The effect of vitamin D3 supplements on the 25(OH)D levels in the II and III trimester of pregnant women in Sleman, Indonesia randomized controlled trial

by Martha Irene Kartasurya

International Journal of Research in Medical Sciences
Susilani AT et al. Int J Res Med Sci. 2021 Jan;9(1):22-26
www.msjonline.org pISSN 2320-6071 | eISSN 2320-6012

Original Research Article

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20205826

The effect of vitamin D3 supplements on the 25(OH)D levels in the II and III trimester of pregnant women in Sleman, Indonesia: randomized controlled trial

Amalina T. Susilani[1]*, Hertanto W. Subagio[2], Noor Pramono[3], Martha I. Kartasurya[4]

[1]Student, [2]Department of Clinical Nutrition, [3]Department of Obstetrics and Gynecology, Faculty of Medicine, [4]Department of Nutrition, Faculty of Public Health, Diponegoro University, Semarang, Indonesia

Received: 22 October 2020
Revised: 04 December 2020
Accepted: 05 December 2020

***Correspondence:**
Dr. Amalina T. Susilani,
E-mail: doktoramalina@gmail.com

ABSTRACT

Background: Pregnant women are among the groups at high risk of vitamin D3 deficiency due to the increased need for micro and macro nutrients during pregnancy. Vitamin D3 deficiency is associated with pregnancy complications, namely preterm birth, pre-eclampsia, gestational diabetes, and babies born small according to their gestational age.
Methods: The study involved a randomized pretest-posttest control group design. Subjects selected include 80 pregnant women in second trimester. Data were collected in June 2020 to September 2020. The respondents were then randomly divided into 2 groups, comprising 40 each, where the first received 400 IU/day vitamin D3 supplementation for 12 weeks, and the second served as a control. Furthermore, 25 (OH) D were measured by using the ELISA method.
Results: The mean value of the 25(OH)D levels after D3 supplementation and statistically showed a significant difference with a significance value of $p<0.05$ (0.01), compared to the control group. Furthermore, the mean value of the 25(OH)D levels in the control group actually decreased by 2.7 ng/ml which was statistically significant with a p value of 0.00, compared to the control group. Furthermore, the mean value of the 25(OH)D levels in the control group actually decreased by 2.7 ng/ml which was statistically significant with a p value of 0.00.
Conclusions: Vitamin D3 supplement of 400 IU per day can increase the levels of 25(OH)D in the II and III trimester of pregnant women in antenatal care (ANC), Sleman Regency, Yogyakarta.

Keywords: II and III trimester pregnant women, 25(OH)D levels, Vitamin D3 supplement

INTRODUCTION

Pregnant women are among the groups at high risk of vitamin D3 deficiency, and this has become a global problem for them. Meanwhile, this deficiency is due to their increased need for both macro and micro nutrients, and it the quality and function of intrauterine fetal development.[1,2] To determine the levels of this vitamin in a person, a 25-Hydroxyvitamin D [25(OH)D] examination is carried out.[3] Physiologically, the metabolism of this vitamin increases from the second to the third trimester of pregnancy.[4] However, complications such as preterm birth, pre-eclampsia, gestational diabetes, and babies born small according to their gestational age sometimes occur during this period, which leads to its deficiency. This poses the risk of infection and respiratory problems when the baby is born, and affects the child with expensive treatment costs.[5]

Vitamin D3 is a fat soluble vitamin which is synthesized by the skin on exposure to sunlight. Meanwhile, lifestyle changes, such as the habit of protecting oneself from the sun, is considered to be a factor that leads to its deficiency in pregnant women.[6] Research conducted in some tropical Asian countries such as China, Bangkok and Malaysia where sunlight is seen all year round also found the same result.[7,8]

In Indonesia, where the majority are Muslims, pregnant women that wear the hijab are capable of being deficient in vitamin D3. According to the research results in 2019, the best time to be exposed to ultra violet (UV) rays is from 10:00 am to 01:00 pm, with an exposure duration of 64.5 minutes for women that wear hijab and 37.5 minutes for those that do not. The use of vehicles such as cars with windshield blocks the exposure of these rays to the skin.[9,10]

Supplements of this vitamin administered during the II and III trimesters at a dose of 400 IU/day oral from the 24th to 28th weeks of gestation are expected to affect the levels of 25(OH)D. This is an experimental study with a randomized controlled trial design which aims to evaluate the levels of this vitamin in late trimester pregnant women in the Sleman region. Furthermore, the levels of this vitamin were seen based on the characteristics of age, education, occupation, height, weight before pregnancy, LILA, BMI, and 25(OH)D levels.

METHODS

Clinical trial

This study used a randomized controlled trial design conducted at the Public Health Center in Sleman Regency, Yogyakarta Province.

Respondent

Data were collected in June 2020 to September 2020. Twenty-two out of the 134 II and III trimester pregnant women were excluded because they did not fulfil the inclusion criteria, 112 fulfilled the criteria, and 80 were randomly selected with 40 as the intervention group and 40 as the control group.

Inclusion criteria

Mothers with II and III TM gestational age (24-28 weeks), ages of 20-35 years who didn't forget the first day of last menstruation (HPHT), BMI: 18.5-24.9, not currently suffering from HIV/AIDS, willingness to participate in the research and signing the informed consent.

Exclusion criteria

Mothers who had no medical history, such as pre-eclampsia and eclampsia, bleeding, PROM, Gemelli pregnancy, abortion and immature birth, as well as mothers with comorbidities such as heart, lung, liver, intestinal, bone, kidney, thyroid, and immunological diseases (Figure 1).

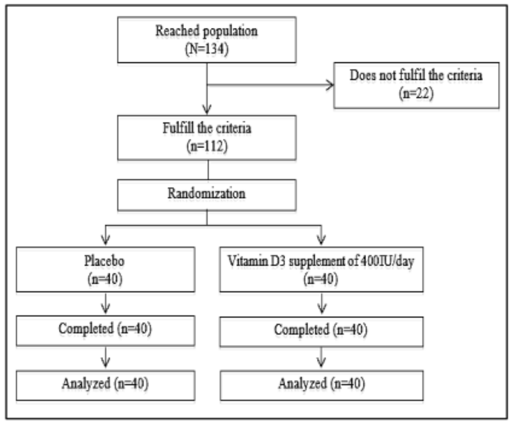

Figure 1: The Flowchart showing subject enrollment and follow up.

Procedure

A recall was performed 7 times on weekdays and weekends. 1.5 ml of venous blood samples were taken for 25(OH)D examination (Kalbiotech VD220B) using the ELISA method which had been centrifuged and the serum extracted.

Outcome measurement

The 25(OH)D examination was carried out at the GAKI Laboratory, Faculty of Medicine, Diponegoro University. Ethical Clearance was issued from the Ethical Commission of the Faculty of Medicine, Gadjah Mada University with the number KE/FK/0328/EC/2020. Statistical analysis was performed using the statistical software Stata version 14 license UGM, while the bivariate statistical test used the Wilcoxon sign rank with a significance <0.05.

RESULTS

The category of early adult was more dominant in the two groups, with 67.5% in the treatment group and 60% in the control group and statistically showed a significant difference with a p value of 0.00. The most dominant education in both groups was secondary school. Furthermore, the most dominant income in both groups was above the regional minimum wage (UMR) standard for the Yogyakarta area and they include 65% and 45% in the treatment and control groups. Meanwhile, the most dominant height in the two groups was ≥150 cm, and the body weight before pregnancy was 40-50 kg and 50-60 kg in the treatment and control groups with a percentage of 45% respectively. The most dominant upper arm circumference (LILA) in the two groups was greater than 23cm with 77.5% and 87.7% in the treatment and control groups. Furthermore, on the body mass index (BMI), there was no significant difference in the mean value between the two groups, which had a significant value of 0.43. The most dominant 25(OH)D level in the two groups was in the insufficiency category with a percentage of 90% respectively (Table 1).

Table 1: Comparison of subject characteristics between treatment and control groups.

Variable	Treatment group		Control Goup		P value
	n=40	%	n=40	%	
Age category					
Early adult (16-30)	27	67.5	24	60	0.00
Middle adult (31-65)	13	32.5	16	40	
Education					
Primary (elementary school-junior high school)	5	12.5	8	20	0.05
Secondary (senior high school)	21	52.5	24	60	
Tertiary (higher education)	14	35	8	20	
Income					
Below the UMR standard (<IDR 1,500,000)	1	2.5	0		0.59
the UMR standard (IDR 1,500,000)	12	32.5	22	55	
Above the UMR standard (≥ IDR 1,500,000)	27	65	18	45	
Body height					
<150 cm	5	10	10	25	0.78
≥150 cm	35	90	30	75	
BW before pregnancy					
30-40 kg	2	5	1	2.5	0.22
41-50 kg	18	45	17	42.5	
51-60 kg	15	37.5	18	45	
>60 kg	5	12.5	4	10	
LILA					
<23 cm	9	22.5	5	12.5	0.31
≥23 cm	31	77.5	35	87.5	
Minimal-maximal	19-33		21-35		0.83
Rerata (SD)	25.1 (3.7)		26.3 (3.1)		
BMI					
Minimal-maximal	17.9-28.4		18.5-28.9		0.43
Mean (SD)	21.6 (2.6)		22 (2.4)		
25(OH)D level					
Insufficiency/less (<30 ng/ml)	36	90	36	90	0.67
Sufficiency/normal (>30 ng/ml)	4	10	4	10	

Table 2: Comparison of protein, energy, zinc and vitamin D intake in the treatment and control groups.

Variable	Treatment group N (%)	Control group N (%)	P value
Food intake	**n=40**	**n=40**	
TKP (g)	44.9 (16.4)	44.3 (13.6)	0.71
TKE (kcal)	1123.3 (329)	1174.7 (310.9)	0.55
Zinc nutrition intake (mg)	4.8 (1.5)	4.6 (1.3)	0.74
Vitamin D intake (µg)	2.6 (2.6)	2.2 (2.6)	0.58

According to the results, food intake based on the adequacy level of protein (TKP) and energy (TKE) in both groups was still below standard (90% AKE and AKP). Furthermore, based on the zinc nutrition and vitamin D intake, the two groups were still below the recommended nutritional intake standard. Based on Hb levels, the most dominant was in the normal category with 60% and 65% for the treatment and control groups (Table 2).

The results obtained through statistical analysis using the Wilcoxon signed rank test showed an increase in the mean value of the 25(OH)D levels before and after vitamin D3 supplementation, and statistically showed a significant difference with a p value of 0.01 compared to the control group in pregnant women who performed a routine antenatal examination. Furthermore, the mean value of the 25(OH)D levels in the control group actually decreased by 2.7 ng/ml and was statistically significant with a p value of 0.00 (Table 3).

Table 3: Differences in the mean value of the 25(OH)D levels before and after vitamin D3 supplementation between the treatment and control groups.

25(OH)D levels (ng/ml)	Treatment Group				Control Group				P value
	Mean±SD	Median	Min.	Max.	Mean±SD	Median	Min.	Max.	
Before	22.5±6.6	22.2	13.2	48.6	23.6±6.5	23.4	10.8	38.7	0.51
After	24.6±6.5	24.2	13.7	48.4	21.6±6.6	20.7	9.9	38.2	0.11
P value		0.01				0.00			

DISCUSSION

Table 1 shows the different characteristics of respondents using the chi-square correlation test. Both groups in the age and education category showed a significant difference with a p value <0.05. Furthermore, in the category of food intake, there was no significant difference in the two groups shown in Table 2. This means that the food intake in the two groups is almost the same in terms of quantity. However, most food ingredients contain a few vitamins and the fulfillment of vitamin D mostly comes from external factors.[11]

According to Table 3, the mean value of the 25(OH)D levels in the two groups did not experience a significant difference. There was an increase in the 25(OH)D levels in the treatment group after vitamin D3 supplementation at a dose of 400 IU/day for 3 months when compared to the control group using paired t-test, and a significant value <0.01. Therefore, the deficiency of this vitamin is common in both Asia and Europe.[7,12] In addition, during the late trimester period, it causes problems for them and their babies, such as preterm birth, pre-eclampsia, gestational diabetes, and babies born small according to their gestational age. This causes the risk of infection and respiratory problems when the baby is born.[5] The fetus is very dependent on fulfilling its nutritional needs in the mother, which will lead to premature birth, LBW and other problems after birth such as respiratory problems that will affect their childhood.[13]

The limitation of this study is only to provide vitamin D3 supplementation at a dose of 400 IU for 3 months to increase levels of 25(OH)D by looking at vitamin D intake during treatment. Further research is needed to include exposure to sunlight in order to obtain an increase in levels 25(OH)D.

CONCLUSION

Vitamin D3 supplementation at a dose of 400 IU/day can increase the 25(OH)D levels in II and III TM pregnant women in Sleman, Indonesia.

ACKNOWLEDGEMENTS

We are grateful to the Midwifery, staff laboratory and respondent at the Puskesmas Sleman, Yogyakarta and laboratory at GAKI Faculty of Medicine, Diponegoro University, Semarang, Indonesia.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee of the Faculty of Medicine, Gadjah Mada University with the number KE/FK/0328/EC/2020

REFERENCES

1. Singh G, Singh G, Brar H, Malik S. Vitamin D levels in preterm and term neonates at birth. Int J Contemp Pediatr. 2017;4(1):48-52.
2. Aji AS, Erwinda E, Yusrawati Y, Malik SG, Lipoeto NI. Vitamin D deficiency status and its related risk factors during early pregnancy: a cross-sectional study of pregnant Minangkabau women, Indonesia. BMC Pregnanc Childbirth. 2019;19(1):1-10.
3. WHO. Guideline: Vitamin D supplementation in pregnant women. Geneva, World Health Organization, 2012. 2012;1-32.
4. Olmos-Ortiz A, Avila E, Durand-Carbajal M, Díaz L. Regulation of calcitriol biosynthesis and activity: Focus on gestational vitamin D deficiency and adverse pregnancy outcomes. Nutrients. 2015;7(1):443-80.
5. Singh D, Hariharan D, Bhaumik D. Role of vitamin D in reducing the risk of preterm labour. Int J Reprod Contracept Obstet Gynecol. 2015;4(1):1.
6. Nurbazlin M, Chee WSS, Rokiah P, Tan ATB, Chew YY, Nusaibah ARS, et al. Effects of sun exposure on 25(OH) vitamin D concentration in urban and rural women in Malaysia. Asia Pac J Clin Nutr. 2013;22(3):391-9.
7. Woon FC, Chin YS, Ismail IH, Batterham M, Latiff AHA, Gan WY, et al. Vitamin D deficiency during pregnancy and its associated factors among third trimester Malaysian pregnant women. PLoS One. 2019;14(6):1-12.
8. Pratumvinit B, Wongkrajang P, Wataganara T, Hanyongyuth S, Nimmannit A, Chatsiricharoenkul S, et al. Maternal vitamin d status and its related factors in pregnant women in Bangkok, Thailand. PLoS One. 2015;10(7):1-14.
9. Judistiani RTD, Nirmala SA, Rahmawati M, Ghrahani R, Natalia YA, Sugianli AK, et al.

Optimizing ultraviolet B radiation exposure to prevent vitamin D deficiency among pregnant women in the tropical zone: Report from cohort study on vitamin D status and its impact during pregnancy in Indonesia. BMC Pregnanc Childbirth. 2019;19(1):1-9.
10. Aji AS, Yerizel E, Desmawati, Lipoeto NI. The association between lifestyle and maternal vitamin D during pregnancy in West Sumatra, Indonesia. Asia Pac J Clin Nutr. 2018;27(6):1286-93.
11. Sabet Z, Ghazi AA, Tohidi M, Oladi B. Vitamin D supplementation in pregnant Iranian women: Effects on maternal and neonatal Vitamin D and parathyroid hormone status. Acta Endocrinologica. 2012;8(1):59-66.
12. Al-Musharaf S, Fouda MA, Turkestani IZ, Al-Ajlan A, Sabico S, Alnaami AM, et al. Vitamin D deficiency prevalence and predictors in early pregnancy among Arab women. Nutrients. 2018;10(4):1-12.
13. WHO. Recommendations on interventions to improve preterm birth outcomes. Geneva: World Health Organization; 2015:1-10.

Cite this article as: Susilani AT, Subagio HW, Pramono N, Kartasurya MI. The effect of vitamin D3 supplements on the 25(OH)D levels in the II and III trimester of pregnant women in Sleman, Indonesia: randomized controlled trial. Int J Res Med Sci 2021;9:22-6.

The effect of vitamin D3 supplements on the 25(OH)D levels in the II and III trimester of pregnant women in Sleman, Indonesia randomized controlled trial

ORIGINALITY REPORT

17%	12%	13%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	"European Congress on Osteoporosis & Osteoarthritis (IOF-ECCEO12)", Osteoporosis International, 2012 Publication	2%
2	www.aimdrjournal.com Internet Source	2%
3	"Abstracts", Transplant International, 2021 Publication	1%
4	www.sarahstogryn.com Internet Source	1%
5	www.orthopaper.com Internet Source	1%
6	ijcc.chemoprev.org Internet Source	1%
7	e-journal.unair.ac.id Internet Source	1%

8	Submitted to Fakultas Ekonomi dan Bisnis Universitas Gadjah Mada Student Paper	1 %
9	Masaaki Inaba, Kazuhiko Yukioka, Yutaka Furumitsu, Mayuko Murano, Hitoshi Goto, Yoshiki Nishizawa, Hirotoshi Morii. "Positive correlation between levels of IL-1 or IL-2 and 1,25(OH)2D/25-OH-D ratio in synovial fluid of patients with rheumatoid arthritis", Life Sciences, 1997 Publication	1 %
10	Submitted to South Bank University Student Paper	<1 %
11	apps.who.int Internet Source	<1 %
12	xb.njucm.edu.cn Internet Source	<1 %
13	Www.japsonline.com Internet Source	<1 %
14	Natasja van Schoor, Paul Lips. "Global Overview of Vitamin D Status", Endocrinology and Metabolism Clinics of North America, 2017 Publication	<1 %
15	ajslp.pubs.asha.org Internet Source	<1 %

16	www.danonenutrindo.org Internet Source	<1 %
17	www.ncbi.nlm.nih.gov Internet Source	<1 %
18	bmcpublichealth.biomedcentral.com Internet Source	<1 %
19	journals.lww.com Internet Source	<1 %
20	puipk.poltekkesbengkulu.ac.id Internet Source	<1 %
21	www.indianpediatrics.net Internet Source	<1 %
22	www.scielo.br Internet Source	<1 %
23	Economos, C.D.. "Vitamin D deficiency is common in young children in Boston: Vitamin D3 in orange juice was an effective treatment", Bone, 200706 Publication	<1 %
24	Harpreet Kaur, Sushmita Sharma, Minni Verma. "Vitamin D Deficiency in Pregnancy and Its Effect on Maternal and Perinatal Outcome", International Journal of Infertility & Fetal Medicine, 2021 Publication	<1 %

25 Marianne S. Aloupis. "Influence of Neurological Medication on Nutritional Status", Handbook of Drug-Nutrient Interactions, 2009 <1%
Publication

26 Z. Mohaghegh, P. Abedi, T. Dilgouni, F. Namvar, S. Ruzafza. "The Relation of Preeclampsia and Serum Level of 25-Hydroxyvitamin D in Mothers and Their Neonates: A Case Control Study in Iran", Hormone and Metabolic Research, 2015 <1%
Publication

27 Cimi Ilmiawati, Athica Oviana, Andi Friadi, Mohamad Reza. "Sunlight exposed body surface area is associated with serum 25-hydroxyvitamin D (25(OH)D) level in pregnant Minangkabau women, Indonesia", BMC Nutrition, 2020 <1%
Publication

28 Natércia Neves Marques de Queiroz, Franciane Trindade Cunha de Melo, Fabrício de Souza Resende, Luísa Corrêa Janaú et al. "Vitamin D and PTH: data from a cross-sectional study in an equatorial population", Endocrine Connections, 2020 <1%
Publication

29 Veerabhadrappa, S.T., Anoop Lal Vyas, and Sneh Anand. "Changes in heart rate variability <1%

and pulse wave characteristics during normal pregnancy and postpartum", International Journal of Biomedical Engineering and Technology, 2015.
Publication

Exclude quotes Off
Exclude bibliography On
Exclude matches Off

The effect of vitamin D3 supplements on the 25(OH)D levels in the II and III trimester of pregnant women in Sleman, Indonesia randomized controlled trial

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5