



## ASSOCIATION OF LOW VITAMIN D WITH PRE ECLAMPSIA.

Dr Nazia Tufail<sup>1</sup>, Dr Sadia Shafiq<sup>2</sup>, Dr Qudsia Nawaz<sup>3</sup>, Dr Nosheen Bano<sup>4</sup>, Dr Munazzah Bashir<sup>5</sup>, Dr Sumreen Anjum<sup>6</sup>

<sup>1,4</sup> MBBS, FCPS, Assistant Professor Gyne and Obs, Khwaja Muhammad Safdar Medical College, Sialkot.

<sup>2,5</sup> MBBS, FCPS, Assistant Professor Gyne and Obs, M.Islam Medical College, Gujranwala.

<sup>3</sup> MBBS, FCPS, Assistant Professor Gyne and Obs, CMH, Lahore

<sup>6</sup> MBBS, FCPS, Consultant Gyne and Obs, Medix Hospital, Lahore.

Conflicts of Interest: Nil

Corresponding author: Dr Nazia Tufail

DOI: <https://doi.org/10.32553/ijmsdr.v4i12.733>

### Abstract:

**Objective:** To determine the association of preeclampsia and vitamin D deficiency.

**Study design:** Cohort study.

**Place and duration of study:** Gynecology Department, Khwaja Muhammad Safdar Medical College, during 01-07-2018 to 31-12-2018.

**Material and Methods:** In this study the pregnant females irrespective of their gravida and parity status and having gestational age more than 20 weeks were included. The cases that had vitamin D level lower were labelled as cases and those with normal levels as controls. They these cases were followed monthly until delivery and during this period they were followed for protein urea and BP to label pre eclampsia.

**Results:** In this study 100 cases were selected. 50 in each group. Mean age in case and control group was  $29.57 \pm 4.57$  vs  $28.43 \pm 3.79$  years and mean duration of gestation at presentation was  $26.43 \pm 5.11$  vs  $27.42 \pm 5.23$  weeks. There were 39 vs 41 multigravida and 37 vs 38 uneducated females in cases and control group respectively. Preeclampsia was seen in 4 (08%) of control and 14 (28%) cases with odd ration of 4.47 (1.35 to 14.75) with p value 0.01.

**Conclusion:** There is significant association of low vitamin D level and risk of pre eclampsia.

**Key words;** pre eclampsia, vitamin D, Hypertension.

### Introduction

Preeclampsia (PE) is one of the highly morbid and can be fatal entity if converted into eclampsia. Its one of the hypertensive disorders of the pregnancy and seen in the later stages of pregnancy. Its incidence is relatively low; though not that uncommon and is seen in less than 10% of the cases.<sup>1-2</sup>

There are number of factors that can lead to its development and can be both maternal, fetal or mixed. Furthermore, they can also be attributed on the basis of underlying pathophysiology comprising angio-genetic, endothelial dysfunction, syncytio-tropho blastic microparticles (STMP), and inflammatory cells activation that results in wide cascade of interactions and lead to pre eclampsia. Still there are around hundred factors that can predispose to this entity.<sup>3-4</sup>

Dietary factors are one important aspect of the offending factors that can result in hypertensive disorders like pre eclampsia and among them role of vitamin A, C and D have been seen in the past and great emphasis is being given to the latter one. It has shown to impact the angiogenesis and anti inflammatory properties and also inhibition of various factors that can result in better control of the disease, however the mechanism is complex.<sup>5-6</sup>

There is further data regarding the co administration of calcium along with vitamin D and that is even been recommended by World Health Organization (WHO) in the prevention of pre eclampsia.<sup>7-8</sup>

### Objective;

To determine the association of preeclampsia and vitamin D deficiency.

### Patients and methods;

This cohort study was carried out at Department of Gynecology Department, Khwaja Muhammad Safdar Medical College during 01-07-2018 to 31-12-2018. In this study the pregnant females irrespective of their gravida and parity status and having gestational age more than 20 weeks were included. The cases with prior history of pre eclampsia or eclampsia, the known cases of hypertension and those with end organ liver, renal or hepatic failure were excluded from this study. Then two groups were made. Group 1 as cases and group 2 as healthy controls. The vitamin D levels of all the subjects were assessed at 1<sup>st</sup> visit and then these cases that had vitamin D level lower were labelled as cases and those with normal levels as controls. They these cases were followed monthly until delivery and during this period they were followed for protein urea and BP to label pre eclampsia.

### Statistical analysis;

The data was entered and analysed by SPSS-version 23.0. qualitative variables were presented as frequencies and quantitative as mean and standard deviation. Odd ratios were calculated to look for association.

### Results;

In this study 100 cases were selected. 50 in each group. Mean age in case and control group was  $29.57 \pm 4.57$  vs  $28.43 \pm 3.79$  years and mean duration of gestation at presentation was  $26.43 \pm 5.11$  vs  $27.42 \pm 5.23$  weeks. There were 39 vs 41 multigravida and 37 vs 38 uneducated females in cases and control group respectively as in table I. Preeclampsia was seen in 4 (08%) of control and 14 (28%) cases with odd ratio of 4.47 (1.35 to 14.75) with p value 0.01 as in table II.

**Table I: Study variables (n= 50 each)**

Variables	Case	Control
	Mean $\pm$ SD	Range
Age	$29.57 \pm 4.57$	$28.43 \pm 3.79$
Age of gestation	$26.43 \pm 5.11$	$27.42 \pm 5.23$
Variables	Frequency	Frequency
Primigravida	11	9
Multigravida	39	41
Educated	13	12
Uneducated	37	38
Rural	40	37
Urban	10	13
Smoker	4	3
Non smoker	46	47

**Table II: Association of vitamin D deficiency and pre eclampsia**

	Pre eclampsia		Odd ratio (95% CI)	p value
	Yes	No		
Control	4 (8%)	46 (92%)	4.47 (1.35 to 14.75)	0.01
Case	14 (28%)	36 (72%)		

### Discussion;

Pre eclampsia is not uncommon and can be a precursor of a highly morbid and even fatal entity as eclampsia. There are number of maternal and fetal related factors that are addressed and being managed to decrease the risk and still there are many un noticed and work is being done to explore. Dietary deficiencies especially with lower levels of vitamin D is being highly considered for this and for which this study was planned to look its degree of association.<sup>8-9</sup>

Preeclampsia was seen in 4 (08%) of control and 14 (28%) cases with odd ratio of 4.47 (1.35 to 14.75) with p value 0.01. These results were comparable to the findings of the

previous studies. According to a study done by Bondar LM et al they also found that there was significant association of the risk of pre eclampsia and low vitamin D and they further described that the risk is even doubles if there is a 50 nmol/l decrease in its level with odd ratio of 2.5 95% CI 1.1-54.<sup>10</sup>

The data from 2 other studies done by Crikshank DP and Seely EW et al also revealed increased risk of pre eclampsia in cases with low vitamin D with p values  $< 0.05$ .<sup>11-12</sup> In another recent study from Iceland by Olafsdottir AS revealed a U shaped curve to look for risk of pre eclampsia and vitamin D levels.<sup>13</sup>

This was also supported by the data of the two randomized trials where they supported the role of vitamin D in the prevention of preeclampsia. In an uncontrolled trial, supplementation with a multivitamin/mineral supplement and halibut liver oil (containing 900 IU/d vitamin D) provided at 20 wk gestation reduced the odds of preeclampsia by 32% (95% CI, 11–47%).<sup>14-15</sup> Marya *et al* randomized 400 women at 20–24 wk gestation to vitamin D (1200 IU/d) and calcium (375 mg/d) supplements or no treatment and found a significant reduction in blood pressure ( $P < 0.001$ ) and a non significant reduction in the incidence of preeclampsia in the treated group compared with the untreated (6 vs. 9%).<sup>16</sup> In a cohort study, investigators found that regular supplementation with vitamin D in the first year of life halved the risk of preeclampsia in the female offspring's first pregnancy (28). Studies of seasonal patterns in preeclampsia show the lowest incidence in summer, when sunlight is plentiful and serum 25(OH)D concentrations are at their peak, and the highest incidence in winter, when synthesis of vitamin D<sub>3</sub> is limited in temperate zones and serum 25(OH)D levels are at their nadir.<sup>17,18</sup>

### Conclusion;

There is significant association of low vitamin D level and risk of pre eclampsia.

### References;

- Schneuer FJ, Roberts CL, Guilbert C, Simpson JM, Algert CS, Khambalia AZ, Tasevski V, Ashton AW, Morris JM, Nassar N. Effects of maternal serum 25-hydroxyvitamin D concentrations in the first trimester on subsequent pregnancy outcomes in an Australian population. *Am J Clin Nutr.* 2014;99(2):287–295.
- Purswani JM, Gala P, Dwarkanath P, et al. The role of vitamin D in pre-eclampsia: a systemic review. *BMC Pregnancy Childbirth.* 2017;17:231.
- Zhou J, Su L, Liu M, Liu Y, Cao X, Wang Z, Xiao H. Associations between 25-hydroxyvitamin D levels and pregnancy outcomes: a prospective observational study in southern China. *Eur J Clin Nutr.* 2014;68 (8):925–930.
- Gidlof S, Silva AT, Gustafsson S, Lindqvist PG. Vitamin D and the risk of preeclampsia--a nested case-

- control study. *Acta Obstet Gynecol Scand.* 2015;94 (8):904–908.
5. Anderson CM, Ralph JL, Johnson L, Scheett A, Wright ML, Taylor JY, Ohm JE, Uthus E. First trimester vitamin D status and placental epigenomics in preeclampsia among Northern Plains primiparas *Life Sci.* 2015;129:10–15.
  6. Mirzakhani H, Litonjua AA, McElrath TF, O'Connor G, Lee-Parritz A, Iverson R, Macones G, Strunk RC, Bacharier LB, Zeiger R, et al. Early pregnancy vitamin D status and risk of preeclampsia. *J Clin Invest.* 2016;126(12):4702–4715.
  7. Mirzakhani H, Litonjua AA, McElrath TF, O'Connor G, Lee-Parritz A, Iverson R, Macones G, Strunk RC, Bacharier LB, Zeiger R, et al. Early pregnancy vitamin D status and risk of preeclampsia. *J Clin Invest.* 2016;126(12):4702–4715.
  8. March KM, Chen NN, Karakochuk CD, Shand AW, Innis SM, von Dadelszen P, Barr SI, Lyon MR, Whiting SJ, Weiler HA, et al. Maternal vitamin D(3) supplementation at 50 mug/d protects against low serum 25-hydroxyvitamin D in infants at 8 wk of age: a randomized controlled trial of 3 doses of vitamin D beginning in gestation and continued in lactation. *Am J Clin Nutr.* 2015;102(2):402–410.
  9. Eskenazi B, Fenster L, Sidney S. A multivariate analysis of risk factors for preeclampsia. *JAMA* 1991; 266:237–241.
  10. Bodnar LM, Catov JM, Simhan HN, et al. Maternal vitamin D deficiency increased the risk of preeclampsia. *J Clin Endo Metab.* 2007;92: 3517-22.
  11. Cruikshank DP, Chan GM, Doerrfeld D. Alterations in vitamin D and calcium metabolism with magnesium sulfate treatment of preeclampsia. *Am J Obstet Gynecol* 168:1170–1176;discussion 1993;1176–1177.
  12. Seely EW, Wood RJ, Brown EM, Graves SW. Lower serum ionized calcium and abnormal calciotropic hormone levels in preeclampsia. *J Clin Endocrinol Metab* 1992;74:1436–1440.
  13. Olafsdottir AS, Magnusardottir AR, Thorgeirdottir H, Hauksson A, Skuladottir GV, Steingrimsdottir L. Relationship between dietary intake of cod liver oil in early pregnancy and birthweight. *BJOG* 2005;112: 424–429.
  14. Olsen SF, Secher NJ. A possible preventive effect of low-dose fish oil on early delivery and pre-eclampsia: indications from a 50-year-old controlled trial. *Br J Nutr* 1990;64:599–609.
  15. Marya RK, Rathee S, Manrow M. Effect of calcium and vitamin D supplementation on toxemia of pregnancy. *Gynecol Obstet Invest* 1987;24:38–42.
  16. Hypponen E, Hartikainen AL, Sovio U, Jarvelin MR, Pouta A. Jan 31 Does vitamin D supplementation in infancy reduce the risk of pre-eclampsia? *Eur J Clin Nutr* [Epub ahead of print] PMID: 2013;17268418.
  17. Burris HH, Rifas-Shiman SL, Huh SY, Kleinman K, Litonjua AA, Oken E, Rich-Edwards JW, Camargo CA, Jr, Gillman MW. Vitamin D status and hypertensive disorders in pregnancy. *Ann Epidemiol.* 2014;24(5):399–403.
  18. Alvarez-Fernandez I, Prieto B, Rodriguez V, Ruano Y, Escudero AI, Alvarez FV. Role of vitamin D and sFlt-1/PlGF ratio in the development of early- and late-onset preeclampsia. *Clin Chem Lab Med.* 2015;53 (7): 1033–1040.