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Maternal vitamin D intake and serum 25-hydroxyvitamin D (25(OH)D) levels associated with blood pressure: A cross-sectional study in Padang, West Sumatra

Nur Indrawaty Lipoeto[1*], Arif Sabta Aji[2], Fanny Ayudia[2], Faradila Faradila[2] & Nazla Putri Sukma[3]

[1]Department of Nutrition, Faculty of Medicine, Universitas Andalas, West Sumatra, Indonesia; [2]Department of Biomedical Science, Faculty of Medicine, Universitas Andalas, West Sumatra, Indonesia; [3]Department of Medical Science, Faculty of Medicine, Universitas Andalas, West Sumatra, Indonesia

ABSTRACT

Introduction: The association between vitamin D inadequacy and blood pressure (BP) has been studied in several populations. We examined the association of maternal vitamin D intake and serum 25(OH)D levels and BP among pregnant women in West Sumatra. **Methods:** This study was conducted using a comparative cross-sectional study in a maternal clinic selected by convenience in Padang. Pregnant mothers who attended the clinic in July-August 2015 were recruited. Inclusion criteria were pregnancy between 28-42 weeks, aged 20-35 years, and with less than three parity status. A total of 56 women were recruited and divided equally into either normotension or hypertension groups. Subjects with blood pressure less than 120 mmHg (SBP) and 80 mmHg (DBP) were placed in the normotension group, while subjects with ≥140 mmHg (SBP) and/or ≥90 mmHg) were in the hypertension group. Subjects completed a pre-tested semi-quantitative food frequency questionnaire. Three ml of non-fasting blood was drawn from each subject for determination of 25(OH)D, urea, creatinine, leukocyte, and blood glucose levels. **Results:** There was a significant difference in mean serum 25(OH)D, between the normotension and hypertension groups, at 36.85±21.58 pg/ml and 17.36±7.91 pg/ml, respectively. Only 20% of participants from the hypertension group had adequate vitamin D intake. Blood pressure status had a significant association with vitamin D intake status (p=0.001). **Conclusion:** Maternal vitamin D intake and 25(OH)D levels were associated with blood pressure status in this sample population. Further studies with a larger sample population are suggested to verify the findings of this study.

Keywords: Blood pressure, pregnancy, 25(OH)D, vitamin D intake

INTRODUCTION

One of the most common medical problem encountered during pregnancy is hypertension, which complicates 10% of all pregnancies (Berhan, 2016). Hypertensive disorders of pregnancy (HDP) include chronic hypertension (occurring before 20 weeks gestation, or persisting longer than 12 weeks after delivery), gestational hypertension

*Corresponding author: Nur Indrawaty Lipoeto, MSc, PhD
Department of Nutrition Science, Faculty of Medicine, Universitas Andalas, West Sumatra, Indonesia
Tel: (+62) 751-31746; Fax: (+62) 751-32838; E-mail: indra.liputo@gmail.com

(occurring after 20 weeks gestation), pre-eclampsia (occurring after 20 weeks gestation and either proteinuria or thrombocytopenia), and eclampsia (pre-eclampsia followed seizure) (Leeman *et al.*, 2016). In addition, more than 8% of all pregnancies are related to cardiovascular death as a result of hypertensive disorders during pregnancy (HDP) (Naderi *et al.*, 2017). Hypertension may also increase the risk of adverse maternal and foetal outcomes, such as preterm birth, intrauterine growth restriction (IUGR), perinatal death, acute renal or hepatic failure, antepartum haemorrhage, postpartum haemorrhage, low birth weight and maternal death (Kendrick *et al.*, 2015; Seyom *et al.*, 2015).

The United Nations Children's Fund (UNICEF) has found that women living in developing countries of the world are 300 times more likely to die because of childbirth or pregnancy-related complications than women living in developed countries. Maternal mortality is the global health indicator with the largest disparity between developed and developing countries. Every year, more than half a million women die because of pregnancy or childbirth complications.

The mean maternal mortality ratio (MMR) in Indonesia fell from 385 to 216 deaths per 100,000 live births in 1990-2015. Despite the 44% reduction, this condition is still far from the recommendation of Millennium Development Goal (MDG), which must reach 75%. Sustainable Development Goal (SDG) is targeting maternal deaths to be less than 70 per 100 000 live births in 2030. One of the main causes of maternal death is gestational hypertension (Alkema *et al.*, 2016; Statistics Indonesia *et al.*, 2013).

Vitamin D plays a critical role in regulating the Renin-Angiotensin System (RAS) and vascular smooth muscle. Thus, vitamin D has the potential to affect blood pressure (Wong *et al.*, 2010). Ullah *et al.* (2009) reported that vitamin D deficiency could increase the risk of hypertension by as much as 67%. The effect of lifestyle, inadequate maternal vitamin D intake, and lack of exposure to sunlight may lead to low vitamin D status (Ullah *et al.*, 2009). Li *et al.* (2004) had reported that low serum 25(OH)D levels could enhance Renin-Angiotensinogen II production, causing elevated blood pressure.

Low levels of 25(OH)D during the third trimester may lead to increased blood pressure or hypertension. Liu *et al.* (2013) studied low vitamin D status in pregnant mice leading to symptoms of pre-eclampsia that influenced Renin-Angiotensinogen II receptor. This condition affects the flow of blood, causing constrictions that may lead to increased blood pressure during pregnancy (Liu *et al.*, 2013). This study aimed to assess the association between maternal vitamin D intake and 25(OH)D serum levels with blood pressure status in pregnant subjects.

MATERIALS AND METHODS

Study design and subjects

This study was a comparative cross-sectional study with 61 pregnant mothers recruited from a maternal clinic selected by convenience in Padang, Indonesia. Pregnant mothers with a history of diabetes mellitus, kidney disorder, pre-eclampsia, eclampsia, anaemia, multiple pregnancies, and those taking medications that might affect vitamin D metabolism were excluded. This study was conducted from July-August 2015.

The subjects were healthy pregnant mothers with hypertension. The inclusion criteria were pregnant mothers within 28-42 weeks of gestation, aged 20-35 years, and with less than three parity statuses. All subjects were informed of the purpose of the study

and requested to participate after giving written consent; five subjects opted to drop out at this point. The subjects were divided equally into two groups namely, subjects with normotension (*n*=28) and those with hypertension (*n*=28).

Demographic and anthropometry data

Age, parity status, actual maternal body weight at third trimester, and height were recorded when the pregnant mothers attended antenatal care (ANC) in the selected maternal clinic. Unfortunately, we were not able to get pre-pregnancy body weight data. Body Mass Index (BMI) was presented in kg/m^2.

Dietary assessment

Maternal vitamin D intake was assessed by using a semi-quantitative food frequency questionnaire (SQ-FFQ) that was developed and validated by Lipoeto *et al.* (2004). The SQ-FFQ had been adapted to food habits of *Minangkabau*, an ethnic group inhabiting the Highlands of West Sumatra. The SQ-FFQ consisted of 223 general food items including potential sources of vitamin D in the targeted population.

Energy and nutrient intake were determined using the SQ-FFQ, which provided a snapshot of the dietary intake among the Minangkabau ethnic group residing in Padang. The SQ-FFQ also provided detailed information of the food choices and sources of nutrients consumed by the subjects in the last three months. Potential vitamin D-rich foods in the area were added to the questionnaire. The Bowes & Church's Food Values of Portions and the U.S. Department of Agriculture (USDA) Foods database (Pennington & Spungen, 2010; USDA, 2015) were used to estimate vitamin D content in the foods consumed. Intakes of energy, macronutrients (carbohydrate, protein, fat) and micronutrients were obtained using the Indonesian Food Database and Nutrisurvey (Version 2007, SEAMEO-TROPMED RCCN University of Indonesia, Jakarta, Indonesia).

Subjects with a daily energy intake of <500 kcal or >3500 kcal were excluded from further data analyses of food or nutrient intake because extreme values could interfere with the results (Willett, 1990). Nutrient intake was expressed in actual grams/day for macronutrients, µg/day for maternal vitamin D intake and as a percentage of total energy intakes. Maternal vitamin D intake status was defined as <15 µg/day for inadequate and ≥15 µg/day for adequate.

Vitamin D blood samples

Non-fasting venous blood samples (3ml) were collected from each pregnant mother in the third trimester of pregnancy. The blood samples were centrifuged at 3500 rpm for 10 min at 4^0C (Eppendorf Centrifuge 5810R, Hamburg, Germany). The serums were placed in aliquot vials and stored at -20^0C to 70^0C until analysed. Serum samples were protected from light oxidation and thawed once before analysis, which was completed after 6 months of data collection.

The blood samples were centrifuged at Dr M. Djamil Hospital, Padang and brought to Biomedical Laboratory of The Medical Faculty of Andalas University for Enzyme-linked Immunosorbent Assay (ELISA). The 25(OH)D for human reagent was checked by E-EL-0016 DVD/DHVD3 (1,25-Dihydroxyvitamin D3), using ELISA kit (Elabscience Biotechnology Inc., Wuhan, Hubei, China) utilising the Sandwich-ELISA method.

The micro ELISA plate provided in this kit had been pre-coated with an antibody specific to 25(OH)D. The enzyme-substrate reaction was terminated by the addition of a sulphuric acid solution whose colour turned to yellow. The optical density (OD) was measured spectrophotometrically at a wavelength of 450±2 nm. The OD value

is proportional to the concentration of 25(OH)D. The serum 25(OH)D results were expressed in pg/ml. The lower and upper limits of detection were 2.0 and 200.0 pg/ml, respectively. In the third trimester of pregnant mothers, the recommended level for 25(OH)D levels was 60-119 pg/ml (Abbassi-Ghanavati *et al.*, 2009).

Blood pressure measurement

Two measurements of general blood pressure were taken within a 5-minute period with a random zero sphygmomanometer with subjects in a sitting position with their backs supported and their legs uncrossed. Measurements were taken by trained midwives on-site during antenatal care check-up. The definition of hypertension as defined by the American College of Cardiology (ACC) and the American Heart Association (AHA), which had released a clinical practice guideline for the prevention, detection, evaluation, and treatment of high blood pressure (BP) in adults (Carey *et al.*, 2018) was used.

This guideline defines hypertension as a systolic blood pressure (SBP) equal to or greater than 140 mmHg or a diastolic blood pressure (DBP) equal to or greater than 90 mmHg. Pregnant mothers with blood pressure less than 120 mmHg (SBP) and 80 mmHg (DBP) were placed in the normotension group, 120-139 mmHg (SBP) or 80-89 mmHg (DBP) were in the prehypertension group, and with either ≥140 mmHg (SBP) and/or ≥90 mmHg) were in the hypertension group.

Statistical analysis

All data analyses were performed by statistical software package SPSS 20 and were expressed by mean (SD), and as frequencies and percentages for categorical variables. The presence of a normal distribution for each variable was tested by the Shapiro Wilk test. The subjects were stratified by hypertension and normotension group, and by maternal vitamin D intake status as defined previously. Comparisons between groups were performed using a chi-square test for categorical variables. Continuous variables were compared between groups by independent samples t-tests for normally distributed variables and the Mann–Whitney U test for non–normally distributed variables. Pearson chi-square, Yates corrected chi-squared, and Fisher's exact tests were performed for categorical variables. The student's t-test was used to compare the differences of mean of 25(OH)D serum levels between blood pressure classification. Finding at $p<0.05$ for a two-sided test was considered statistically significant with 95% Confidence Interval (CI) to see the relationship.

Ethics approval

The Research Ethics Committee of Medical Faculty, Andalas University, West Sumatera, Indonesia approved the study protocol. The letter number is 347/KEP/2014.

RESULTS

A total of 56 pregnant mothers aged 21-35 years participated in this study. The characteristics of the subjects according to blood pressure status are shown in Table 1. The association between maternal characteristics and blood pressure status showed variable results. There was no significant difference between parity status, age groups, and BMI status and blood pressure status.

Out of the 56 subjects, only twenty (35.7%) had adequate vitamin D intake of more than 15 *μg/day*. There was a significant difference in vitamin D intake between normotension and hypertension subjects (Table 2).

Table 1. Characteristics of study participants according to blood pressure status

Characteristics	*N (%)*	*Normotension*		*Hypertension*		*p-value*† *OR (95%CI)*
Age (years)			(%)		(%)	
a. 21-25	15(26.8)	7	(46.7)	8	(53.3)	0.666
b. 26-30	25(44.6)	14	(56.0)	11	(44.0)	
c. 31-35	16 (28.6)	7	(43.8)	9	(56.2)	
Parity status						0.060
a. Nulliparous	31 (55.4)	12	(38.7)	19	(61.3)	0.35 (0.11-1.05)
b. Multiparous	25 (44.6)	16	(64.0)	9	(36.0)	
Vitamin D intake (µg/day)						<0.001*
a. Adequate (≥15)	20 (35.7)	17	(85.0)	3	(15.0)	0.078 (0.019-0.32)
b. Inadequate (<15)	36 (64.3)	11	(30.5)	25	(69.4)	
Height T3 (cm)	56 (100.0)	28	(50.0)	28	(50.0)	0.904
BMI T3, (kg/m^2)						
a. <18	0	0	(0.0)	0	(0.0)	
b. 18-25	17 (30.4)	9	(52.9)	8	(47.1)	0.685
c. 25-30	33 (58.9)	17	(51.5)	16	(48.5)	
d. ≥30	6 (10.7)	2	(33.3)	4	(66.7)	
Urea (mg/dL)	56 (100.0)	28	(50.0)	28	(50.0)	0.818
Creatinine (mg/dL)	56 (100.0)	28	(50.0)	28	(50.0)	0.283
Blood glucose (mg/dL)	56 (100.0)	28	(50.0)	28	(50.0)	0.528
Leucocyte (mm$^{3)}$	56 (100.0)	28	(50.0)	28	(50.0)	0.069

SD=Standard deviation; BMI=Body mass index; T3=Third trimester.
†Categorical variables were expressed as numbers and percentages, and analysed using a chi-square test.
*Significant at p<0.01 level.

The difference in serum 25(OH) D levels between hypertension and normotension pregnant mothers was significant. Table 3 shows that the mean serum 25(OH)D level in normotension pregnant mothers was 6.85±21.58 pg/ml, while that of hypertension pregnant mothers was 17.36± 7.91 pg/ml. The minimum and maximum values of 25(OH)D for all subjects was 5.72 pg/ml and 93.92 pg/ml respectively.

The mean systolic blood pressure of pregnant mothers was 108.29±10.21 mmHg for normotension group, and 152.14±6.23 mmHg for hypertension group. The mean diastolic blood pressure of pregnant mothers was 71.93±5.56 for normotension group and 95.36±2.61 for hypertension group.

The mean maternal vitamin D intake

Table 2. Association of dietary vitamin D intake and blood pressure status

Vitamin D consumption (µg/day)	*Blood pressure*				*Total*		*p-value*†	*OR (95%CI)*
	Hypertension		*Normotension*		*N*	*%*		
	n	*%*	*n*	*%*				
≤15	25	69.4	11	30.6	36	64.3		
>15	3	15.0	17	85.0	20	35.7	0.0001	0.078
Total	28	50.0	28	50.0	56	100.0		

µg=microgram
†Categorical variables were expressed as numbers and percentages, and analysed using a chi-square test. Differences were considered statistically significant at p<0.05 level.

Table 3. Mean of 25(OH)D serum levels, blood pressure, and maternal Vitamin D intake between normotension and hypertension pregnant mothers

Variables	*Normotension*		*Hypertension*		*p-value*
	Mean	*SD*	*Mean*	*SD*	
25(OH)D levels (pg/ml)	36.85	21.58	17.36	7.91	0.0001*
Vitamin D intake (µg)	16.61	9.39	10.22	7.23	0.006*
Blood pressure (mmHg)					
a. Systolic	108.29	10.21	152.14	6.23	0.002*
b. Diastolic	71.93	5.56	95.36	2.61	0.006*

SD=Standard Deviation; Mean of variables were analysed using independent sample *t*-test. Mean differences were considered statistically significant at $p<0.05$ level.
*Independent sample *t*-test significant at $p<0.01$ level.

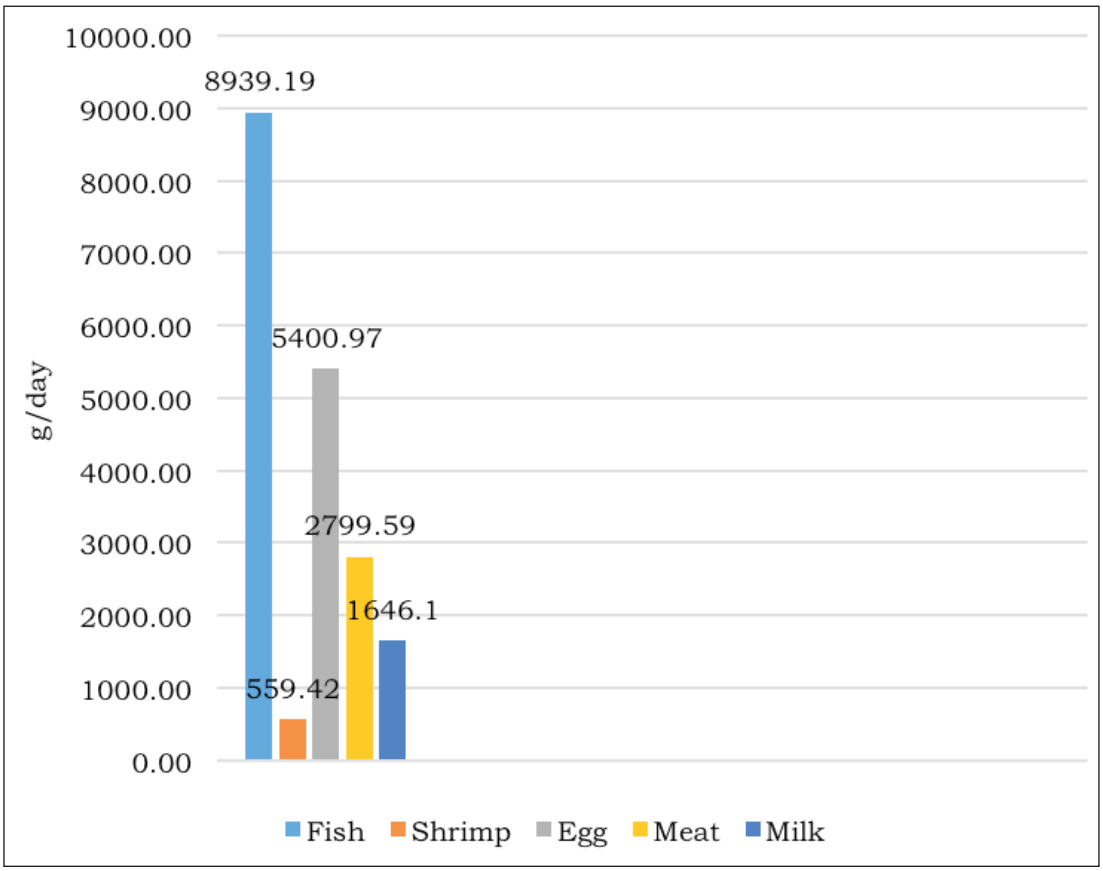

Figure 1. Sources of vitamin D-rich food (gram/day) consumed by pregnant mothers.

of normotension and hypertension was 16.61±9.39 µg/day and 10.22±7.23 µg/day, respectively. The minimum-maximum value of maternal vitamin D intake for all subjects was 4-36 µg/day. Based on the independent sample *t*-test analysis, maternal vitamin D intake was significantly different between normotension and hypertension mothers.

Vitamin D is not found naturally in foods commonly consumed by the subjects, and the highest sources of dietary vitamin D were fish, fortified

foods (mostly from milk and dairy products), and egg and meat (Figure 1).

The mean difference of dietary consumption of vitamin D-rich foods in pregnant mothers with normal blood pressure was 834.93±242.49 g/day, and 385.08±145.14 g/day for high blood pressure. Those with a higher intake of vitamin D-rich foods had lower blood pressure compared to those with lower intake of vitamin D-rich foods during pregnancy. The average intake of vitamin D sources during pregnancy in high blood pressure pregnant mothers was lower than that of normal blood pressure pregnant mothers (p=0.001).

DISCUSSION

Vitamin D deficiency and insufficiency are common throughout the world. Large epidemiological studies showed high prevalence of vitamin D deficiency in women, including antenatal and lactating mothers (Mithal *et al.*, 2009). This study revealed that the average maternal vitamin D intake was 13.42±8.91 µg/day, with the lowest and highest intake at 4 µg/day and 36 µg/day, respectively

There was a significant relationship between maternal vitamin D intake and blood pressure among the third trimester pregnant mothers. A total of 64.3% pregnant mothers in their third trimester consumed less than the recommended amount of vitamin D. Hyppönen *et al.* (2005) reported a relationship between the risk of high blood pressure with vitamin D deficiency. Low maternal vitamin D status may influence the risk of pre-eclampsia because of its effect on transcriptional gene, immune function, and blood pressure. Some experts suggest that 25(OH)D plays a role in the regulation of genes that are responsible for placental invasion and blood vessel formation (Evans *et al.*, 2004). The role of vitamin D in the modulation of immune function may affect immunologic response to the foetus.

In our previous study, we reported that 94.9% of young women aged 20-50 years had low 25(OH)D serum levels (Keumala Sari, 2013). Synthesis of vitamin D during pregnancy is higher than in non-pregnant mothers. Kidney and placenta produce vitamin D, 25(OH) D, by CYP27B1 enzyme activity. The production of 25(OH)D increases two folds in the third trimester of pregnancy. Their body's need for 25(OH)D serum leads to increased absorption of calcium in the intestine (Ma *et al.*, 2012).

During the third trimester, pregnant mothers should increase their vitamin D intake. The need for vitamin D may be greater during pregnancy because of the physiologically higher levels of 25(OH)D seen in the second and third trimester (Hollis and Wagner, 2013). The physiological increase of active metabolite vitamin D during pregnancy, due to elevated intestinal calcium absorption, raises the foetal need of calcium (250 mg/day in the third trimester), and may affect the immunomodulation system and placental development. This evidence again indicates the importance of having sufficient vitamin D intake during pregnancy (Specker, 2012).

Vitamin D supplementation is suggested for women with vitamin D deficiency, dark skin, less sun exposure, usage of long dress and veil daily, vitamin D metabolism disorders, pregnancy and breastfeeding mothers (Mithal & Kalra, 2014). Vitamin D supplementation during pregnancy is suggested at 2000-4000 IU/day for a safe dose (Hollis & Wagner, 2013).

The recent study by Bean e*t al.* (2017) in the U.S. population reported that vitamin D and calcium supplementation showed a positive association with reducing blood pressure. Low levels of vitamin D may impair calcium homeostasis by the renin-angiotensin

system in the kidneys. Systolic blood pressure was negatively and significantly associated with increasing 25(OH) D levels and an interaction between 25(OH)D and calcium intake levels was significantly associated with diastolic blood pressure. The results of this study suggest that the association between 25(OH)D levels and diastolic blood pressure may differ depending on the amount of calcium intake.

This study had several limitations, which include the small sample size, intake of vitamins from supplements and other potential confounding factors that were not assessed. The taking of repeated samples of maternal serum 25(OH)D concentrations during pregnancy should be considered for future studies.

CONCLUSION

Maternal 25(OH)D serum levels and vitamin D intake showed associations with blood pressure levels during the third trimester of pregnancy in this sample of subjects. Further studies with larger samples are suggested to verify these findings.

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Author contributions

Conceiving and conducting the experiments: NIL, NPS, FA. Performing the experiments: NPS, FA. Analyse the data: ASA, FF. Drafting of the manuscript: ASA. Primary responsibility for the final content of manuscript: NIL. All authors reviewed and approved the manuscript.

Conflicts of interest

The authors have no conflict of interest.

References

Abbassi-Ghanavati M, Greer LG & Cunningham FG (2009). Pregnancy and laboratory studies: a reference table for clinicians. *Obstet. Gynecol.* 114: 1326–1331.

Alkema L, Chou D, Hogan D, Zhang S, Moller A-B, Gemmill A, Fat DM, Boerma T, Temmerman M, Mathers C & Say L (2016). Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. *The Lancet* 387: 462–474.

Bean S, Kramer H, Durazo-Arvizu R & Bhattacharya D (2017). Vitamin D, calcium, and blood pressure in the US. Poster presented at the National Kidney Foundation's 2017 Spring Clinical Meetings in Orlando, Florida, April 18-22. Poster 306. From: https://ww3.aievolution.com/nkf1701/index.cfm?do=abs.viewAbs&abs=1048. [Retrieved July 6 2017].

Berhan Y (2016). No Hypertensive Disorder of Pregnancy; No Preeclampsia-eclampsia; No Gestational Hypertension; No Hellp Syndrome. Vascular Disorder of Pregnancy Speaks for All. *Ethiop. J. Health Sci.* 26: 177–186.

Carey RM, Whelton PK & 2017 ACC/AHA Hypertension Guideline Writing Committee (2018). Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Synopsis of the 2017 American College of Cardiology/American Heart Association Hypertension Guideline. *Ann. Intern. Med.* 168: 351–358.

Evans KN, Bulmer JN, Kilby MD & Hewison M (2004). Vitamin D and Placental-Decidual Function. *J. Soc. Gynecol. Investig.* 11: 263–271.

Frølich A, Rudnici M, Storm T, Rasmussen N & Hegedüs L (1992). Impaired 1,25-dihydroxyvitamin D production in pregnancy-induced hypertension. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 47: 25–29.

Hollis BW & Wagner CL (2013). Vitamin D and pregnancy: skeletal effects, nonskeletal effects, and birth outcomes. *Calcif. Tissue Int.* 92: 128–139.

Hyppönen E (2005). Vitamin D for the prevention of preeclampsia? A hypothesis. *Nutr. Rev.* 63: 225–232.

Institute of Medicine (2011). *Dietary Reference Intakes for Calcium and Vitamin D.* The National Academia Press, Washington, DC.

Kendrick J, Sharma S, Holmen J, Palit, S, Nuccio E & Chonchol M (2015). Kidney Disease and Maternal and Fetal Outcomes in Pregnancy. *Am. J. Kidney Dis.* 66: 55–59.

Sari DK, Damanik HA, Lipoeto NI & Lubis Z (2013). Low serum 25(OH)D levels are associated with single nucleotide polymorphisms of the vitamin D receptor gene and lifestyle factors, especially in women with higher body fat percentage. O*bes. Res. Clin. Pract.* 7: 12–13.

Kumar R, Cohen WR, Silva P & Epstein FH (1979). Elevated 1,25-dihydroxyvitamin D plasma levels in normal human pregnancy and lactation. *J. Clin. Invest.* 63: 342–344.

Leeman, Lawrence, Dresang, Lee T, Fontaine & Patricia (2016). Hypertensive Disorders of Pregnancy. *Am. Fam. Physician* 92: 121–127.

Li YC, Kong J, Wei M, Chen Z-F, Liu SQ & Cao L-P (2002). 1,25-Dihydroxyvitamin D(3) is a negative endocrine regulator of the renin-angiotensin system. *J. Clin. Invest.* 110: 229–238.

Li YC, Qiao G, Uskokovic M, Xiang W, Zheng W & Kong J (2004). Vitamin D: a negative endocrine regulator of the renin–angiotensin system and blood pressure. *J. Steroid Biochem. Mol. Biol.* 89–90: 387–392.

Lipoeto NI, Agus Z, Oenzil F, Wahlqvist M & Wattanapenpaiboon N (2004). Dietary intake and the risk of coronary heart disease among the coconut-consuming Minangkabau in West Sumatra, Indonesia. A*sia Pac. J. Clin. Nutr.* 13: 377–384.

Liu NQ, Ouyang Y, Bulut Y, Lagishetty V, Chan SY, Hollis BW, Wagner C, Equils O & Hewison M (2013). Dietary vitamin D restriction in pregnant female mice is associated with maternal hypertension and altered placental and fetal development. *Endocrinology* 154: 2270–2280.

Ma R, Gu Y, Zhao S, Sun J, Groome LJ & Wang Y (2012). Expressions of vitamin D metabolic components VDBP, CYP2R1, CYP27B1, CYP24A1, and VDR in placentas from normal and preeclamptic pregnancies. *Am. J. Physiol. - Endocrinol. Metab.* 303: E928–E935.

Ministry of Health Republic of Indonesia (2013). Dietary Intake Reference in Indonesia. Ministry of Health Republic of Indonesia, Jakarta.

Mithal A & Kalra S (2014). Vitamin D supplementation in pregnancy. *Indian J. Endocrinol. Metab.* 18: 593–596.

Mithal A, Wahl DA, Bonjour J-P, Burckhardt P, Dawson-Hughes B, Eisman JA, El-Hajj Fuleihan G, Josse RG, Lips P & Morales-Torres J (2009). Global vitamin D status and determinants of hypovitaminosis D. *Osteoporos. Int. J. Establ. Result Coop. Eur. Found. Osteoporos. Natl. Osteoporos. Found. USA* 20: 1807–1820.

Naderi S, Tsai SA & Khandelwal A (2017). Hypertensive Disorders of Pregnancy. *Curr. Atheroscler. Rep.* 19: 15.

Pennington JA & Spungen JS (2010). Bowes & Church's Food Values of Portions Commonly Used. Philadelphia: Lippincott Williams & Wilkins.

Seyom E, Abera M, Tesfaye M & Fentahun N (2015). Maternal and fetal outcome of pregnancy related hypertension in Mettu Karl Referral Hospital, Ethiopia. *J. Ovarian Res.* 8: 1–7.

Specker BL (2012). Does vitamin D during pregnancy impact offspring growth and bone? *Proc. Nutr. Soc.* 71: 38–45.

Statistics Indonesia, National Population and Family Planning Board, Kementrian Kesehatan & ICF International (2013). *Indonesia Demographic and Health Survey 2012*. Statistics Indonesia, Jakarta.

Ullah MI, Uwaifo GI, Nicholas WC & Koch CA (2009). Does Vitamin D Deficiency Cause Hypertension? Current Evidence from Clinical Studies and Potential Mechanisms. *Int. J. Endocrinol.* 2010(579640): 1-11. doi: 10.1155/2010/579640.

US Department of Agriculture, Agricultural Research Service, Nutrient Data Laboratory (2015). USDA National Nutrient Database for Standard Reference, Release 27 (slightly revised). From: http://www.ars.usda.gov/ba/bhnrc/ndl. [Retrieved July 6 2017].

Viswanath D (2013). Dietary Reference Intakes for Calcium and Vitamin D. *J. Sci. Innov. Res.* 2: 710–715.

Willett W (1990). *Nutritional epidemiology*. Oxford University Press, New York.

Wong MSK, Delansorne R, Man RYK, Svenningsen P & Vanhoutte PM (2010). Chronic treatment with vitamin D lowers arterial blood pressure and reduces endothelium-dependent contractions in the aorta of the spontaneously hypertensive rat. *Am. J. Physiol. Heart Circ. Physiol.* 299: H1226-1234.