

## Serum Vitamin D and Calcium Levels in Preeclampsia

Bushra Iftikhar, Mahwish Shahzad, Mehwish Iftikhar, Mirza Ameer Faizan Ali, Mehwish Rana, Shabbir Hussain

### ABSTRACT

**Objective:** To measure and compare serum vitamin D and calcium levels in primigravida women with preeclampsia (PE) and normotensive primigravida.

**Methodology:** This cross-sectional comparative study was conducted at the Department of Biochemistry, University of Health Sciences after ethical approval. Vitamin D and calcium levels were measured and compared from the venous blood of 45 pregnant females with preeclampsia (group A) and 45 pregnant normotensive females (group B) taken as controls. Vitamin D & calcium levels were measured by enzyme-linked immunosorbent assay (ELISA) and atomic absorption spectrometer, respectively.

**Results:** The mean serum calcium level of the controls was  $9.25 \pm 0.98$  mg/dL and that of preeclamptic females was  $8.92 \pm 0.84$  mg/dL. The difference between the two groups was not statistically significant ( $p$ -value=0.073). The mean serum vitamin D level of normotensive pregnant females was  $19.25 \pm 9.25$  ng/mL whereas it was  $14.88 \pm 6.57$  ng/mL in the preeclamptic pregnant females. The difference in these findings was significant between the two groups ( $p$ -value=0.038). A significant negative correlation between weight and BMI was observed with vitamin D in the preeclamptic group while no such correlation was found in the control group.

**Conclusion:** Preeclampsia is associated with lower levels of vitamin D. The pathophysiology of PE also involves altered metabolism of calcium however, a strong correlation was not found between altered levels of calcium and PE in the present study.

**Keywords:** Preeclampsia. Gestational age. Calcium. Vitamin D. Hypertension.

### INTRODUCTION

Hypertensive disorders of pregnancy are important public health challenges and research efforts are yet to unravel the exact aetiology and pathogenesis of these disorders. Preeclampsia (PE) is a condition that is characterized by increased blood pressure ( $>140/90$  mmHg) measured on two separate occasions at least 6 hours apart and proteinuria ( $>100$  mg/dL) on urine analysis or  $>300$  mg/24 hour urine collection, after 20 weeks of gestation in previously normotensive women.<sup>1,2</sup> The two mechanisms which play a major role in the pathogenesis are insufficient trophoblastic invasion and endothelial dysfunction leading to inappropriate growth of the placenta and reduced placental perfusion. In addition, exaggerated inflammatory and immune responses also contribute to PE.<sup>3</sup>

Vitamin D, also known as calcitriol plays a key role in the pathophysiology of PE. It binds to its nuclear vitamin D receptors, which are present in almost all the tissues of the body including the placenta.<sup>4</sup> Preeclampsia is thought to occur due to an abnormal maternal immune response that prevents a maternal placental invasion. Its deficiency leads to immune dysfunction, placental inflammation, and release of the

placental-derived vasoconstrictive substance causing maternal hypertension and proteinuria.<sup>5</sup> Vitamin D suppresses renin synthesis in the renin-angiotensin system. Therefore, if the vitamin D level would be optimum in the body it will prevent hypertension by preventing the formation of renin and its deficiency can cause preeclampsia. In addition to its effects on the renin-angiotensin system, it also has a direct effect in suppressing the proliferation of vascular smooth muscle cells, improving endothelial cell-dependent vasodilation, and inhibiting anticoagulant activity.<sup>6</sup> In vascular smooth muscle cells, expression of vascular endothelial growth factor is also regulated by vitamin D. Vascular endothelial growth factors are essential for regulating the early changes which occur in the vasculature of placenta; improving angiogenesis of placenta and remodelling of maternal spiral arteries.<sup>7</sup> Calcium plays important role in maintaining blood pressure. How calcium is involved in the pathogenesis of preeclampsia is nowadays receiving growing interest. A link between low serum calcium levels and increased incidence of preeclampsia and supplementation with calcium has been found to prevent PE and its related complications.<sup>8</sup> Several physiological events lead to a decline in maternal serum levels of calcium such as plasma volume expansion, decrease in the level of albumin, increase in glomerular filtration rate, increased calciuria, and transfer of calcium from the maternal system to the growing fetus.<sup>9</sup> The decrease in serum calcium levels causes an increase in parathyroid hormone (PTH) levels which helps to maintain constant serum calcium levels by increasing the absorption from the gastrointestinal

Sharif Medical & Dental College, Sharif Medical City,  
Sharif Medical City Road, Off Raiwind Road, Jati Umra,  
Lahore 54000, Pakistan.

Correspondence: Dr. Bushra Iftikhar  
Assistant Professor Department of Biochemistry  
Azra Naheed Medical College, Lahore  
E-mail: bushra.iftikhar14@gmail.com

Received: October 1, 2022; Accepted: November 15, 2022

tract. If calcium supplementation is provided, particularly late in pregnancy, this hyperparathyroidism state may be reduced. The elevation of parathyroid hormone causes an increase in free intracellular ionized calcium, which results in vasoconstriction and increased vascular resistance causing high blood pressure.<sup>10</sup>

The association between the pathophysiology of PE and calcium is still controversial and further studies are required to establish this fact. This study was planned to measure vitamin D and calcium in preeclampsia and normotensive women during 30-34 weeks of pregnancy and see whether these parameters give some insight into the role of these metabolites in PE.

### METHODOLOGY

This was a cross-sectional comparative study conducted at the Department of Biochemistry, University of Health Sciences, Lahore. After approval from the ethical review board and Advanced Studies & Research Board of the University. Subjects were recruited from the Department of Gynecological, Government Kot Khawaja Saeed Teaching Hospital, Lahore. The study was conducted from July 2018 to July 2019.

Informed consent was taken and all the data information was recorded on a subject datasheet. Ninety subjects were included in this study and were divided into two groups. Group A included 45 preeclamptic patients and 45 normotensive pregnant females were included in group B. The two groups were matched in maternal age, gestational age, and socioeconomic status. Inclusion criteria for group A were gestational age between 30-34 weeks, primigravida females with a single pregnancy, blood pressure >140/90 mmHg, and proteinuria of >300 mg/24 hours on urine sample analysis after 20 weeks of pregnancy. Inclusion criteria for group B were pregnant females of gestational age between 30-34 weeks, primigravida females with a single pregnancy, and normotensive. Exclusion criteria for both groups were multiple pregnancies, females taking vitamin D and calcium supplements, diabetes, renal disease, infections, obesity, and family history of hypertension. Blood samples were taken by a convenient sampling technique. Blood pressure was recorded by a digital sphygmomanometer device. Serum vitamin D level was determined by competitive enzyme-linked immunosorbent assay by using 25-OH vitamin D3 human ELISA kit (ORGENTEC Diagnostika GmbH, Germany). Normal serum vitamin D level was taken as 20-40 ng/mL. Serum calcium levels were measured by colourimetric method using a spectrophotometer (Hitachi Z2000) and its normal value was considered as 8.5-10.2 mg/dL.

### STATISTICAL ANALYSIS

The data was analyzed by using Statistical Package for the Social Sciences version 22.0. Mean & standard deviation (SD) was calculated for normally distributed quantitative variables and median and interquartile range (IQR) were given for non-normally distributed quantitative variables. Student t-test was used to compare means in both groups for normally distributed quantitative variables. Mann-Whitney U test was used to compare non-normally quantitative variables between study groups. Pearson's correlation (r) was used to see a correlation between normally distributed quantitative variables and Spearman's rho correlation (rho) was used to find a correlation between non-normally distributed quantitative variables. A p-value of  $\leq 0.05$  was taken as statistically significant.

### RESULTS

In the control group, the mean age was  $22.4 \pm 2.85$  years while it was  $23.5 \pm 3.97$  years for the preeclamptic women. No significant difference was seen in the age of the healthy primigravida females and primigravida preeclamptic patients (p-value=0.148). The median (IQR) gestational age of normotensive pregnant females was 32(31-33) weeks while the median (IQR) gestational age of preeclamptic females was also 32(30.5-33) weeks. No significant difference was found between the gestational age of both groups (p-value=0.179). The mean BMI of the normal pregnant females was  $27.5 \pm 1.48$  kg/m<sup>2</sup> while the BMI of the preeclamptic patients was  $28.8 \pm 1.42$  kg/m<sup>2</sup>. This difference in values was significant (p-value=0.001). Mean systolic blood pressure in group A & B was  $156.86 \pm 8.27$  mmHg and  $112.8 \pm 10.62$  mmHg, respectively. Mann-Whitney U test was used to compare the results of the two groups and a significant difference was seen (p-value=0.001). The mean value of diastolic blood pressure of the controls was  $74.0 \pm 10.27$  mmHg while it was  $106.9 \pm 11.66$  mmHg for the females with preeclampsia. The mean serum calcium level of the controls was  $9.25 \pm 0.98$  mg/dL and that of preeclamptic females was  $8.92 \pm 0.84$  mg/dL. No statistically significant difference was found between the two groups (p-value=0.073). The mean serum vitamin D level of normotensive pregnant females was  $19.25 \pm 9.25$  ng/mL whereas it was  $14.88 \pm 6.57$  ng/mL for the preeclamptic pregnant females. The difference in these findings was significant between the two groups (p-value=0.038) (Table 1).

A positive correlation between systolic and diastolic blood pressure was seen in the control group and the patient group. The correlation between weight, height, and BMI was also positive in both groups. A significant positive correlation between vitamin D with calcium was seen in the control group (Table 2).

The Spearman's rho correlation for this association was 0.408 and the p-value was 0.005. A significant positive correlation between vitamin D with calcium was also found in the preeclamptic group (Spearman's

rho=0.368; p-value=0.013). A negative correlation between weight and BMI was observed with vitamin D in the preeclamptic group. However, no such correlation was found in the control group.

**Table 1: Comparison of Parameters in the Preeclamptic and Control Groups**

Parameters	Group A (Preeclamptic Patients)		Group B (Control)		p-value
	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	
Age (Years)	23.5±3.97	23(20.5-26)	22.4±2.85	22(20-25)	0.148 <sup>a</sup>
Gestational Age (Weeks)	31.68±1.32	32(30.5-33)	32±1.44	32(31-33)	0.179 <sup>a</sup>
Systolic Blood Pressure (mmHg)	156.8±8.27	156(150-164)	112.8±10.62	112(102-123)	0.001* <sup>a</sup>
Diastolic Blood Pressure (mmHg)	106.9±11.6	106(96-118)	74±10.27	72(65-83)	0.001* <sup>a</sup>
BMI (kg/m <sup>2</sup> )	28.8±1.42	28.76(27.7-29.76)	27.5±1.48	27.6(26.45-28.1)	0.001* <sup>β</sup>
Vitamin D (ng/mL)	14.88±6.57	13.29(10.63-16.5)	19.25±9.25	17.25(11.09-24.8)	0.038* <sup>a</sup>
Calcium (mg/dL)	8.92±0.84	8.6(8.4-9.5)	9.25±0.98	8.9(8.5-10.25)	0.073* <sup>a</sup>

<sup>a</sup>p-value calculated by Mann-Whitney U Test

<sup>β</sup>p-value calculated by Independent Sample t-test

\*Significant p-value ≤0.05

**Table 2: Correlation Matrix of Clinical and Biochemical Variables of Study Groups**

Correlation Matrix of Clinical and Biochemical Variables of Preeclamptic Patients						
Parameters	Correlation	Systolic Blood Pressure	Weight	BMI	Vitamin D	Calcium
Diastolic Blood Pressure	r/rho	0.801 <sup>β</sup>				
	p-value	0.001*				
Height	r/rho	-0.070 <sup>β</sup>	0.773 <sup>β</sup>			
	p-value	0.649	0.001*			
BMI	r/rho	-0.193 <sup>β</sup>	0.704 <sup>a</sup>			
	p-value	0.205	0.001*			
Vitamin D	r/rho	-0.036 <sup>β</sup>	-0.343 <sup>β</sup>	-0.319 <sup>β</sup>		
	p-value	0.814	0.021	0.033*		
Calcium	r/rho	0.055 <sup>a</sup>	0.056 <sup>β</sup>	0.196 <sup>β</sup>	0.368 <sup>β</sup>	
	p-value	0.719	0.713	0.202	0.013*	
Correlation Matrix of Clinical and Biochemical Variables of Healthy Controls						
Diastolic Blood Pressure	r/rho	0.570 <sup>β</sup>				
	p-value	0.001*				
Height	r/rho	-0.267 <sup>β</sup>	0.651 <sup>β</sup>			
	p-value	0.077	0.001*			
BMI	r/rho	-0.101 <sup>β</sup>	0.557 <sup>a</sup>			
	p-value	0.507	0.001*			
Calcium	r/rho	-0.192 <sup>β</sup>	0.040 <sup>β</sup>	0.140 <sup>β</sup>	0.408 <sup>β</sup>	
	p-value	0.207	0.794	0.359	0.005*	

<sup>a</sup>Correlation coefficient (r) & p-values are calculated by Pearson's Correlation coefficient

<sup>β</sup>Correlation coefficient (rho) & p-values are calculated by Spearman's Rho Correlation coefficient

\*Significant p-value ≤0.05

## DISCUSSION

Establishing an exact relationship between vitamin D, calcium, and preeclampsia is complicated. We found a remarkable difference in the level of vitamin D between the control and patient groups. Although vitamin D in both groups had deficiency but it was more severe in the preeclamptic group and this difference in the serum vitamin D levels among the two groups was statistically significant ( $p=0.046$ ). Similarly, many studies have supported the hypothesis on the role of vitamin D in the aetiology of preeclampsia.<sup>11-14</sup>

For an adequate synthesis of vitamin D (3000 IU), a minimum exposure of at least 10 minutes to direct sunlight in the wavelength between 290-315 nm is required. One of the reasons for vitamin D deficiency in both the pregnant female groups included in this study was maybe due to the reason that most of the Pakistani females cover their whole body to observe purdah while going outside and many of the females wear burqa (a black colored garment worn by Muslim females). It has been documented that clothing preference affects vitamin D synthesis by decreasing the absorbance of ultraviolet (UV) rays by the skin.<sup>15</sup>

Another observation in this study was that most of the females in the preeclamptic group were housewives and spent most of their time indoors, thus they had minimum sun exposure during the times when the sun is the brightest accounting for more severe vitamin D deficiency in preeclamptic group. The finding is in contrast with the findings of some other studies which did not report any association between vitamin D deficiency and preeclampsia.<sup>16</sup> There are several possible explanations for the inconsistent and equivocal findings about the association of vitamin D & preeclampsia. It can be related to the differences in lifestyle, differences in dietary intake of vitamin D, skin color, genetic differences in the metabolism of vitamin D, duration of exposure to sunlight, climate changes, and method of measurement of vitamin D.

We found out that the PE women were heavier ( $p=0.018$ ) and had higher ( $p < 0.001$ ) BMI than the women with a healthy pregnancy. Also, a negative correlation between vitamin D was observed with weight and BMI in the preeclamptic group of this study (Spearman's  $\rho = -0.319$ ,  $p=0.033$ ). This finding is similar to the study of Delle Monache et al., who reported that an increase in BMI (obesity) can proportionally reduce the vitamin D level in women regardless of their ages.<sup>17</sup> It is hypothesized that the metabolic clearance of vitamin D might increase in obesity possibly due to the increased sequestration of vitamin D in adipocytes and consequently alteration of its release into the circulation. Another explanation for the correlation between an increase in BMI and low vitamin D levels can be that overweight patients usually have a sedentary lifestyle and spend more time indoors.

This also deprives them of vitamin D since UV rays are essential for its synthesis.<sup>18</sup>

Calcium is an important bivalent ion which not only maintains good bone health but also acts as a cofactor for many enzymes. The maternal serum calcium levels directly affect the fetal serum calcium levels. Calcium is very essential for the development of fetal bones, muscles, and nerves. As a result of the increasing demand for calcium in the mother and fetus during pregnancy, calcium deficiency is a commonly encountered issue, especially in developing countries. It also maintains the smooth muscle vascular tone hence, it is involved in the regulation of blood pressure.<sup>19</sup>

Our results showed that the mean serum calcium levels in the preeclamptic females ( $8.92 \pm 0.84$  mg/dL) were lower as compared to controls ( $9.25 \pm 0.98$  mg/dL). The difference between the two groups was not statistically significant ( $p$ -value= $0.073$ ). This is in agreement with the findings of other studies which observed no significant difference in the serum calcium levels between preeclamptic and normotensive pregnant females.<sup>20,21</sup> The finding of the present study and the previous studies can be explained by the fact that these studies reported decreased serum vitamin D levels with the consequent increase in parathyroid hormone levels. This rise in PTH levels tries to maintain the serum calcium levels within the normal range by increasing its reabsorption from the intestines and the kidney tubules.<sup>22</sup>

On contrary, Winarno et al., & Al-Jameil et al., have reported a statistically significant decrease in serum calcium levels in PE.<sup>23,24</sup> It is possible that this difference is due to the different methods of assay, sample size, genetics, dietary habits, and lifestyle of the population studied.

## CONCLUSION

Preeclampsia is associated with lower levels of vitamin D. The pathophysiology of PE also involves altered metabolism of calcium however, a strong correlation was not found between altered levels of calcium and PE in the present study.

## LIMITATIONS & RECOMMENDATIONS

The sample size was taken smaller due to the financial constraints, however, further prospective studies with large sample sizes should be conducted to confirm or refute these findings. In addition to vitamin D and calcium, parathyroid hormone levels and bone-related parameters should also be investigated. The current study utilized the ELISA technique for measuring vitamin D levels. Other modern techniques such as high-performance liquid chromatography should also be explored. This study recommends that improvement in nutrition can have a beneficial effect on the overall

health of pregnant females and it can prevent pregnancy-related complications such as preeclampsia.

## REFERENCES

- Duvekot J, Bouter A. 44. Evaluation of the clinical impact of the revised ISSHP and ACOG definitions on preeclampsia and on severe preeclampsia. *Pregnancy Hypertens.* 2018; 13(1):S61. doi:10.1016/j.preghy.2018.08.182.
- Soomro S, Kumar R, Lakhan H, Shaukat F. Risk Factors for preeclampsia and eclampsia disorders in tertiary care center in Sukkur, Pakistan. *Cureus.* 2019; 11(11):e6115. doi:10.7759/cureus.6115.
- Ives CW, Sinkey R, Rajapreyar I, Tita ATN, Oparil S. Preeclampsia-pathophysiology and clinical presentations: JACC state-of-the-art review. *J Am Coll Cardiol.* 2020; 76(14):1690-1702. doi:10.1016/j.jacc.2020.08.014.
- Alvarez-Silvares E, Vilouta-Romero M, Borrajo-Hernandez E, Morales-Serrano ML, Alves-Perez MT. Maternal serum 25-hydroxy vitamin D levels in the first trimester and adverse gestational outcomes. *Ginecol Obstet Mex.* 2016; 84(3):150-63. Available from: <https://pubmed.ncbi.nlm.nih.gov/27424441>.
- Cyprian F, Lefkou E, Varoudi K, Girardi G. Immunomodulatory effects of vitamin D in pregnancy and beyond. *Front Immunol.* 2019; 10:2739. doi:10.3389/fimmu.2019.02739.
- Gernand AD, Simhan HN, Baca KM, Caritis S, Bodnar LM. Vitamin D, pre-eclampsia, and preterm birth among pregnancies at high risk for pre-eclampsia: an analysis of data from a low-dose aspirin trial. *BJOG.* 2017; 124(12):1874-82. doi:10.1111/1471-0528.14372.
- Nema J, Sundrani D, Joshi S. Role of vitamin D in influencing angiogenesis in preeclampsia. *Hypertens Pregnancy.* 2019; 38(4):201-7. doi:10.1080/10641955.2019.1647231.
- Gebreyohannes RD, Abdella A, Ayele W, Eke AC. Association of dietary calcium intake, total and ionized serum calcium levels with preeclampsia in Ethiopia. *BMC Pregnancy Childbirth.* 2021; 21(1):532. doi:10.1186/s12884-021-04005-y.
- Avidime O, Avidime S, Randawa AJ, Kawu MU, Mohammed A, Yama OE, et al. Physiological changes in serum calcium, phosphate, vitamin D, parathyroid hormone and calcitonin during pregnancy and lactation in randomised population of Zaria women. *Niger J Physiol Sci.* 2022; 37(1):77-82. doi:10.54548/njps.v37i1.1.
- Goltzman D, Mannstadt M, Marcocci C. Physiology of the calcium-parathyroid hormone-vitamin D axis. *Front Horm Res.* 2018; 50:1-13. doi:10.1159/000486060.
- Pashapour S, Golmohammadlou S, Behroozi-Lak T, Ghasemnejad-Berenji H, Sadeghpour S, Ghasemnejad-Berenji M. Relationship between low maternal vitamin D status and the risk of severe preeclampsia: a case-control study. *Pregnancy Hypertens.* 2019; 15:161-5. doi:10.1016/j.preghy.2019.01.003.
- Huang XM, Liu YH, Zhang H, Cao Y, Dou WF, Duan DD, et al. Dietary and serum vitamin D and preeclampsia risk in Chinese pregnant women: a matched case-control study. *Br J Nutr.* 2021; 28(1):84-92. doi:10.1017/S0007114521002956.
- Zhao X, Fang R, Yu R, Chen D, Zhao J, Xiao J. Maternal vitamin D status in the late second trimester and the risk of severe preeclampsia in Southeastern China. *Nutrients.* 2017; 9(2):138. doi:10.3390/nu9020138.
- Serrano NC, Guio E, Quintero-Lesmes DC, Becerra-Bayona S, Luna-Gonzalez ML, Herrera VM, et al. Vitamin D deficiency and pre-eclampsia in Colombia: PREVitD study. *Pregnancy Hypertens.* 2018; 14:240-4. doi:10.1016/j.preghy.2018.03.006.
- Al-Yatama FI, AlOtaibi F, Al-Bader MD, Al-Shoumer KA. The effect of clothing on vitamin D status, bone turnover markers, and bone mineral density in young Kuwaiti females. *Int J Endocrinol.* 2019; 2019:6794837. doi:10.1155/2019/6794837.
- Abbasalizadeh S, Abam F, Mirghafourvand M, Abbasalizadeh F, Taghavi S, Hajizadeh K. Comparing levels of vitamin D, calcium and phosphorus in normotensive pregnant women and pregnant women with preeclampsia. *J Obstet Gynaecol.* 2020; 40(8):1069-73. doi:10.1080/01443615.2019.1678575.
- Delle Monache S, Di Fulvio P, Iannetti E, Valerii L, Capone L, Nespoli MG, et al. Body mass index represents a good predictor of vitamin D status in women independently from age. *Clin Nutr.* 2019; 38(2):829-34. doi:10.1016/j.clnu.2018.02.024.
- Ruiz-Ojeda FJ, Anguita-Ruiz A, Leis R, Aguilera CM. Genetic factors and molecular mechanisms of vitamin D and obesity relationship. *Ann Nutr Metab.* 2018; 73(2):89-99. doi:10.1159/000490669.
- Oh C, Keats EC, Bhutta ZA. Vitamin and mineral supplementation during pregnancy on maternal, birth, child health and development outcomes in low- and middle-income countries: a systematic review and meta-analysis. *Nutrients.* 2020; 12(2):491. doi:10.3390/nu12020491.
- Wadhvani N, Dangat K, Randhir K, Poddar A, Joshi P, Pisal H, et al. Longitudinal assessment of calcium and magnesium levels in women with preeclampsia. *Biol Trace Elem Res.* 2022. doi:10.1007/s12011-022-03440-y.
- Owusu Darkwa E, Antwi-Boasiako C, Djagbletey R, Owoo C, Obed S, Sottie D. Serum magnesium and calcium in preeclampsia: a comparative study at the Korle-Bu Teaching Hospital, Ghana. *Integr Blood Press Control.* 2017; 10:9-15. doi:10.2147/IBPC.S129106.
- Hashemipour S, Esmailzadehha N, Ziaee A, Khoeiniha MH, Darvishgoftar E, Mesgari Z, et al. The relationship of vitamin D and calcium level with preeclampsia severity: a case-control study. *Int J Pediatr.* 2017; 5(6):5203-10. Available from: [https://ijp.mums.ac.ir/article\\_8181\\_876583a8655c6e3742ecf e15b73aff47.pdf](https://ijp.mums.ac.ir/article_8181_876583a8655c6e3742ecf e15b73aff47.pdf).
- Winarno GNA, Pribadi A, Maruli HJ, Achmad ED, Anwar R, Mose JC, et al. Ratio of serum calcium to magnesium levels on pregnancy with and without preeclampsia. *Med Sci Monit.* 2021; 27:e932032. doi:10.12659/MSM.932032.
- Al-Jameil N, Tabassum H, Ali MN, Qadeer MA, Khan FA, Al-Rashed M. Correlation between serum trace elements and risk of preeclampsia: a case-controlled study in Riyadh, Saudi Arabia. *Saudi J Biol Sci.* 2017; 24(6):1142-8. doi:10.1016/j.sjbs.2015.02.009.

