

## Effectiveness of Vitamin D Supplementation in Pregnant Women with Vitamin D Deficiency to Improved Fetal Biometry

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### Abstract

**Objective:** The aim of this study was to determine the effect and effectiveness of vitamin D on fetal biometry.

**Methods:** This study was a Quantitative Study of two quasi-experimental groups. The research was conducted in Rupert District, Bengkalis Regency, Riau Province from June 2022 to August 2022. The research sample was pregnant women with vitamin D deficiency who were divided into an intervention group of 20 subjects and a control group of 20 subjects.

**Result:** Examination of vitamin D levels in pregnant women and examination of fetal biometry was carried out. Then given a 1000 IU vitamin D supplement to pregnant women with vitamin D deficiency levels, re-evaluated after 3 months vitamin D levels in pregnant women and re-measured fetal biometry. There were significant differences in Fetal Biometrics between the pre-Intervention and post-Intervention studies in the intervention group with  $p=0.001$ . The intervention group also showed that there was an increase in the proportion of Normal Biometrics from 8 subjects before the intervention compared to 13 subjects after 3 months of vitamin D supplementation intervention

**Conclusion:** Vitamin D supplementation for 3 months in pregnant women with Vitamin D deficiency is proven to improve fetal health through Fetal Biometry examination.

**Key words:** Biometry, Pregnancy, Vitamin D Deficiency

## Efektivitas Suplemen Vitamin D dalam Meningkatkan Biometri Janin pada Wanita Hamil dengan Defisiensi Vitamin D

### Abstrak

**Tujuan:** Studi ini bertujuan mengetahui dampak dan efektivitas vitamin D terhadap biometri janin.

**Metode:** Studi kuantitatif ini menggunakan dua grup dengan pendekatan kuasi-eksperimental. Penelitian ini dilaksanakan di Rupert, Kabupaten Bengkalis, Provinsi Riau dari Juni 2022 hingga Agustus 2022. Sampel penelitian ini adalah Wanita hamil dengan defisiensi vitamin D yang dibagi menjadi grup intervensi sebanyak 20 orang dan grup kontrol sebanyak 20 orang.

**Hasil:** Dilakukan pengukuran kadar vitamin D pada Wanita hamil dan biometri janin. Pada grup intervensi diberikan suplementasi vitamin D 1000IU dan dievaluasi kembali kadar vitamin D setelah tiga bulan dan dilakukan kembali biometri janin. Terdapat perbedaan signifikan pada biometri janin sebelum dan sesudah intervensi dengan  $p=0.001$ . Grup intervensi juga menunjukkan peningkatan proporsi biometri normal dari 8 orang menjadi 13 orang setelah tiga bulan suplementasi vitamin D

**Kesimpulan:** Suplementasi vitamin D selama tiga bulan pada Wanita hamil dengan defisiensi vitamin D terbukti membantu kesehatan janin melalui pemeriksaan biometri janin.

**Keywords:** Biometri, Defisiensi Vitamin D, Kehamilan

## Introduction

Vitamin D is known to have an important role during pregnancy, especially for fetal growth. Vitamin D is a precursor to the potent steroid hormone calcitriol known as 1,25-dihydroxyvitamin D<sub>3</sub> (1,25(OH)<sub>2</sub>D<sub>3</sub>). Research proves that vitamin D supplementation during pregnancy can reduce the risk of small babies during pregnancy / KMK (small for gestational age) or low birth weight babies.<sup>1-4</sup>

Vitamin D<sub>3</sub> or oral vitamin D is converted to 25(OH)D in the liver and then to a hormonal metabolite, namely 1,25(OH)<sub>2</sub>D (calcitriol) in the kidneys or other organs as needed. During pregnancy, 1,25(OH)<sub>2</sub>D production increases and exceeds clearance rates, twofold higher in women with third trimester pregnancies compared to non-pregnant or postpartum women.<sup>6</sup>

Observational studies and randomized controlled trials of vitamin D supplementation in pregnancy have demonstrated an association between adequate vitamin D levels and a reduced incidence of preeclampsia, gestational diabetes, and primary caesarean section in women who are at term. RCT studies of Vitamin D supplementation have consistently shown success in increasing 25(OH)D levels in pregnant women and neonates even with varying doses of 25(OH)D. <sup>2</sup> Vitamin D deficiency in pregnant women is an important public health problem because it has been hypothesized that Low maternal vitamin D can be associated with reduced fetal growth. <sup>3</sup> Although there have been many recommendations for taking vitamin D supplements during pregnancy, there has not been a guideline for routine vitamin D supplementation in pregnant women.

One of the main objectives of an ultrasound examination in the field of obstetrics is to determine gestational age more precisely, monitor fetal growth and perform early detection of fetal abnormalities in the

antenatal period. In every obstetric ultrasound examination, regardless of the indication, fetal biometry and fetal anatomical structure must be examined carefully and systematically.<sup>6</sup> Based on the description above, researchers are interested in examining the relationship of vitamin D with fetal biometry. The aim of this study was to determine the effect and effectiveness of vitamin D on fetal biometry.

## Methods

This study was a Quantitative Study of two quasi-experimental groups. The research was conducted in Rupert District, Bengkalis Regency, Riau Province from June 2022 to August 2022. The research sample was pregnant women with vitamin D deficiency who were divided into an intervention group of 20 subjects and a control group of 20 subjects. Examination of vitamin D levels in pregnant women and examination of fetal biometry was carried out. Then given a 1000 IU vitamin D supplement to pregnant women with vitamin D deficiency levels, re-evaluated after 3 months vitamin D levels in pregnant women and re-measured fetal biometry. In the control group, strict observation of fetal well-being was carried out by checking antenatal care regularly, to avoid intrauterine growth restriction. The research was conducted after going through an ethical review by the Medical and Health Research Ethics Unit, Faculty of Medicine, University of Riau (123/UN.19.5.1.1.8/UEPKK/2021).

Statistical analysis was performed using SPSS software (Statistical Package for Social Sciences, Chicago, IL, USA). Univariate analysis (numerical data, categorical) is presented in an overview of the characteristics of the research subjects presented in the form of tabulations and descriptions.

## Result

The study was conducted in Rupert District on

pregnant women with vitamin D deficiency who were divided into intervention and control groups. There were 20 mothers who then entered the intervention group and 20 mothers who entered the control group.

A total of 40 pregnant women with Vitamin D deficiency were involved in this study. Table 1 shows that in each study group it was shown that the majority were in the third semester of pregnancy, ethnic Malay, unemployed, were outdoors for less than 1 hour/day, and did not routinely take vitamin D supplementation prior to the study. Then, the test for different proportions of respondents' characteristics between the intervention group and the control group showed  $p > 0.05$ , which means that there was no significant difference in the proportions between the study groups before the research was carried out.

**Table 2 Comparison of Intervention and Control Group Fetal Biometrics**

Group	Pre	Post	*p
<b>Intervention (n=20)</b>			
Normal Biometry	8 (40%)	13 (65%)	0.001
IUGR	12 (60%)	7 (35%)	
<b>Control (n=20)</b>			
Normal Biometry	7 (35%)	8 (40%)	0.785
IUGR	13 (65%)	12 (60%)	
**p	0.865	0.027	

\* Test for difference in pre-post proportions in each study group was carried out by the Wilcoxon test with a significance of  $p < 0.05$   
 \*\*Independent Group Proportion Difference Test was carried out by Chi-Square Test with a significance of  $p < 0.05$

Table 2 shows that there were significant differences in Fetal Biometrics between the pre-Intervention and post-Intervention

**Table 1 Characteristics of Research Subjects**

Characteristic	Intervention Group (n=20)		Control Group (n=20)		*p
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)	
<b>Gestational Ages</b>					
Semester I	5	25%	5	25%	0.456
Semester II	5	25%	6	30%	
Semester III	10	50%	9	45%	
<b>Ethnicity</b>					
Malay	10	50%	15	75%	0.287
Non-Malay	10	50%	5	25%	
<b>Occupational Status</b>					
Unemployed	13	65%	15	75%	0.386
Employed	7	35%	5	25%	
<b>Be Outdoors</b>					
<1 hour/day	13	65%	12	60%	0.467
>1 hour/day	7	35%	8	40%	
<b>Vitamin D Supplementation</b>					
Not Routine	14	70%	15	75%	0.238
Routine	6	30%	5	25%	

\*Independent Group Proportion Difference Test was carried out by Chi-Square Test with a significance of  $p < 0.05$

studies in the intervention group with  $p=0.001$ . The intervention group also showed that there was an increase in the proportion of Normal Biometrics from 8 subjects before the intervention compared to 13 subjects after 3 months of vitamin D supplementation intervention. Meanwhile, the control group showed no significant difference in Fetal Biometrics between pre-Intervention and post-Intervention. with  $p=0.785$ .

## Discussion

There were significant differences in Fetal Biometrics between the pre-Intervention and post-Intervention studies in the intervention group with  $p=0.001$ . The intervention group also showed that there was an increase in the proportion of Normal Biometrics from 8 subjects before the intervention compared to 13 subjects after 3 months of vitamin D supplementation intervention.

Previous studies have indeed shown a strong relationship between maternal serum vitamin D levels and several anthropometric measurements of the fetus using ultrasound examination, namely biparietal diameter and abdominal circumference. In one study, low levels of maternal calcidiol interfered with fetal bone growth which was detected by ultrasound. The meta-analysis conducted by Theodoratou et al and Wei et al stated that there was a significant association between low vitamin D status during pregnancy and the incidence of KMK. Several systematic reviews found a positive association between maternal serum vitamin D and neonatal anthropometric measurements although a recent Cochrane review suggested inconclusive results.

Broadly speaking, the benefits of vitamin D for pregnant women have indeed been described in some literature. Serum 25(OH)D is widely recognized as the best biochemical indicator of vitamin D status because it reflects the cumulative exposure

to sunlight and dietary vitamin D intake of an individual. Identification of circulating 25(OH)D levels is important for the diagnosis and monitoring of vitamin D deficiency. The physiological adaptations of pregnancy alter maternal vitamin D metabolism, thereby affecting fetal availability, which may have a marked effect on vitamin D requirements during pregnancy. Beginning at the end of the first trimester and continuing after delivery, circulating levels of both vitamin D binding protein (DBP) and serum 1,25-dihydroxyvitamin D [1,25(OH)<sub>2</sub>D] increase. DBP levels begin to increase at 8-10 weeks of gestation, before a steady increase in serum 1,25(OH)<sub>2</sub>D, which begins approximately 2 weeks later. The mechanism controlling the increase in circulating DBP in pregnancy is not defined, but estrogen regulation has been suggested. At term, pregnant women have approximately twice the circulating concentration of 1,25(OH)<sub>2</sub>D than nonpregnant women, which is produced by increased renal synthesis of 1,25(OH)<sub>2</sub>D plus production of placental or decidual tissue. 8 During pregnancy, 1,25(OH)<sub>2</sub>D production increases and exceeds clearance rates, twofold higher in women with third trimester pregnancies compared to non-pregnant or postpartum women. Collectively, data indicate that 1,25(OH)<sub>2</sub>D aids implantation and maintenance of normal pregnancy, supports fetal growth through calcium delivery, controls placental hormone secretion, and limits proinflammatory cytokine production.

Randomized controlled trials are available to support the need for and benefit of vitamin D supplementation in pregnancy. While the older studies were relatively smaller, and limited to 3-4 months in duration, more recent data prove the safety and efficacy of 4000 IU of vitamin D, given daily for 6 months of pregnancy. This study by Holles et al. demonstrated a significant reduction in pregnancy complications including primary

caesarean section, hypertensive disorders of pregnancy, and comorbidities of pregnancy. However, no correlation has been found between maternal vitamin D and birth weight. Simultaneously, no adverse effects due to vitamin D were documented in any subject. The study conducted by Holles et al. significant, due to study duration (from 12 weeks of gestation onwards), doses used (400, 2000, and 4000 IU daily), the ethical decision to have a control group supplemented with 400 IU/day large subject size, the need to take new drug approvals under investigation from the US Food and Drug Administration, and the fact that this is the first study to address this question in nearly three decades. Similar results were found by Dawodu et al., who supplemented vitamin D in doses of 2000 and 4000 IU/day, from 12 to 16 weeks of gestation onwards, in antenatal Arab women from vitamin D deficient areas. Thus, the results of the two studies This can be extrapolated to other heliophobia countries that are deficient in vitamin D such as India. However, another study from New Zealand has proven the safety and efficacy of supplementing 2000 IU/day of vitamin D from 27 weeks onwards, and continuing supplementation of 800 IU/day in infants up to 6 months of age.

These studies have not been included in the most recent Cochrane review (2012) of vitamin D supplementation for women during pregnancy. This may be the reason for the Cochrane authors to conclude that there is a requirement for “further rigorous randomized trials” to evaluate this subject.

## Conclusion

Vitamin D is known to have an important role during pregnancy, especially for fetal growth. Vitamin D deficiency in pregnant women is an important public health problem because it has been hypothesized that Low maternal vitamin D can be associated with reduced fetal growth.<sup>3</sup> Although there have been

many recommendations for taking vitamin D supplements during pregnancy, there has not been a guideline for routine vitamin D supplementation in pregnant women. Through this study we conclude that vitamin D supplementation in pregnant women with Vitamin D deficiency for 3 months is proven to improve fetal health through Fetal Biometry examination.

## Conflict of Interest

All authors declare that they have no conflicts of interest.

## Ethical approval

This research has passed the ethical review stage with letter number 123/UN.19.5.1.1.8/UEPKK/2021 issued by the Ethical Clearance Committee of the Faculty of Medicine, University of Riau.

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