

The Effect Of Applying Vitamin D Onrepairing Of Thorax Photo Of Tuberculosis Patients Of Batak Ethnic In Medan

Seri Rayani Bangun^{1,*}, Bintang Y.K. Sinaga², Nasipta Ginting²

¹STIKes Santa Elisabeth Medan BungaTrompet No. 118, Medan, North Sumatra, Indonesia

²Bintang Yinke Magdalena Sinaga, Departemen Pulmonology and Respiratory Medicine, University of North Sumatera

²Nasipta Ginting, Departemen MIK STIKes Santa Elisabeth Medan

ARTICLE INFO

Keywords:

Levels of Vitamin D,
Thorax Photo Fix

E-mail:

serirayani2009@gmail.com

ABSTRACT

This study aims to determine the effect of vitamin D on the repairing of thoracic on patients with pulmonary tuberculosis of Batak ethnic in Medan, conducted on 42 patients with TB, vitamin D group of 21 people and 21 placebo. Giving vitamin D dose of 2.5 mg (100,000 IU) for 4 times (weeks 0, 2, 4, 6) and placebo for 4 times (weeks 0, 2, 4, 6). B. The assessment of vitamin D and thorax photo were done before and after intervention. The results showed that the levels of vitamin D results before and after there is a difference, the measurement results using the enzyme linked immunosorbent assay (ELISA) provisions of the absorbance of each well at a wavelength of 450 ± 10 nm. Vitamin D levels were measured 25 (OH) D nmol / L then further analyzed using paired T test on vitamin D group $p = 0:00$, mean difference $29.27 +$ vitamin D levels were 22 ng / ml , whereas the placebo group $p = 0:27$, the difference of the mean levels of vitamin D $1:36 + 5:53 \text{ ng / ml}$. After examination of thorax photo in hospital then analyzed using Chi-square test. Vitamin D group showed a total improvement (66.7%) while the placebo treatment (33.3%), $p = 0:06$ concluded there was no effect of vitamin D on the restoration of thorax photo on patients pulmonary tuberculosis Batak ethnic.

Copyright © 2021 Science Midwifery.

1. Introduction

Tuberculosis is an infectious disease caused by the bacterium Mycobacterium tuberculosis which aerobic bacteria that can live mainly in the lungs or in various other organs of the body that has a high oxygen partial pressure. This disease spreads through droplets of infected people who have tuberculosis bacillus [1-2]. Particularly in Indonesia at the time of the VIII century Borobudur temple built, tuberculosis had become a disease of the people since spread across the archipelago with characteristic thin, shoulder and upper interested and bones jutted out. [3] Until now, pulmonary tuberculosis disease remains a major health problem, both globally and in Indonesia. Approximately 75% of patients with pulmonary TB is the economically productive age group (15-50 years). Pulmonary tuberculosis is also having a devastating effect more socially and sometimes ostracized by society. [4] The tuberculosis death rate is still very high in the world so that by 2015 global targets to reduce TB tuberculosis are set in the context of the Millennium Development Goals (MDGs). [5] The population of North Sumatra there are 12 million people, the tuberculosis patients in this area as many as 19,000, [6]

Vitamin D functions as an immunomodulator, which is involved in macrophage activation. Invitro study conducted by Liu, [7] shows the active metabolite of vitamin D is 1,25-dihydroxy. Vitamin D is able to help the macrophages suppress the growth of *M. tuberculosis* through increased intracellular levels of cathelicidin. Cathelicidin is an anti-microbial protein that can kill gram negative and positive bacteria which have antimicrobial properties. Cathelicidin present in the human body in the form of Human LL-37 Peptide or h-CAP18 that play a role in immune system-specific and non-specific. [8-9]

Vitamin D has a function in the body immune system, both of which are naturally non-specific and specific immunity, which has an important role in the activation of 1 α -hydroxylase to convert 25 (OH) D to its active form [1, 25 (OH) 2D] that improve the function of cathelicidin to *M. tuberculosis*. [10-11]

Genetic factors are among the factors that could explain why some people are more resistant to infection with *M. tuberculosis*. Vitamin D receptor gene (RVD) is one of the important candidate

gene from non-MHC genes that plays a role in the incidence of tuberculosis. Vitamin D will give effect after interacting with RVD, which is a hormone receptor core. Most polymorphisms known to show different results on ethnicity, culture, diet, [12-13]

This results of this study is supported by Salahuddin research, [14] the subject of research in Saudi Arabia population with pulmonary tuberculosis, showed that high doses of vitamin D3 supplementation, 2x 600,000 IU intramuscularly accelerate clinical improvement and radiological improvement in all patients with tuberculosis. Results of Martineau research [11] in London that an oral dose of 2.5mg (100,000 IU) of ergocalciferol shows the significant results reducing the growth of mycobacteria.

Studies of Eun-Kyeong confirm that antimicrobial peptides play a central role in innate immunity to mycobacteria, immediately kill and immune modulation. It has been proven that the cathelicidin LL-37 becomes component key of vitamin D3-dependent immunity and autophagy link. [9,13]

Giving vitamin D to pulmonary tuberculosis patients showed the restoration of thoracic photoresults by giving oral of 800 IU of vitamin D per day after 1 month the vitamin D is given. [9] Batak ethnic is majority population in North Sumatra that consists of a Batak Karo

2. Experimental Section

Materials

All chemicals used by Elisa Kit Vitamin D is obtained from Belgium, vitamin D D3-5 5,000iu obtained from Bio-Tech Pharmacal USA, placebo (sac lactis) were obtained from Rudang drug store Medan serum blood plasma of the study sample, sterile aquades and available materials in elisa kit vitamin D, sensitivity of 1.6 ng / ml, a dynamic range of 4-120 ng / ml, with 20µl samples of serum plasma, [17]

Instrumentation

Elisa kit vitamin D, centrifuge, vortex, micropipette (10-200µl, 100-1000µl), eppendorf tube, the freezer, shelf eppendorf tube, 1x size 96 wells

Procedure

Blood samples were taken 3 cc then centrifuged to separate serum from its cell and placed in ice box then brought to laboratory stored in -20 ° C freezer for vitamin D levels checked, Serum plasma stored in a freezer and then measured the levels of vitamin D early in FK USU laboratory, patients were randomized into two (2) intervention group (control) and comparators (placebo), the intervention group were given OAT according DOTS program and oral vitamin D at a dose of 2.5 mg to 4 (four) times a week at week 2, 4, 6 and 8th week. OAT and the comparison group was given a placebo, [14] Patients were followed later development after given drug the 8th week 3 cc blood samples taken to measure levels of vitamin D and lung examination with rontgen.

The Level of Vitamin D Assessment

Measured vitamin D levels is 25 (OH) serum level. The assessment of level 25 (OH) D serum using the method of enzyme linked immunosorbent assay (ELISA). The assessment results in units of nmol / L. Vitamin D deficiency is declared when the levels of 25 (OH) D serum of 10-20 nmol / L vitamin D insufficiency is declared when the levels of 25 (OH) D serum 21-29 nmol / L, vitamin D sufficiency is declared when the levels of 25 (OH) D serum > 30. Insert 25 µl standard solution, control and sample to be checked into the vial, with the tip of a new micropipette every time, insert 50 µl of denaturation buffer into each vial, close the vial and incubation for 30 minutes at a temperature of 37°C, Add 200 µl buffer neutralization into the vial, add 50 µl of enzyme conjugate into vial, Add 50 µl enzyme complex into vial, Mix solution in each vial for 10 seconds, use 200 µl

Science Midwifery

journal homepage: www.midwifery.iocspublisher.org

solution from the vial to the next process, Insert 200 ul solution standard, control and sample, into a well plate, close the vial and incubate for 60 minutes at a temperature of 37°C, shake fast the plate well, wash 4 times with wash solution (300 ul per well). Knock the wells on paper absorbent to remove the remaining residual, add 200 ul substrate solution into each well, incubate for 15 min in room temperature, stop the enzymatic reaction by adding 100 ul stop solution into the well, Determine the absorbance of each well by readings at a wavelength of 450 ± 10 nm. Recommended readings were taken within 10 minutes after the addition of stop solution, [17]

The Thorax Photo Assessment

The lung assessment with rongent were conducted in both the intervention group and the comparator to pre (beginning before vitamin D being given) intervention and post-intervention (after completion of vitamin D) by rongent department in hospital.

3. Results

Samples General Character

There are 42 samples with pulmonary tuberculosis with different characteristics, age, sex, and occupation

TABLE 1.
DISTRIBUTION BASED ON CHARACTERISTICS OF PULMONARY TUBERCULOSIS PATIENTS

Characteristics	Intervention					
	Vitamin D		Plasebo		Total	
	n	%	n	%	n	%
Umur						
18 – 34	3	52.4	4	19	7	16.7
35 – 52	13	42.9	9	42.9	22	52.4
53 – 69	5	4.8	8	38.1	13	30.9
Sex						
Male	14	66.7	13	61.9	27	62.5
Female	7	33.3	8	38.1	15	37.5
Status Vitamin D						
< 20 ng/ml (Deficiency)	3	14.3	2	9.5	5	11.9
20-30 ng/ml (insufficiency)	6	28.6	8	38.1	14	33.3
> 30 ng/ml (Optimal)	12	57.1	11	52.4	23	54.7
Vitamin D Level						
Mean	21	30.93	21	29.81	21	
SD		8.78		8.65		

Table 1 shows the frequency of the largest age 35-52 years 22 (52.4%), the highest frequency of sex was male with a number of 27 people (62.5%), women 15 (37.5%), the highest frequency of vitamin D status > 30 ng / ml (Optimal) 23 (54.7%), the average levels mean of vitamin D in the group given vitamin D 30.93 ng / ml in the placebo group 29.81 ng / ml

TABLE 2
FREQUENCY DISTRIBUTION TO TOTAL ZONE ON VITAMIN D AND PLASEBO GROUPS

Amount Zone	Vitamin D				Plasebo			
	Pre		Post		Pre		Post	
	n	%	n	%	N	%	n	%
0	-	-	-	-	-	-	1	4.8
1	-	-	2	9.5	1	4.8	1	4.8
2	2	9.5	5	23.8	5	23.8	7	33.3
3	6	28.6	7	33.3	2	9.5	2	9.5
4	8	38	5	23.8	2	9.5	2	9.5
5	2	9.5	1	4.8	8	38.1	6	28.6
6	3	14.2	1	4.8	3	14.3	2	9.5
Amount	21	100	21	100	21	100	21	100

Table 2 shows the difference of frequency in both treatment was before being given vitamin D 1 as many as 1 people (4.8%), 2 zones as many as 5 people (23.8%), 3 zones as many as 2 people (9.5%), 4 zones as many as 2 people (9.5%), 5 zones of 8 people (38.1%), 6 zones as many as 2 (9.5%) while the frequency after being given vitamin D net 2 (9.5%) 1 zone as many as 1 people (4.8%), 2 zones as many as 6 people (28.6%), 3 zones as many as 2 people (9.5%), 4 zones as many as 2 people (9.5%), 5 zones as many as 6 people (28.6%), 6 zones as many as 2 people (9.5%), while the difference of frequencies on the group given the placebo were 2 zones with 2 people (9.5%), 3 zones as many as 6 people (28.6%), 4 zones of as many 8 people (38.1%), 5 zones as many as 2 (9.5%), 6 zones as many as 8 people (38.1%), 6 zones as many as 3 people (14.3%), while the frequency difference after given placebo 1 zone as many as 2 people (9.5%), 2 zones as many as 5 people (23.8%), 3 zones as many as 7 people (33.3%), 4 zones as many as 5 people (23.8%), 5 zones as many 1 people (4.8%), 6 zones as many as 1 people (4.8%).

TABLE 3.
THE ANALYSIS OF VITAMIN D LEVEL TO PATIENTS OF PULMONARY TUBERCULOSIS THAT ARE GIVEN VITAMIN D

Vitamin D					
Group	N	Mean + sd	Difference average	P* Value	
Pre vitamin D treatment	21	31.35 ± 1.99	29.27 ± 22	0.000	
Post vitamin D treatment	21	60.62 ± 4.63			

*Couple T Test

Table 3 shows that there are differences of the average of vitamin D level before and after administration of vitamin D $p = 0.000$ ($p < 0.05$), the average difference between the two time measurement was 29.2 ng / ml with a standard deviation of 22.0 ng / ml.

TABLE 4.
ANALYSIS OF VITAMIN D LEVELS ON PULMONARY TUBERCULOSIS PATIENTS GROUP THAT ARE GIVEN PLASEBO

Vitamin D				
Group	n	Average + SD	Difference average	P* Value
Pre plasebo treatment	21	29.81 ± 7.54	1.36 ± 5.53	0.271
Post plasebo treatment	21	31.18 ± 8.23		

*Couple T Test

Table 4 shows that there is no differences of lever of vitamin D average before and after 2 months of

Science Midwifery

journal homepage: www.midwifery.iocspublisher.org

placebo in the placebo group $p = 0.271$ ($p > 0.05$ the average difference vitamin D levels before and after is 1:36 ng / ml with standard deviation of 5:53 ng / ml).

TABLE 5.
AVERAGE OF VITAMIN D LEVEL SUBJECT RESEARCH BEFORE AND AFTER TREATMENT IN BOTH

Group	N	Average \pm	Average	Difference	P*value
		SD Pre	\pm SD Post		
Vitamin D	21	31,35 \pm 1.9 9	60,62 \pm 4.63	29,27 \pm 22	0,00
Plasebo	21	29,81 \pm 7,5 4	31,18 \pm 8,23	1,36 \pm 5,53	0,27

*Couple T Test

Table Table 5, showed that the group which were given vitamin D there is an increase of 33.3%. The difference of average vitamin D levels before and after treatment in the vitamin D group was 29.27 ng / ml (SD = 22), whereas in the placebo group was 1.39 ng / ml (SD = 5.53). In the couple T test $p = 0.00$ results obtained in the group of vitamin D, means there is a significant increase in the average levels of vitamin D before and after treatment. In the same test for the placebo group was found $p = 0.27$ means there is no significant increase of the average level of vitamin D before and after treatment.

TABLE 6.
DIFFERENCES OF TOTAL REPAIR ZONE OF THORAX PHOTOS IN BOTH GROUPS

Amount treatment Zone	Vitamin D		Plasebo		P*value
	N	%	n	%	
0	7	33,33	13	61,9	0,12
1	10	47,6	3	14,3	
2	4	19	4	19	
3	0	0	1	4,8	

* Chi-square test

Table 6 shows the improvement assessment based on zones that have improved lung fields on thorax photo group of vitamin D are 7 people (33.3%) had no improvement, 10 men (47.6%) experienced improvement 1 zone, 4 people (19%) experienced repair 2 zones whereas on placebo group did not experience improvement as many as 14 people (66.7%), 3 people (14.3%) experienced improvement zones 1, 3 people (14.3%) experienced improvement in 2 zones. 1 person (4.8%) experienced improvement as many as 3 zones declared clean. Giving vitamin D showed a total amount of improvement more than placebo (66.7%) compared with (33.3%). However, the chi-square test showed $p = 0:06$ means there is no significant relationship between applying vitamin D with improvements of thorax photo on pulmonary tuberculosis patients of Batak ethnic.

TABLE 7.
FREQUENCY DISTRIBUTION BASE ON PHOTO THORAX LESIONS SIZE BEFORE TREATMENT IN BOTH GROUP.

Lesion area	Vitamin D		Plasebo		Total	
	n	%	n	%	n	%
Minimal	0	0	1	4.8	1	2,4
Moderate	11	52.4	11	52.4	22	52,4
Far advance	10	52.6	9	47.4	19	45,2

Table 7, shows the area of the lesion is minimal, moderate and far advanced. In the group of vitamin D is not found broad subject with minimal lesions, while the placebo group there was 1 person

(4.8%). Moderate lesion area as many as 11 people (52.4%) of vitamin D and placebo groups. Lesion area far advance as many as 10 people (52.6%) on the vitamin D group and 9 people (47.4%) on the placebo group.

TABLE 8
FREQUENCY DISTRIBUTION BASED THE CHANGE OF PHOTOS THORAX LESIONS AREA AFTER TREATMENT IN BOTH GROUPS.

Change of Lesions area	Vitamin D		Plasebo		Total	
	n	%	n	%	n	%
Moderate → Minimal						
Far Advance → Moderate	7	33,3	1	4,8	8	19
Far advance → Minimal	5	23,8	4	19	9	21,4
Far advance → Negative	1	4,8	0	0	1	2,4
No change	0	0	1	4,8	1	2,4
	8	38,1	15	71,4	23	54,8

Table 8, shows that the change of lesion area after treatment there were five categories of change; a change from moderate to a minimum, advance far became moderate, far advanced became minimal, far advanced became negative. On group of vitamin D treatment there were 7 people (33.3%) who experienced the change of moderate lesion area to a minimum, while the placebo group there was 1 person (4.8%). 5 people (23.8%) who experienced a change from the lesions far advance become moderate area, on the vitamin D group and as many as 4 people (19%) on the placebo group. 1 person (4.8%) who experienced a change of photo from far advance became minimal lesions and 1 person (4.8%) in the group of placebo who experienced a change of photo of far advance became negative. On the vitamin D group of 8 people (19%) had no change and 15 people in the placebo group did not experience changes.

4. Discussion

The results of the study vitamin D levels in this study was consistent with broad research like Africa [18-19] Pakistan [20] and the UK [11] levels of vitamin D group that was given vitamin D treatment is higher than with placebo. Differences of vitamin D occur due to differences in sunlight exposure and different dietary intake factors. Results of research conducted [21], in 1994 in Hong Kong, showing the optimal vitamin D level in the case group.

Another study in Indonesia also in line with this study, [9] research in Malang, there were significant differences in vitamin D levels in the intervention group and placebo, where the group given vitamin D had higher vitamin D levels. Vitamin D2 and D3 followed the same metabolic pathway, while the exposure to the sunlight is considered to be the same as being in the same demographic and climate.

Vitamin D has an important role in increasing the production and activity of macrophages katelisinidin in inhibiting the growth of germ M. tuberculosis. Vitamin D levels in each patient with pulmonary tuberculosis will be reduced because it is used for the activity of the immune system. From the results of this study of vitamin D status on the group given vitamin D is deficient 3 people insufficiency 6 people, optimal 12 people, while levels of vitamin D that given a placebo were insufficiency 2 people, optimal 8 people, while optimal were 11 people.

Tuberculosis is a cause of high death in the world with an estimated death and morbidity of 1.5 million people in 2014. This is consistent with previous studies reported that independently vitamin D deficiency has link with susceptibility to tuberculosis. The study [20], in patients tuberculosis in Pakistan reported that vitamin D deficiency on patients tuberculosis occurred due to activities in the fight against tuberculosis germs and independently associated with susceptibility to active tuberculosis.

Theoretically tuberculosis patients who have consumed OAT and addictive supplements will provide resistance against germ M. tuberculosis. Response several germ M. tuberculosis in addition to the death against the host immune system will respond by doing dormancy. Sputum assessment with BTA will be negative for germ M. tuberculosis that had dormant.

Other studies [14] with the same design on the 259 tuberculosis patients by applying vitamin

Science Midwifery

journal homepage: www.midwifery.iocspublisher.org

D injections dose of 600,000 iu 2 times of applying that it was obtained sputum conversion insignificant ($p = 0.39$), while significant radiological improvement ($p = 0.004$). This difference is possibly due to a broad effect of Vitamin D on muscle, blood vessels and the body's homeostasis in patients tuberculosis.

This may be the reason that the healing process for tuberculosis can be influenced by many factors other than vitamin D levels, including the factors the body's immunity, the virulence of the bacteria and lifestyle or habits (smoking and alcohol) based on the survey results revealed that the group was given vitamin D and placebo in average experienced a reduction in density after a given intervention. The result difference can be caused by many things other than the patient's immune status, the virulence of the bacteria and ethnicity [14].

5. Conclusion

Overall, the subject of this study amounted to 42 people and be divided into vitamin D group as many as 21 people and placebo group as many as 21 people, the highest frequency characteristics in patients pulmonary tuberculosis at the age of 35-52 years (52.4%), the largest gender was male (62.5%), levels of vitamin D (25 OH-vitamin D) on patients pulmonary tuberculosis of Batak ethnic before and after treatment for 8 weeks to the group given vitamin D found differences of meaningful significant $p = 0.000$, levels of vitamin D on patients tuberculosis of Batak ethnic before and after treatment for 8 weeks in the placebo group found that there were no differences of meaningful significant $p = 0.27$.

Comparative levels of vitamin D on patients pulmonary tuberculosis of Batak ethnics in both groups, vitamin D levels influence susceptibility to tuberculosis, because most of the subjects in this study, both groups showed different vitamin D level status.

It was found the different significant of the level vitamin D average before treatment in both groups, the average levels of vitamin D $29.27 + 22$ ng / ml ($p = 0:00$), while the placebo group $1:36 + 5:53$ ng / ml ($p = 0:27$), the improvement thorax photo differences in both groups based on the frequency distribution after treatment wason the vitamin D group that experienced improvement of thorax photo as many as 14 people (66.7%), 7 people (33.3%) experienced no thorax photo improvement. Whereas in the placebo group who experienced thorax photo improvement were 7 people (33.3%) while those not improved thorax photo were 14 people (66.7%).

References

- [1] Basir D, Yani FF. Tuberkulosis dengan Keadaan Khusus. 2012. Buku Ajar Respirologi Anak. Fakultas Kedokteran Universitas Indonesia. Jakarta;. p. 228-45
- [2] Tabrani Rab. 2010. Ilmu Penyakit Paru. Editor sandy qlintang diterbitkan oleh hipokrates; 157-168
- [3] Halim Danusantoso. 2012. Buku saku penyakit paru. jakarta. Edisi 2. EGC.
- [4] Bambang Ruswanto, Nurjazuli, Mursid Raharj. 2012. Analisis Spasial Sebaran Kasus Tuberkulosis Paru Ditinjau Dari Faktor Lingkungan Dalam dan Luar Rumah di Kabupaten Pekalongan . Vol. 11 No. 1, 22-28
- [5] WHO, 2014. Global Tuberculosis Report 2014; 13-61. Tersedia di <http://www.who.int/TB/data>. Diakses 29 November 2014
- [6] Profil kesehatan provinsi sumatera utara tahun 2012
- [7] Liu PT, Stenger S, Li H et al. 2006. Scienceexpress. *Toll Like Receptor Triggering of a Vitamin D-Mediated Human Antimicrobial Response*. 24:1770-1773
- [8] Dini, C and Bianchi, A. 2012. The potential role of vitamin D for prevention and treatment of tuberculosis and infectious diseases *Ann Ist Super Sanità. Italy;* 319-327
- [9] Siswanto, at al. 2009. Jurnal Kedokteran Brawijaya, Vitamin D as Supportive Treatment Improve The Sputum Conversion and Radiographic Finding in Tuberculosis Patients. Vol. XXV, No. 3, Desember 2009; 128-132
- [10] Martineau AR, Honecker FU, Wilkinson RJ, Griffiths CJ. 2007. Journal of Steroid Biochemistry & Molecular Biology. Vitamin D in the treatment of pulmonary tuberculosis.103;793-8
- [11] Martineau AR, at al. 2011. High-dose vitamin D3 during intensive-phase antimicrobial treatment of pulmonary tuberculosis: a double-blind randomised controlled trial. Centre for Health Sciences Barts dan The London School of Medicine and Dentistry *Lancet.*; 377: 242-50

- [12] Hemant K Bid, Dhruva K Mishra, Rama D Mittal. 2005. Asian Pasific Journal of cancer prevention. Vitamin-D Receptor (VDR) Gene (Fok-I, Taq-I & Apa-I) Polymorphisms in Healthy Individuals from North Indian Population. volume 6. edisi 2; 147-152
- [13] Shaden, Haddad. 2014. Meta Gene, Syria. Vitamin-D receptor (VDR) gene polymorphisms (Taq-I & Apa-I) in Syrian healthy population ; 646-650
- [14] Salahuddin N, Ali F, Hasan Z, Rao N, Aqeel M, Mahmood F. 2013. Vitamin D accelerates clinical recovery from tuberculosis: results of the SUCCINCT Study [Supplementary Cholecalciferol in recovery from tuberculosis]. A randomized, placebo-controlled, clinical trial of vitamin D supplementation in patients with pulmonary tuberculosis. BMC Infectious Disease.; 13-22
- [15] Badan Pusat Statistik Provinsi Sumatera Utara. 2013. Jurnal Kesehatan Lingkungan Indonesia. Sumatera Utara dalam Angka 2013/ Sumatera Utara in Figures 2013. Medan
- [16] Arbeitsanleitung/Manual. Valid from 17.01.2012. 25(OH)-Vitamin D direct ELISA Kit For the determination of 25(OH)-Vitamin D in human serum. Immundiagnostik AG Stubenwald-Allee 8a D-64625 Bensheim
- [17] <https://Kebudayaanindonesia.net/kebudayaan/952/suku-batak-sumatera-utara> diakses pada tanggal 20 Agustus
- [18] Gao L, Tao Y, Zhang L, Jin Q. Vitamin D Receptor Genetics Polymorphisms and Tuberculosis: Update Systemic review and meta-analysis. International Journal of Tuberculosis Lung Disease. 2010; 14 (1): 15-23
- [19] Keflie, M.Sc. *Vitamin D deficiencies among tuberculosis patients in Africa: A systematic review.* Nutrition 31, review, Elsevier 2015; p.1204-1212
- [20] Junaid, Kashaf et al. High prevalence of vitamin D deficiency among women of child-bearing age in Lahore Pakistan, associating with lack of sun exposure and illiteracy. BMC Women's Health. 2015; p. 1-8
- [21] Chan TY, Poon P, Pang J, Swaminathan R, Chan CH, Nisar M, Williams CS, Davies PD. A Study of Calcium and Vitamin D Metabolism in Chinese Patients With Pulmonary Tuberculosis. J Trop Med Hyg. 1994 Feb; 97(1): 26-30