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Original Article

The Effect of Vitamin D Supplementation on Sputum Conversion, Erythrocyte Sedimentation Rate and Neutrophil-Lymphocyte Ratio in Pulmonary Tuberculosis Patients – A Randomized Controlled Trial

Muchamad Regi Sonjaya[1], Mohamad Isa[1], Alfi Yasmina[2], Isa Ansori[1], Ira Nurrasyidah[1], Erna Kusumawardhani[1]

[1]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Lambung Mangkurat University, Ulin Hospital Banjarmasin, South Kalimantan, Indonesia
[2]Department of Pharmacology, Faculty of Medicine and Health Sciences, Lambung Mangkurat University, Banjarmasin, South Kalimantan, Indonesia

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Author's affiliation:
Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Lambung Mangkurat University, Ulin Hospital Banjarmasin, Banjarmasin, Indonesia

Author's correspondence:
Muchamad Regi Sonjaya
Veteran Sungai Bilu Street, Num.128, Melayu, Banjarmasin, South Kalimantan 70122, Indonesia

E-mail:
Regisonjaya017@gmail.com

Abstract

Background : The health issue of pulmonary tuberculosis (TB) remains a concern in Indonesia. Vitamin D supplementation is one way to manage tuberculosis, which is a crucial case control metric. It is anticipated that vitamin D's anti-inflammatory properties will lower erythrocyte sedimentation rate (ESR) and inflammatory indicators, hence speeding up sputum conversion.
Aims : To analyze the effect of vitamin D supplementation on sputum conversion, ESR and neutrophil-lymphocyte ratio (NLR) among pulmonary tuberculosis patients
Methods : Patients with pulmonary tuberculosis who were treated as outpatients at Ulin Banjarmasin Hospital and Pekauman Health Centre between May–July 2024 and who satisfied the study's inclusion requirements were included in the randomised controlled trial. Subjects were randomly divided into 2 groups (19 subjects in the treatment group and 19 subjects in the control group) using random selection with sealed envelopes. The treatment group received antituberculosis drugs (ATD) and vitamin D supplementation at a dose of 10,000 IU/day for eight weeks after the initiation of TB therapy, while the control group received ATD and a placebo. ESR and NLR examinations were performed prior to treatment, in weeks 4 and 8, whereas sputum evaluations were conducted at weeks 2, 4, 6, and 8. Statistical Product and Service Solutions (SPSS) was used for data analysis. *P*-value <0.05 was significant statistically.
Results : The study subjects were 38 pulmonary TB patients, most of whom were women (65.0%) with an average age of 50.42 ± 18.61 years. Overall, during the 8 weeks of intervention, there was a significant effect of vitamin D supplementation on sputum conversion (OR = 1.61, 95%CI = 0.030–0.931, p = 0.037). There was no significant effect of vitamin D supplementation on NLR (regression coefficient = 0.549, 95%CI = -1.769–2.858, p = 0.641) and ESR (regression coefficient = -5.529, 95%CI = -20.658–9.599, p = 0.474).
Conclusion : Vitamin D supplementation significantly affects sputum conversion. In the 8th week, almost all subjects who initially had positive BTA became negative. But does not significantly affect ESR and NLR.

Keywords : Pulmonary Tuberculosis, Vitamin D, Sputum Conversion, Neutrophil-Lymphocyte Ratio, Erythrocyte Sedimentation Rate

INTRODUCTION

A worldwide health concern, tuberculosis (TB) is particularly prevalent in Indonesia. According to data gathered by the Republic of Indonesia's Ministry of Health (Kemenkes RI), there were 443,235 TB cases overall in 2021, and that figure rose by 503,712 cases in 2022.[1] After receiving rigorous treatment, the patient's response to treatment is evaluated by the conversion of positive acid-fast bacilli (AFB) to negative AFB. After six months of treatment, TB patients are considered to have failed therapy if their sputum does not become negative.[2]

TB treatment monitoring can also be assessed by ESR. The inflammatory process in TB causes the ESR value to increase, although it is not specific to TB infection.[3] ESR can show normal results even though the patient has TB, but the use of ESR values can still be used as an indicator of patient improvement.[3,4] NLR value can also be used to evaluate systemic inflammation.[5] Research conducted by Harun *et al*. examining NLR in TB with positive and negative AFB showed that there was a significant increase in the number of neutrophils, a decrease in lymphocytes and an increase in NLR in positive AFB TB compared to negative AFB TB.[6]

Since vitamin D is believed to play a role in the host cell immunological response to M. tuberculosis infection, vitamin D supplements are considered to be helpful in the treatment of TB. The addition of vitamin D supplementation (250 ug vitamin D/day) for 6 weeks to ATD in TB patients increased clinical improvement, as well as sputum conversion time and improved radiological images, according to research by Sugiarti *et al*. However, the dosage of vitamin D supplementation must be changed to achieve meaningful changes.[7]

There has not been much research on the effect of vitamin D supplementation on sputum conversion and inflammatory indicators such as ESR and NLR in TB patients. The purpose of this study was to assess the effect of vitamin D supplementation on sputum conversion and ESR and NLR in TB patients in Ulin Banjarmasin Hospital and Pekauman Health Centre, considering that there has been no such research in this area.

METHODS

This study was an experimental study with a randomized controlled trial study design. The study was conducted at Ulin Banjarmasin Regional Hospital and Pekauman Health Center, from May to July 2024. This research has obtained research ethics permission from the Research Ethics Commission of Lambung Mangkurat University and Ulin Banjarmasin Hospital, with permit number: No.64/PPDS.Pulmo/Litbang/RSUDU/V/2024.

The study subjects were pulmonary TB patients aged ≥18 years, diagnosed with bacteriologically confirmed pulmonary TB (TCM and AFB), Patients willingness to participate in this study by signing an informed consent. Patients who consumed vitamin D supplementation in the past month, suffered from MDR TB and lung tumors, had comorbid diseases such as kidney failure and impaired liver function, had a history of intolerance or hypersensitivity to vitamin D, and women who were pregnant, or planning to become pregnant, and were breastfeeding were excluded from this study. The sample size in this study used the unpaired numerical comparative minimum formula with the results of 19 subjects in the treatment group and 19 subjects in the control group.

After obtaining the research subjects based on the research criteria, it was then divided into 2 groups, namely the control group (given first-line ATD + placebo), and the treatment group (given first-line ATD + vitamin D) randomly, using a sealed envelope. AFB evaluation was carried out in weeks 2, 4, 6 and 8. ESR and NLR evaluations were carried out in weeks 4 and 8. Sputum conversion is defined as a change from AFB positive to negative. NLR changes were assessed based on a comparison of the mean NLR before, 4 weeks, and 8 weeks after the intervention. ESR changes were assessed based on a comparison of the mean ESR before, 4 weeks, and 8 weeks after the intervention.

After the data was collected, data analysis was carried out using the Statistical Package for the Social Sciences (SPSS) Version 29.0 software program. Subject characteristics are presented in the form of frequencies and percentages, with an assessment of differences in the characteristics of the two groups using the Chi-square test. The generalized estimating equation (GEE) was used to determine the effect of vitamin D supplementation on sputum conversion, ESR and NLR. If the p-value is <0.05, it is said to be significant.

RESULTS

Subject Characteristics

The number of subjects consisted of 38 research subjects that were included until the end of this study, and were divided into two groups, namely 19 research subjects in the control group given ATD line 1 + placebo, and 19 research subjects in the treatment group given ATD line 1 + vitamin D, without drop out subjects. Table 1 shows the characteristics of the subjects in this study.

There was no significant difference in subject characteristics between the two groups (p>0.05). There were more women in the control group compared to the treatment group. The mean age of the control group was 47.31±14.94 years and 50.42±18.61 years in the treatment group. New cases were the most dominant in this study. In both the control and intervention groups, most subjects did not have comorbidities, but some subjects did have comorbidities such as hypertension, diabetes mellitus, or others. Based on BMI, the control group was dominated

TABLE 1
Characteristics of Research Subjects

Characteristics	Control (n=19)	Intervention (n=19)	Total	*p*-value
Gender				0.051*
Men	6 (31.6%)	12 (63.2%)	18 (47.4%)	
Women	13 (68.4%)	7 (36.8%)	20 (52.6%)	
Age (meanSD)	47.31±14.94	50.42±18.61		0.228**
Case Classification				1.000***
New Case	17 (89.5%)	18 (94.7%)	35 (92.1%)	
Relaps	2 (10.5%)	0 (0%)	2 (5.3%)	
Drop out	0 (0%)	1 (5.3%)	1 (2.6%)	
Comorbid				0.794***
None	14 (73.6%)	14 (73.6%)	28 (73.6%)	
HT	0 (0%)	1 (5.3%)	1 (2.6%)	
DM	2 (10.5%)	1 (5.3%)	3 (7.8%)	
Others	3 (15.9%)	3 (15.8%)	6 (16%)	
BMI				0.194*
Underweight	12 (63.2%)	8 (42.1%)	20 (52.6%)	
Normal	7 (36.8%)	11 (57.9%)	18 (47.4%)	
Smoking				0.179*
Smoking	5 (26.3%)	9 (47.4%)	14 (36.8%)	
No Smoking	14 (73.7%)	10 (52.6%)	10 (63.2%)	
Occupation				0.972***
No Occupation	0 (0%)	3 (15.8%)	3 (5.3%)	
Employee	4 (21.1%)	4 (21.1%)	4 (21.1%)	
Businessman	4 (21.1%)	3 (15.8%)	3 (18.4%)	
Housewife	9 (47.4%)	5 (26.3%)	14 (36.8%)	
Civil Servant	0 (0%)	1 (5.3%)	1 (2.6%)	
Farmer	2 (10.5%)	3 (15.8%)	3 (13.2%)	
AFB Before Treatment				0.152***
3+	3 (15.8%)	2 (10.5%)	5 (13.2%)	
2+	7 (36.8%)	1 (5.3%)	8 (21.0%)	
1+	9 (47.4%)	16 (84.2%)	25 (65.8%)	
Gene Xpert				1.000***
Very Low	1 (5.3%)	2 (10.5%)	3 (7.3%)	
Low	9 (47.4%)	10 (52.6%)	19 (50.0%)	
Medium	7 (36.8%)	4 (21.1%)	11 (28.9%)	
High	2 (10.5%)	3 (15.8%)	5 (13.2%)	

DM: Diabetes Melitus, HT: Hypertension. *Chi Square, **Independent t-test, ***Kolmogorov Smirnov

TABLE 2
The Effect of Vitamin D Supplementation on Sputum Conversion

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
Intercept	0.465	0.2013	0.070	0.859	5.329	1	0.021
Intervention Group	0.480	0.2298	0.030	0.931	4.363	1	0.037
Control Group	0						
(Scale)	1						

Dependent variable: Sputum Conversion

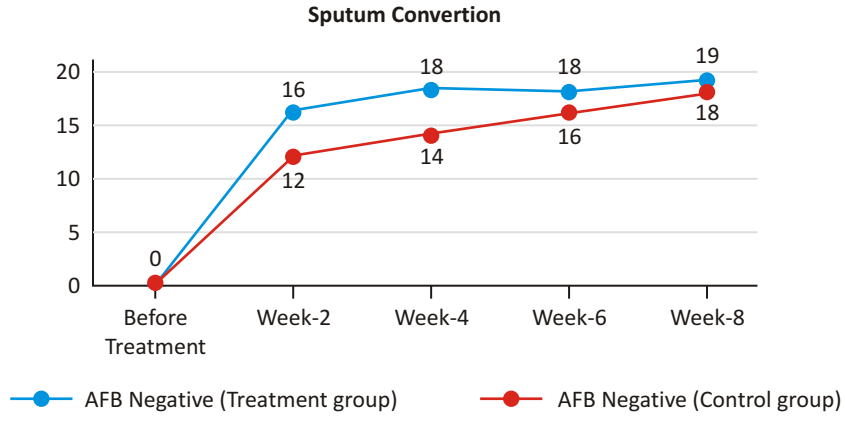

Figure 1. AFB Conversion Chart

by subjects with an underweight BMI; while the intervention group was dominated by subjects with a normal BMI. There were more non-smokers than smokers. The study subjects had various occupations, such as employee, businessman, housewife, civil servant, and farmer. Based on AFB examination before therapy, there were more subjects in the control group +1 (47.4%); as well as in the intervention group (84.2%). Based on the results of gene expert, the findings of gene expert low were more numerous than very low, medium, and high, with the number in the control group being 47.4% and in the intervention group being 52.6%.

Vitamin D and Sputum Conversion

The effect of vitamin D supplementation on sputum conversion was assessed in this study, and is presented in the Table 2.

Based on Table 2, there is a significant relationship between vitamin D supplementation and sputum conversion (p = 0.037). Figure 1 shows that more subjects experienced sputum conversion in the treatment group compared to the control group. In the second week, 12 people experienced sputum conversion in the control group and 16 people in the treatment group. In the fourth week, 14 people experienced sputum conversion in the control group and 18 people in the treatment group. In the sixth week, 16 people experienced sputum conversion in the control group and 18 people in the treatment group. In the eighth week, 18 people experienced sputum conversion in the control group and 19 people experienced sputum conversion in the treatment group.

Vitamin D and NLR

NLR was assessed before treatment, week 4 and week 8 after treatment. The following table shows the effect of vitamin D supplementation on NLR after 8 weeks.

Table 3 shows that there is no significant relationship between vitamin D supplementation and NLR (p = 0.641). The graph of NLR changes before treatment, week 4 and week 8 can be seen in Figure 2. Before treatment, the mean NLR in the control group was 7.15 and in the treatment group was 5.52. At week 4, the mean NLR in the control group was 3.52 and in the treatment group was 3.05. At week 8, the mean NLR in the control group was 2.36 and in the treatment group was 2.84.

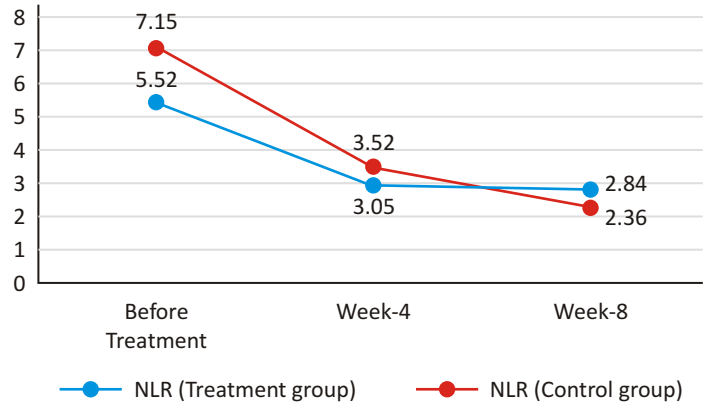

Figure 2. NLR Chart

TABLE 3
The Effect of Vitamin D Supplementation on NLR

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
Intercept	3.863	0.4030	3.073	4.653	91.881	1	0.000
Intervention Group	0.549	1.1779	-1.769	2.858	0.217	1	0.641
Control Group	0						
(Scale)	28.109						

Dependent variable: NLR

Vitamin D and ESR

ESR was assessed before treatment, week 4 and week 8. Figure 3 shows the changes in ESR before treatment, week 4 and week 8 in both groups. Before treatment, the LED in the control group was 63.63 and in the treatment group was 55.15. At week 4, the LED in the control group was 60.57 and in the treatment group was 50.36. At week 8, the LED in the control group was 42.26 and in the treatment group was 42.05.

Based on Table 4, there was no significant relationship between vitamin D supplementation and ESR ($p = 0.474$).

DISCUSSION

Sputum smear negativity (becoming non-infectious) after a specific period of anti-TB treatment initiation is a critical indicator for assessing the efficacy of anti-TB treatment in developing countries.[8] Despite the complete elimination of new TB transmission today, an estimated 5%–15% of individuals with tuberculosis (TBI) develop active TB disease during their lifetimes, thereby functioning as a vast reservoir for future TB disease.[9] Isoniazid, rifampicin, pyrazinamide, and ethambutol comprise the conventional treatment regimen for tuberculosis. The dosage must be adjusted in accordance with the patient's clinical condition, as each substance has a distinct mechanism of action. Nevertheless, this treatment is frequently confronted with a variety of obstacles, such as the emergence of substantial adverse effects. Hepatotoxicity, neuropathy, gastrointestinal disorders, and hypersensitivity reactions are potential side effects that may impact patient adherence to therapy.[10]

Recently, there has been a lot of research linking vitamin D with the prevention of tuberculosis and helping in the treatment of tuberculosis. Vitamin D (calciferol) and its metabolites are hormones and hormone precursors that can be synthesized endogenously in the appropriate biological environment. Vitamin D from plant sources is vitamin D2 (ergocalciferol), while from animal sources it is vitamin D3 (cholecalciferol). The skin is a significant source of vitamin D, which is synthesized upon exposure to ultraviolet B radiation (UV-B; wavelength, 290–320 nm). Vitamin D, whether synthesized cutaneously or absorbed from the intestine, is transported through the circulation

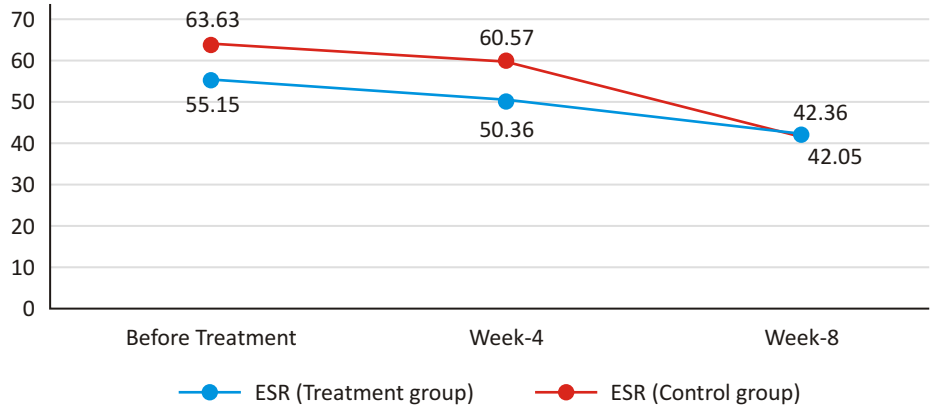

Figure 3. ESR Chart

TABLE 4
The Effect of Vitamin D Supplementation on ESR

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test		
			Lower	Upper	Wald Chi-Square	df	Sig.
Intercept	54.491	5.7033	48.313	65.670	91.285	1	0.000
Intervention Group	-5.529	7.7186	-20.658	9.599	0.513	1	0.474
Control Group	0						
(Scale)	894.349						

Dependent variable: ESR

bound to the vitamin D-binding protein, α-globulin, which is synthesized in the liver. Vitamin D is then 25-hydroxylated in the liver by cytochrome P450 oxidase in mitochondria and microsomes to form 25-hydroxyvitamin D [25(OH)D] (calcidiol). The second hydroxylation, required for the formation of the active hormone 1,25-hydroxyvitamin D [1,25(OH)D] (calcitriol), occurs in the kidneys. 25-hydroxyvitamin D [25(OH)D] (calcidiol) is the primary circulating and stored form of vitamin D.[11]

Vitamin D enhances the antimicrobial activity of macrophages in the context of tuberculosis by promoting the production of cathelicidin and other antimicrobial peptides, as well as by supporting autophagy and phagolysosome fusion–mechanisms that are essential for the host's defense against Mycobacterium tuberculosis. Vitamin D also modulates the adaptive immune system by regulating T cell differentiation and cytokine responses, thereby assisting in the preservation of immune equilibrium. An association between low serum 25-hydroxyvitamin D levels and an increased susceptibility to infection and the development of tuberculosis has been consistently demonstrated in observational studies. It is common for individuals with active or latent tuberculosis to have lower vitamin D levels than healthy controls.[12,13] Furthermore, the biological effects of vitamin D are mediated by vitamin D receptors, also found in most tissues. In addition to its classic endocrine effects on calcium and phosphate metabolism and bone health, binding to these receptors has the potential to extend vitamin D's actions to various cell and organ systems (e.g., immune cells, the brain, breast, colon, and prostate).[11]

According to the study's findings, sputum conversion in patients with pulmonary tuberculosis is significantly impacted by vitamin D administration. Consistent with the findings of Siswanto *et al*. (2009), who found a correlation between sputum conversion and vitamin D provision, group I received 800 IU of vitamin D per day, while group 2 did not get any vitamin D. Compared to the group without receiving vitamin D, those who received it displayed negative AFB results noticeably more quickly ($p = 0.04$).[14] In that study, sputum conversion occurred as early as the first month after intervention. This conversion time was faster than in our study, where sputum conversion was seen 4 weeks after intervention. Because our study only assessed sputum conversion before, 4 weeks, and 8 weeks after

intervention, the results cannot indicate how quickly sputum conversion occurs. According to research by Sugiarti *et al*. (2018), adding 5,000 IU of vitamin D to ATD therapy enhanced radiological imaging, sputum conversion time, and clinical improvement as determined by the TB score in TB patients. To get noticeable effects, the vitamin D dosage must be increased.[15] Because it aids in regulating the immunological response to combat M. tuberculosis, vitamin D as a complement to ATD therapy also has a notable impact on clinical improvement. Vitamin D is able to phagocytose Mycobacterium tuberculosis through TLR2/1 sensitization which will increase the expression of RVD and CYP27B1, which are genes that form the 1-alpha-hydroxylase enzyme that functions to initiate vitamin D into its active metabolite form.[16]

The administration of vitamin D as a supportive treatment in addition to the present conventional short-term treatment is one alternative that should be taken into consideration in order to address the issue of TB treatment. Vitamin D contributes to respiratory system infections in the following ways: it improves mucociliary clearance function in the airways, aiding in the removal of respiratory pathogens and inflammatory mediators; it modulates inflammation by regulating adaptive and innate immune responses, suppressing excessive inflammation that may damage the respiratory tract during infections; and it lowers the risk and severity of acute respiratory infections.[17] Together with ATD that patients consumed, vitamin D acts as an immunomodulator that helps activate macrophages against Mycobacterium Tuberculosis.[8] By generating nitrogen and oxygen reactants, vitamin D has been shown to efficiently stop Mycobacterium Tuberculosis from growing in infected macrophages. It is well known that vitamin D promotes the synthesis of methyl glycol and the antimicrobial peptide β-Phenin 2, which aids in drawing T cells, neutrophils, and monocytes to the infection site. It has a major immunomodulatory effect on TB treatment.[10] Maintaining the activity of monocytes and macrophages linked to human innate immunity to certain infectious agents is the primary function of vitamin D. This function is crucial for the body's natural defense against infection, where macrophages play a significant part in pathogenesis.[13]

The active metabolite of vitamin D or calcitriol has the ability to induce an immune response to produce cathelicidin which functions as an endogenous antibiotic. The role of vitamin D in adaptive immunity is to suppress INF-y, TNF-α as inflammatory interleukins and increase IL-4 as an anti-inflammatory interleukin. The role of active metabolites of vitamin D in adaptive immunity is very necessary to suppress excessive inflammatory reactions so that it can improve and accelerate the healing of tuberculosis patients.[14,16] In addition, Vitamin D works by combining with nuclear receptors on affected cells so that abnormalities in the function and structure of the receptors or low levels of Vitamin D alter immunity to the tubercle bacillus.[18] Based on research by Riefani, *et al* (2024), various factors can increase the risk of TB, one of which is vitamin D deficiency. The results of this study showed that out of 42 research samples, there were 2 with normal vitamin D levels (4.76%), 19 with vitamin D insufficiency (45.2%), 21 with vitamin D deficiency (50%). Vitamin D levels in drug-resistant TB patients were higher than drug-sensitive TB due to differences in the number of samples and drug-resistant TB patients were more often exposed to sunlight related to their work.[19]

However, the results of this study are not in line with the study by Wang *et al*. (2018) who provided 60,000 IU of vitamin D, which showed that vitamin D supplementation did not affect AFB conversion time in TB patients.[20] The study participants were aged 23–47 years. All participants were undergoing intensive treatment at the time of entry. Vitamin D supplementation was administered for 8 weeks. Nearly 50% of the study subjects had vitamin D deficiency. This may have contributed to the differences in our results.[21] Research by Ganmaa *et al*. (2017) who conducted research on 190 patients also showed that vitamin D did not improve AFB conversion time.[21] This difference in results may be due to the fact that this study and the studies of Wang *et al* (2018) and Ganmaa *et al* (2017) did not measure vitamin D levels before the intervention, so they could not describe the initial vitamin D levels that could affect the results after the intervention.[20,21]

The results of this study indicate that there is no significant effect between vitamin D supplementation and NLR levels. They are not in line with the research of Wang *et al*. (2021) which showed that there is a relationship between vitamin D levels and NLR. The higher the vitamin D in the blood, the lower the NLR found.[20] Many studies have shown a relationship between vitamin D levels and inflammation. Research by Akbas *et al*. (2015) showed that subjects with sufficient vitamin D had lower NLR values compared to the group of subjects with vitamin D deficiency, and vice versa (p = 0.001). There isn't a clear consensus about the relationship between vitamin D and inflammatory indicators, despite the fact that the literature has highlighted the connection between vitamin D deficiency and numerous chronic inflammatory illnesses.[22]

The strong anti-inflammatory effects of 1,25-dihydroxyvitamin D, the active form of vitamin D, have been demonstrated to cause a change in response from the more inflammatory Th1/Th17 response to the less inflammatory Th2/Treg response. As a result, pro-inflammatory mediators including interferon gamma (IFN-g), TNF-a, IL-1b, IL-6, IL-8, IL-12, and IL-17 are secreted less frequently, whereas anti-inflammatory cytokines like IL-4 and IL-10 are produced more frequently.[23] Haematopoiesis in cells is influenced by

vitamin D. Vitamin D affects the early development of monocytes and granulocytes in haematopoiesis. The bioactive form of vitamin D (1,25(OH)2D3) will inhibit the development of colony-forming units of granulocyte macrophages (CFU-GM) and subsequently induce colony-forming units of macrophages during the haematopoiesis process. This will suppress the development of granulocyte cells and direct cell development towards monocytes and macrophages. The ratio of neutrophils, lymphocytes, and monocytes is altered by M. tuberculosis infection. It has been demonstrated that variations in the ratio are associated with the inhibition of M. tb growth, and they also indicate an increase in the effective immunological response.[24] Cathelicidin production from vitamin D will rise during TB infection, but this process will only take place if the body has enough vitamin D. Because of its antibacterial properties, this vitamin D can prevent germs from multiplying, which lowers neutrophils and lymphocytes and, consequently, NLR.[25]

This study evaluated ESR in addition to NLR. According to the study's findings, vitamin D supplementation and ESR do not significantly interact. This outcome is consistent with Wang *et al*. (2018)'s study, which found that vitamin D supplementation had no discernible impact on patients with pulmonary tuberculosis' ESR.[21] This, however, contradicts the findings of Kaya *et al*. (2017), who found a correlation between vitamin D levels and ESR. Patients with vitamin D insufficiency had greater ESRs than those with adequate vitamin D ($p < 0.001$), and there was a negative correlation between ESR and 25-hydroxyvitamin D levels ($r = 0.265$, $p < 0.001$).[26] ESR is an inflammatory biomarker that can rise in response to vitamin D insufficiency, according to studies by Etminan *et al*. (2020).[27]

It is known that vitamin D levels in the blood are associated with increased ESR. In accordance with the research of Etminan, *et al* (2020) showed that vitamin D deficiency is significantly associated with increased ESR. ESR has a significant effect on vitamin D levels.[27] In this study, vitamin D levels were not measured. In pulmonary TB, an inflammatory process occurs in pulmonary TB which causes positively charged acute phase proteins to neutralize the erythrocyte membrane, thereby reducing resistance and causing erythrocyte aggregation, forming rouleaux, resulting in increased ESR.[28]

By suppressing the expression of major histocompatibility complex (MHC-II) class 2 molecules on the cell surface, vitamin D has been demonstrated to improve monocyte differentiation into macrophages, stop macrophages from releasing inflammatory cytokines, and lessen the capacity of macrophages to present antigen to lymphocytes. Additionally, vitamin D inhibits the ability of T cells and monocytes to proliferate and stimulate, and it upregulates anti-inflammatory cytokines like IL-10 while downregulating proinflammatory cytokines like c-reactive protein (CRP), tumour necrosis factor-α (TNFα), interleukin (IL) 6, IL-1, and IL-8. Vitamin D may lower ESR because of these anti-inflammatory properties.[29]

The limitation of this study is that it does not include confounding variables in the statistical analysis of the relationship between independent and dependent variables, so it is difficult to see whether the confounding variables in this study can affect the results, including comorbid conditions. This study also did not mention about the diet of the subjects, including vitamin D intake from the food and sunlight exposure. Both of these variables might have confounded the results. The advantage of this study is that researchers studied inflammatory parameters, considering that research related to the effect of vitamin D supplementation on ESR and NLR in pulmonary TB patients has not been widely studied in South Kalimantan. It is hoped that this study can be used as a reference in further research.

CONCLUSION

Vitamin D supplementation can accelerate sputum conversion in pulmonary TB patients; however, it does not have a significant effect on NLR and ESR in pulmonary TB patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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