

The role of honey, curcuma, and black cumin supplements in overcoming stunting on the adaptive immune system

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ABSTRACT

Stunting is strongly associated with impaired immune function, as chronically malnourished children tend to have weaker immunity and are more vulnerable to infection. This study aimed to examine the effect of temulawak-black cumin herbal honey on the adaptive immune system in stunted children. A quasi-experimental one-group pre-test and post-test design was used. The findings showed that the intervention significantly increased height-for-age (TB/U) in the treatment group compared to the control group ($p = 0.014$). Weight-for-age (BB/U) also rose significantly within the treatment group ($p = 0.013$), but no significant difference was found relative to the control group ($p = 0.192$). The supplement significantly elevated IgM levels in the treatment group ($p = 0.001$), though again without a significant difference from the control ($p = 0.546$). CD4 concentration decreased in the treatment group ($p = 0.003$), but the change was not significantly different from the control ($p = 0.682$). In conclusion, temulawak-black cumin herbal honey can improve nutritional status and enhance adaptive immunity by increasing IgM levels, although it does not raise CD4 levels and instead slows CD4 decline. However, its effectiveness in increasing IgM and CD4 concentrations compared to controls is not significant.

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INTRODUCTION

Stunting is defined as a child's height falling more than two standard deviations below the World Health Organization (WHO) growth standard median for age. It represents a chronic nutritional disorder in early childhood, influenced by socioeconomic factors, maternal health during pregnancy, early childhood illness, and inadequate nutrient intake during infancy. Children who experience stunting from an early age are prone to short-term developmental disturbances such as impaired brain development, lower intelligence, suboptimal physical growth, and metabolic irregularities. In the long term, stunting weakens the immune system, increasing susceptibility to illness and infection. For this reason, stunted children are theoretically more vulnerable to

infectious diseases. The issue is closely tied to human resource development in the future, and in Indonesia, childhood nutrition and growth remain pressing concerns. According to the Indonesian Nutritional Status Study (SSGI) in 2021, the national prevalence of stunting among children under five was approximately 24.4%. In 2020, UNICEF reported the prevalence at 31.8%, a figure considered very high. In West Java, prevalence decreased from 26.2% in 2019 to 24.5% in 2021 and 20.2% in 2022. However, achieving the Regional Medium-Term Development Plan (RPJMD) target of 19.2% in 2023 and the National Medium-Term Development Plan (RPJMN) target of 14% in 2024 requires innovation and consistent annual reductions of 3 to 3.5%.

IgM (Immunoglobulin M) is a major antibody found in B cell plasma. Structurally, it is a pentamer containing ten epitope-binding sites and responds rapidly after exposure to antigens as part of the initial immune response, with a half-life of about five days. Besides its pentameric form, IgM also exists as a monomer on the surface of B lymphocytes and B cell receptors. Its importance is evident in the fact that IgM is the first antibody to emerge within the first 20 weeks of fetal development and has phylogenetic origins, making it vital to the immune response. CD4 (Cluster of Differentiation 4) cells are white blood cells found on T-helper cells and play a central role in the human immune system. These cells assist B cells in producing antibodies (immunoglobulins), protecting the body from infection.

Stunting is associated with higher morbidity and mortality due to infection. It affects children's health, including their immune systems. IgM levels rise as part of the response to infection and may be influenced by nutritional status. Poor nutrition can reduce the production of IgM and CD4, weakening the body's ability to combat infection. However, the correlation between IgM, CD4, and stunting is not direct. The link between nutrient deficiency and infection can worsen nutritional conditions and heighten infection susceptibility. Infection impairs nutrition by reducing appetite and inhibiting nutrient absorption through the digestive tract. Meanwhile, nutrient deficiency raises infection risk by impairing the protective epithelial barrier and altering immune system responses.

Traditional medicine, including herbal remedies, has long been used in Indonesia to address childhood illnesses. Herbal medicine is supported by WHO for health maintenance, disease prevention, and treatment, and the organization encourages improved safety and efficacy of herbal therapies. Honey contains active compounds such as saccharides, proteins, enzymes, amino acids, polyphenols, flavonoids, vitamins, and minerals and is known to enhance both innate and adaptive immunity. Suhaenah & Nissa (2013) studied the effects of different pure honey products on IgM activity in male rabbits and found increased IgM activity with average titers of 1/32, 1/38.4, and 1/48 in AS, MR, and EK honey, respectively. Wan Yusuf et al. (2019) found that Tualang honey at daily doses of 40 g and 60 g for six months increased CD4 counts in asymptomatic HIV-infected individuals with baseline CD4 levels between 250 and 600 cells/mL.

Temulawak rhizome contains curcuminoids such as curcumin, demethoxycurcumin, and essential oils composed of α -curcumene, xanthorrhizol, β -curcumene, germacrene, furanodiene, furanodienone, arturmerone, β -atlantone, d-camphor, and starch. Curcumin enhances immunity. Azimah et al. (2015) found that 0.75 mg/mL temulawak extract enhanced immune response by triggering better lymphocyte proliferation than a combined extract with sambiloto. Taner (2021) reported that 400 mg/kg of ethanolic temulawak extract increased CD4 and CD8 expression in rats. Black cumin contains thymoquinone, thymohydroquinone, dithymoquinone, thymol, carvacrol, nigellidine, nigellimine x-oxide, nigellidine, and alpha-hedrin. Thymoquinone supports immune function. Sarker & Mazumder (2011) found that 0.1 mg/mL of black cumin extract increased IgM production by stimulating B cell differentiation into plasma cells. Akrom et al. (2022) showed that thymoquinone from black cumin extract enhanced CD4Th proliferation and differentiation into Th1 and Th2 cells.

Based on existing research on honey, temulawak, and black cumin, their mechanisms support immune modulation and suggest potential as therapeutic agents for addressing stunting.

This forms the rationale for investigating the effectiveness of honey combined with temulawak and black cumin on the adaptive immune system in stunted children. The study aims to determine whether administering this herbal honey can increase IgM production and CD4 concentration in the adaptive immune system of stunted children and to assess its overall effectiveness in improving adaptive immunity in this population

RESEARCH METHOD

Research Design

The type of research used is a quasi-experimental design. A quasi-experiment is a research method in which random assignment is not applied during implementation; instead, it involves the use of existing groups. In this study, the design was used to conduct an experiment aimed at determining the effects of administering temulawak-black cumin herbal honey on IgM and CD4 levels in stunted children. The research was carried out in Tegalwangi Village, Weru District, Cirebon Regency, from March to June 2024.

Population and Sample

The population of this study consisted of stunted children in the Tegalwangi area of Cirebon Regency. A total of 26 children were selected as the sample and divided into two groups: 13 stunted children who received treatment and 13 who did not. The inclusion criteria were children aged 2 to 5 years, residing in Cirebon Regency, and having obtained written consent from a parent or legal guardian. The exclusion criteria included children with a history of allergies to honey or the herbal components in the temulawak-black cumin honey, those with chronic health conditions affecting the immune system, and those undergoing immunosuppressive therapy or other treatments that influence immune function.

Variables

The independent variable in this study is the administration of temulawak-black cumin herbal honey, comparing children with stunting who received the treatment and those who did not. The dependent variable is the effectiveness of the temulawak-black cumin herbal honey on the adaptive immune system of stunted children.

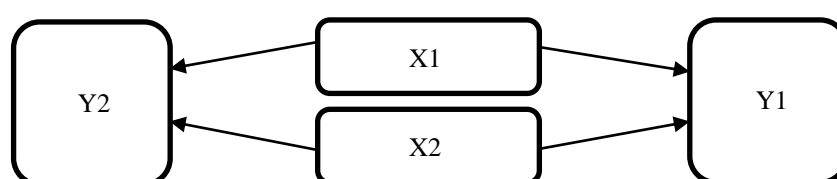


Figure 1. Operational definition

Description:

- X1 : Stunting children aged 2-5 years treated with black cumin turmeric herbal honey
- X2 : Stunting children aged 2-5 years without black cumin turmeric herbal honey
- Y1 : Effectiveness of black cumin turmeric herbal honey on the adaptive immune system of stunted children as seen by increased IgM production
- Y2 : Effectiveness of black cumin turmeric herbal honey on the adaptive immune system of stunted children as seen by increased CD4 cell production

The study focuses on stunted children aged 2 to 5 years, a population characterized by growth delays typically measured through height-for-age ratios. The intervention group (X1) consists of children within this age range who receive herbal honey made from temulawak and black cumin, while the control group (X2) includes stunted children of the same age who do not receive any intervention, serving as a comparison. The primary outcome (Y1) evaluates the

effectiveness of the intervention based on increased IgM production, an indicator of adaptive immune response, and a rise in IgM levels is considered a positive result. The secondary outcome (Y2) assesses effectiveness through increased CD4 production, another key marker of adaptive immunity, with improvements in CD4 levels likewise interpreted as beneficial effects of the intervention.

Data Collection

Data collection involved taking blood samples from stunted children before and after treatment to measure IgM and CD4 levels. The research instruments included informed consent forms, pens, a camera for documentation, syringes for blood collection, a semi-automatic hematology analyzer (Mindray) for blood samples, and ELISA kits for CD4 (ab234569) and IgM (ab137982). The only material tested was the temulawak-black cumin herbal honey. The procedure began with obtaining research permits, including ethical clearance and authorization from KESBANGPOL, the Cirebon District Health Office, and the Tegalwangi Community Health Center, followed by an FGD. Participants were divided into two groups: Group I (stunted children aged 2–5 receiving the herbal honey) and Group II (stunted children without treatment). Blood samples of 1 mL per child were collected using EDTA tubes. IgM and CD4 levels were analyzed at the Physiology Laboratory of the Faculty of Medicine, Universitas Brawijaya, using ELISA techniques involving antigen coating, incubation, washing, blocking, antibody application, substrate reaction, and absorbance measurement at 450 nm. Pretest data were collected from both groups, followed by administering 5 mL of the herbal honey to Group I for four months (adjusted for children under five). Posttest blood samples were then collected from both groups to compare IgM and CD4 outcomes.

Data Processing and Analysis

The study employed bivariate analysis to examine the relationship between two variables, specifically the effect of temulawak-black cumin herbal honey on IgM and CD4 levels in stunted children. The statistical tests used were: (a) the Kolmogorov-Smirnov test to assess data normality, (b) Levene's test to determine data homogeneity, and (c) the paired sample t-test to analyze the mean differences in IgM and CD4 levels before and after the intervention.

RESULTS AND DISCUSSIONS

Sample Preparation Results

The sample used was black cumin and turmeric herbal honey (CXBCH), formulated from a mixture of curcuma (*Curcuma xanthorrhiza*) extract (CXE), black cumin (*Nigella sativa*) seed extract (BCE), and honey. It was processed by CV Al Afiat (a Small Traditional Medicine Company Certified by the Indonesian Food and Drug Authority).

Based on analysis by PT. EBM SAINTIFIK DAN TEKNOLOGI, the active compounds in the honey, xanthorrhizol and thymoquinone, were tested using high-performance liquid chromatography (HPLC) with a Photodiode Array (PDA) detector. The results showed xanthorrhizol at a concentration of 0.0065 mg/mg and thymoquinone at a concentration of 0.000013 mg/mg.

Based on the results of microbiological testing in the test result report number: 017263/LHU/BLK-Y/10/2021 by the Testing and Calibration Laboratory of the Health Laboratory and Calibration Center of the Yogyakarta Special Region Health Service, the honey sample (Sample A2) tested showed the results of the Germ Count/ALT: <10 cfu/gr and *Escherichia coli*: Negative. The requirements for microbial contamination testing in honey according to the Indonesian National Standard (SNI) 7388:2009 concerning the Maximum Limit of Microbial Contamination in Food stipulates that the maximum limit for the germ count or Total Plate Count (ALT) is 5×10^3 cfu/gr. Thus, it shows that the honey sample tested meets the microbiological requirements

stipulated by SNI 7388:2009, that the honey is safe for consumption in terms of microbial contamination.

Anthropometric Measurement Results of Research Subjects

The following are the results of anthropometric measurements of children in Tegalwangi Village, Weru District, Cirebon Regency. In this study, the results of height (H/A) and weight (BW/A) measurements were entered into the formula to obtain the Z-score, as shown in Table 1.

Table 1. Average Z-score results for H/A and W/A

No	Category	Mean \pm SD
1	Zscore TB/U	-2,57 \pm 0,40
2	Zscore BB/U	-1,50 \pm 1,27

The Z-score is used to measure a child's growth against growth standards established by the World Health Organization (WHO). The table of toddler nutritional status categories based on W/A, H/A, and W/H indices based on the WHO (World Health Organization) is shown in Table 2 as follows:

Table 2. Toddler nutritional status categories based on H/A and W/A

Indicator	Nutritional Status	Z-Score
W/A (Weight-for-Age)	Severe Malnutrition	< -3.0 SD
	Moderate Malnutrition	-3.0 SD to < -2.0 SD
	Good Nutrition	-2.0 SD to 2.0 SD
	Overnutrition	> 2.0 SD
H/A (Height-for-Age)	Severely Stunted	< -3.0 SD
	Stunted	-3.0 SD to < -2.0 SD
	Normal	\geq -2.0 SD
W/H (Weight-for-Height)	Severely Wasted	< -3.0 SD
	Wasted	-3.0 SD to < -2.0 SD
	Normal	-2.0 SD to 2.0 SD
	Overweight	> 2.0 SD

Based on Table 2, the mean Z-score for height-for-age (TB/U) is -2.57 ± 0.40 , indicating that children in this population have significantly lower height than the normal standard for their age. The mean Z-score for weight-for-age (BB/U) is -1.50 ± 1.27 , showing that their average weight is also below the normal range. These anthropometric findings confirm that the children in Desa Tegalwangi who participated in the study are categorized as stunted, with Z-score TB/U < -2 SD and Z-score BB/U < -2 SD (Kementrian Kesehatan RI, 2018). Stunting is defined as a failure of growth in children under five caused by chronic malnutrition, leading to physical growth retardation. Children who are stunted or severely stunted have body length-for-age (PB/U) or height-for-age (TB/U) values below the WHO-MGRS standard, with Z-scores less than -2 SD (stunted) and less than -3 SD (severely stunted).

Anthropometric parameters serve as the basis for assessing a child's nutritional and health status. Nutritional status in toddlers is evaluated using three indices: weight-for-age (BB/U), which reflects body weight at a given age, and height-for-age (TB/U), which represents linear growth at a specific age. Two key indicators frequently used to evaluate a child's nutritional status, especially in the context of stunting, are TB/U and BB/U. These parameters are essential for understanding growth delays attributable to chronic malnutrition and are central to identifying stunted children.

Malnutrition, including stunting, is closely associated with impaired immune function. Children suffering from chronic undernutrition often exhibit reduced immunity, making them more susceptible to infections. Systematic studies show that malnutrition causes significant changes in barrier functions, innate immunity, and the adaptive immune system, including a

reduction in white blood cell counts and decreased phagocytic activity vital for combating infections. According to Goodluck A.K et al. (2022), the triple burden of malnutrition – stunting, wasting, and micronutrient deficiencies – significantly affects immune function. Malnutrition leads to altered cellular metabolism and impaired cellular function, increasing the risk of infection. Undernourished children often face a negative cycle in which recurrent infections further disrupt growth and increase the risk of early mortality.

Research by Rohmatika et al. (2020), titled “Hubungan Stunting dengan Kerentanan Penyakit pada Anak Usia 1–5 Tahun di Desa Panyirapan Kecamatan Soreang Kabupaten Bandung,” shows that stunted toddlers are 1.333 times more likely to suffer from disease than non-stunted children. Thus, stunting affects not only physical growth but also has long-term consequences for the immune system. Preventive efforts must include comprehensive nutritional interventions to reduce infection risk and strengthen children’s immune status. This study aims to determine the effect of administering herbal honey made from temulawak and black cumin on adaptive immune function in stunted children. An experimental design was used with treatment and control groups. Initial anthropometric measurements and blood sampling (pretest) were conducted to assess IgM and CD4 concentrations. Children were divided into two groups: the treatment group received the herbal honey daily for three months, while the control group did not. After three months, anthropometric measurements and blood sampling (posttest) were repeated to evaluate changes in height, weight, IgM, and CD4 levels in stunted children.

Test Results on Physical Parameters TB/U and BB/U

The following are the results of physical parameters of height/age before and after in stunted children without the administration of black cumin turmeric herbal honey and stunted children with the administration of black cumin turmeric herbal honey for a period of 3 months, which can be seen in Figure 2.

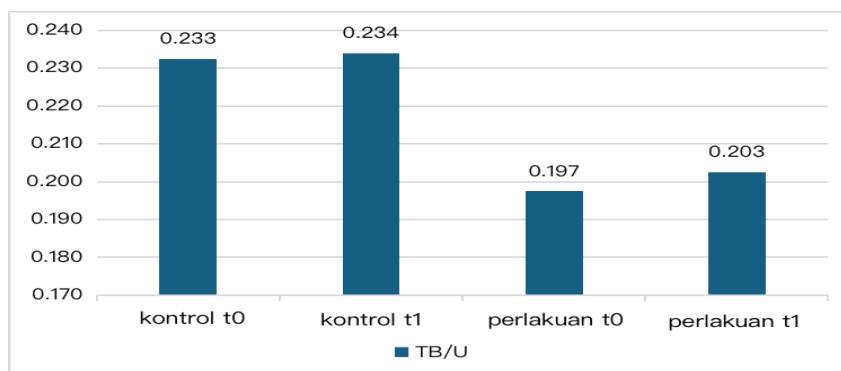


Figure 2. Physical parameter test results: height/age

Based on the pretest average in the control group, it was 0.233 cm and the posttest average was 0.234 cm, indicating minimal increase in height in the control group. The pretest average for the treatment group was 0.197 cm and the posttest average was 0.203 cm, indicating a more significant increase in height in the treatment group. Therefore, the treatment group showed a relatively greater increase in height compared to the control group. Overall, the treatment condition was more effective in increasing height growth compared to the control condition. This demonstrates the effectiveness of the treatment in increasing height for age (H/A) over a 3-month period.

The following are the results of the physical parameters of height for age before and after stunting in children without black cumin turmeric herbal honey and stunting in children with turmeric herbal honey treatment over a 3-month period.

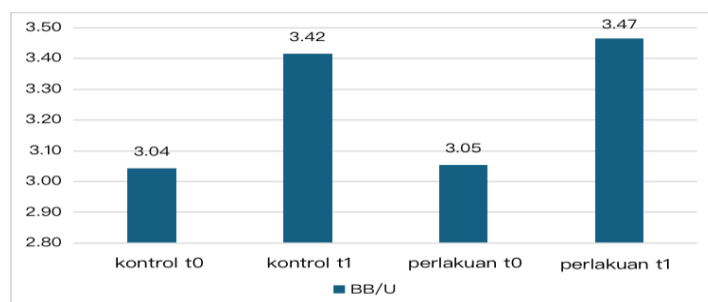


Figure 3. Results of the physical parameter test: weight for age

The pretest average for the control group was 3.04 kg and the posttest average was 3.42 kg, indicating a significant increase in body weight in the control group. The pretest average for the treatment group was 3.05 kg and the posttest average was 3.47 kg, indicating a greater increase in body weight in the treatment group.

Therefore, the treatment group showed a relatively greater increase in body weight compared to the control group. Overall, the treatment condition was more effective in increasing body weight compared to the control condition, thus demonstrating the effectiveness of the treatment in increasing body weight for age (BW/A) over a 3-month period.

The results of the physical parameter test regarding the average BW/A and BW/A were then statistically analyzed using a paired t-test, as shown in Table 3.

Table 3. SPSS results for physical parameters

Category	Group	Mean \pm SD		P1 Value
		Pretest	Posttest	
TB/U	Treatment	0,192 \pm 0,024	0,202 \pm 0,023	0,001
	Control	0,233 \pm 0,051	0,235 \pm 0,050	0,165
	P2 value			0,014
BB/U	Treatment	2,875 \pm 0,592	2,972 \pm 0,633	0,013
	Control	3,043 \pm 0,880	3,416 \pm 1,001	0,122
	P2 value			0,192

The treatment group showed a significant increase in height, with the average TB rising from 0.192 \pm 0.024 at pretest to 0.202 \pm 0.023 at posttest ($P_1 = 0.001 < 0.05$), while the control group showed no significant change, increasing only from 0.233 \pm 0.051 to 0.235 \pm 0.050 ($P_1 = 0.165 > 0.05$). The between-group comparison yielded a P_2 value of 0.014 < 0.05 , indicating a statistically significant difference in height changes between the treatment and control groups. These results suggest that the intervention had a significant effect on height gain compared to no treatment.

In terms of weight, the treatment group experienced a significant increase from 2.875 \pm 0.592 at pretest to 2.972 \pm 0.633 at posttest ($P_1 = 0.013 < 0.05$), while the control group showed a nonsignificant increase from 3.043 \pm 0.880 to 3.416 \pm 1.001 ($P_1 = 0.122 > 0.05$). However, the P_2 comparison between groups was 0.192 > 0.05 , indicating no statistically significant difference in weight gain between the treatment and control groups overall. Thus, while weight gain occurred in the treatment group, it was not significantly different from the control group when compared directly. Improved appetite contributes to better nutritional intake, reflected by increased weight appropriate for age and height. Nutritional intake is influenced by food consumption, which can be enhanced by stimulating appetite. One nutritional intervention is the administration of a traditional herbal blend of black cumin and turmeric honey. Honey contains high levels of fructose and glucose, making it easily absorbed in the small intestine along with other organic compounds, thereby improving digestion and nutrient absorption. Better nutrient absorption can stimulate appetite. Turmeric contains curcuminoids and essential oils that support gallbladder and pancreatic function, improving intestinal absorption. Enhanced bile and pancreatic activity aids

digestion. The combination of honey and Javanese ginger strengthens their appetite-enhancing properties. Regular consumption of Javanese ginger and honey in children can increase appetite, resulting in weight gain.

Javanese ginger's essential oil, xanthorrhizol, is a natural appetite stimulant. Its choleric properties accelerate gastric emptying and digestion while aiding fat absorption. Honey helps meet nutritional needs in children with inadequate diets, boosts immunity, supports recovery from illness or surgery, and stimulates appetite. Weight gain in malnourished children who received black cumin-ginger honey is attributed to ginger's essential oils improving appetite and food enjoyment, resulting in increased weight. In the control group, weight gain may have resulted from supplementary feeding programs that met nutritional needs. However, weight gain was greater in the treatment group, indicating the effectiveness of black cumin-ginger herbal honey. This aligns with findings by Paramita et al. (2022), which showed changes in nutritional status based on height-for-age after a 30-day forest honey intervention. Another study by Ningrum & Ningsih (2022) found that two weeks of honey administration increased appetite and weight gain in 60% of children. Similarly, Novikasari & Setiawati (2021) reported that administering temulawak and honey effectively increased body weight in children with malnutrition.

Immune System Parameter Test Results

The following are the results of IgM immune system parameters before and after treatment in stunted children without black cumin turmeric herbal honey and stunted children with black cumin turmeric herbal honey treatment over a 3-month period. These results are shown in Figure 4.

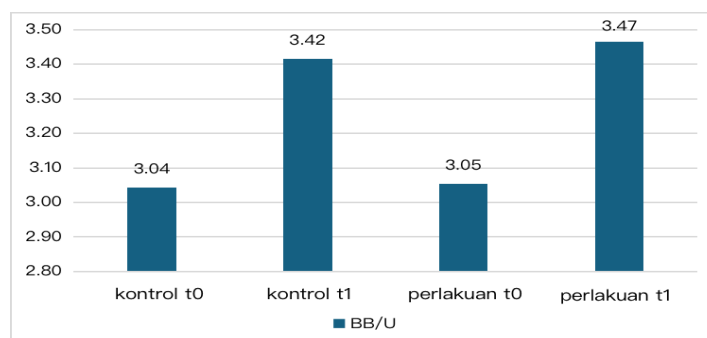


Figure 4. IgM parameter test results

The pretest average for the control group was 12.28 pg/mL and the posttest average was 17.51 pg/mL, indicating a significant increase in IgM concentration in the control group. The pretest average for the treatment group was 10.36 pg/mL and the posttest average was 17.88 pg/mL, indicating a greater increase in IgM concentration in the treatment group.

Therefore, the treatment group showed a relatively greater increase in IgM concentration compared to the control group. Overall, the treatment condition was more effective in increasing IgM concentration compared to the control condition, demonstrating the effectiveness of the treatment in increasing immune system IgM concentration over a 3-month period.

The following are the results of CD4 immune system parameters before and after testing stunted children without black cumin turmeric herbal honey and stunted children with black cumin turmeric herbal honey over a 3-month period. These are shown in Figure 5.

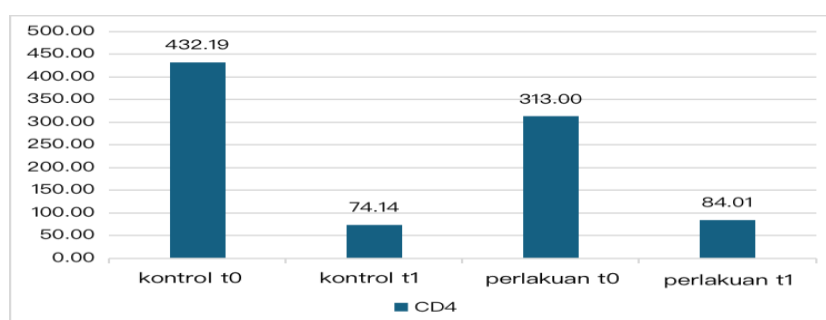


Figure 5. CD4 parameter test results

The average pretest in the control group was 432.19 pg/mL and the average posttest was 74.14 pg/mL, indicating a significant decrease in CD4 concentrations in the control group. The average pretest in the treatment group was 313.00 pg/mL and the average posttest was 84.01 pg/mL, indicating a decrease in CD4 concentrations, but not significantly greater than the control group.

Therefore, the control group showed a relatively greater decrease in CD4 concentrations compared to the treatment group. Overall, the treatment conditions had a protective effect or slowed the decline in CD4 concentrations, thus demonstrating the effectiveness of the treatment in maintaining CD4 concentrations over a 3-month period.

The results of the immune system parameter tests on average IgM and CD4 were then statistically analyzed using a paired t-test, as shown in Table 4.

Table 4. SPSS results of TJH honey administration on immune system parameters

Category	Group	Mean±SD		P1 Value
		Pretest	Posttest	
IgM	Treatment	9,050 ± 1,813	17,877 ± 7,382	0,001
	Control	10,977 ± 2,697	16,507 ± 3,12	0,001
	P2 value			0,546
CD4	Treatment	328,382 ± 218,924	84,01 ± 58,723	0,003
	Control	434,187 ± 223,333	74,140 ± 62,512	0,000
	P2 value			0,682

Both the treatment and control groups showed significant increases in IgM levels from pretest to posttest. In the treatment group, the mean IgM concentration rose from 9,050 ± 1,813 to 17,877 ± 7,382 with a P1 value of 0.001 < 0.005, indicating a significant change. Similarly, the control group showed an increase from 10,977 ± 2,697 to 16,507 ± 3.12, also with a P1 value of 0.001 < 0.005. However, the P2 comparison between the two groups was 0.546 > 0.005, demonstrating no statistically significant difference between the changes in both groups. This means that although IgM levels increased significantly in each group, the treatment did not result in a greater increase compared to the control. Overall, both groups experienced notable improvements, with the treatment group showing a slightly larger increase.

For CD4 levels, both the treatment and control groups experienced significant declines. The mean CD4 concentration in the treatment group decreased from 328,382 ± 218,924 cells/mm³ to 84.01 ± 58,723 cells/mm³, with a P1 value of 0.003 < 0.005, indicating a significant difference. Likewise, the control group declined from 434,187 ± 223,333 to 74,140 ± 62,512, with a P1 value of 0.000 < 0.005. The P2 value of 0.682 > 0.005 showed no significant difference in CD4 decline between groups. Thus, both groups experienced a substantial decrease, but the treatment did not produce a greater decline than the control. Instead, the data suggest that the treatment may have helped slow the reduction in CD4 levels.

Stunting is linked to higher infection-related morbidity and mortality. Conditions such as stunting, wasting, and malnutrition impair the immune system and increase infection risk. Morales et al. (2023) found that both innate and adaptive immunity are compromised in malnourished children. Srimshaw & SanGiovanni (1997) in Noviyanti & Sarbini (2010) reported that nutrient deficiencies can lead to infections and reduced immunoglobulin levels and T cell production. Rytter et al. (2014) also found decreased CD4 lymphocytes in malnourished non-HIV children. In this study, IgM levels were measured using the ELISA KIT, with normal levels in children being 16.5 ± 13.8 mg/dL. The treatment group increased from $9,050 \pm 1,813$ pg/mL to $17,877 \pm 7,382$ pg/mL, while the control group rose from $10,977 \pm 2,697$ pg/mL to $16,507 \pm 3.12$ pg/mL. Although still below normal limits, the increase in the treatment group demonstrates an improved immune response in stunted children.

The rise in IgM in the treatment group reflects the effectiveness of herbal honey containing Javanese ginger and black cumin in enhancing immunity. The bioactive components—fructose, sucrose, xanthorrhizol, and thymoquinone—each contribute to IgM improvement. Fructose and sucrose supply rapid metabolic energy for lymphocyte function, supporting antibody production. Hegazi (2015) demonstrated that honey increased macrophage phagocytic activity and immunoglobulin titers (IgG, IgM, IgA), partly by stimulating TNF- α , IL-1 β , and IL-6 production via TLR4. These cytokines activate B cells to increase immunoglobulin production. Suhaenah & Nissa (2013) similarly found that various honey products increased IgM activity in rabbits, with titers of 1/32, 1/38.4, and 1/48.

Xanthorrhizol in Javanese ginger exerts anti-inflammatory and antioxidant effects that support B and T cell modulation, enhancing antibody production, including IgM. Yuandani et al. (2021) showed that xanthorrhizol increases B cell proliferation. The mechanism involves antigen interaction with T and B cells, triggering G-protein activation, phospholipase C, and production of DAG and IP3, leading to increased Ca²⁺ levels, protein kinase C activation, and IL-2 production to stimulate lymphocyte proliferation (Roitt & Delves, 2001 on (Sofiakmi et al., 2014). Thymoquinone, the active component in black cumin, supports immunomodulation by increasing cytokines such as interleukins and interferons that stimulate B cell activation and IgM production. (El Kadi et al, on Sulistiawati & Radji (2014) showed that black cumin powder increased T-helper to T-suppressor ratios by 72% and boosted T-killer cells. Cytokines such as IL-1 and IL-2 drive proliferation of T and B cells, with IL-2 supporting immunoglobulin secretion (Darwin et al., 2021).

CD4 levels were measured using the ELISA KIT, which assesses protein concentration rather than direct cell counts. Normal CD4 levels are 410–1,590 cells/mL (Widiyanti & Sandy, 2016), but the ELISA KIT measures CD4 concentrations of 0.469–30 ng/mL (Abcam, 2021). In this study, both treatment and control groups showed declines: $328,382 \pm 218,924$ to $84.01 \pm 58,723$ in the treatment group and $434,187 \pm 223,333$ to $74,140 \pm 62,512$ in the control group. The treatment group's decline was smaller, suggesting a protective effect. Xanthorrhizol modulates gene expression related to T cell apoptosis and proliferation, supporting CD4 survival, while increasing IL-2 and IFN- γ (Yuandani et al., 2021). Thymoquinone inhibits NF- κ B, reducing pro-inflammatory cytokines and CD4 damage, while promoting IL-2 and IL-4 for T cell differentiation (Badary et al., 2021). These mechanisms align with findings by Taner (2021), showing Javanese ginger extract increased CD4 and CD8 expression in mice, and Akrom et al. (2022), demonstrating that thymoquinone enhances CD4Th differentiation into Th1 and Th2.

CONCLUSION

The administration of herbal honey containing temulawak and black cumin shows potential in enhancing adaptive immune function in stunted children by increasing IgM concentrations and slowing the decline of CD4 levels. However, its overall effectiveness is not significantly different from the control group in improving both IgM and CD4 concentrations. These findings indicate that while the intervention may offer partial immune benefits, it does not produce substantial

immunological improvements within the studied timeframe. Future research is recommended to extend the intervention period beyond three months to allow sufficient time for more measurable changes in IgM and CD4 levels. Additionally, subsequent studies should employ highly accurate and precise measurement methods, such as ELISA Reader for IgM and Flow Cytometer for CD4, to ensure more reliable and detailed evaluation of immunological outcomes.

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