

## ASSOCIATION OF VITAMIN D DEFICIENCY WITH PRETERM BIRTH

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## ABSTRACT

**Background:** Every year, 15 million neonates worldwide are born preterm. Of these, 1.1 million die as a result of complications of being born too soon and even more suffer from serious prematurity-related complications including learning disabilities. Several studies point to the fact that vitamin D is involved in the regulation of acquired and innate immune responses at the fetal-maternal interface across gestation. Vitamin D reduces the risk of spontaneous preterm birth also by maintaining myometrium quiescence. This study was conducted to determine the role of Vitamin D deficiency with preterm labor in our population. **Objective;** To determine the frequency of vitamin D deficiency in preterm labour. **Setting;** Department of Obstetrics and Gynaecology, Fatima Memorial Hospital Lahore. **Results;** A total of 167 pregnant women were registered mean age of our study cases was  $28.48 \pm 3.58$  years. Mean parity was  $3.95 \pm 1.15$ . Mean gestational age of our study cases was  $30.29 \pm 3.02$  weeks. Majority of our study cases i.e. 105 (62.9%) had poor socioeconomic status, while 62 (37.1%) were from middle class while none of them were from rich class. Mean vitamin D level was  $40.86 \pm 8.51$  ng/dl (with minimum vitamin D level was 22 ng/dl and maximum vitamin D level was 56 ng/dl). Vitamin D deficiency was seen in 27 (16.2%) of our study cases. **Conclusion;** High frequency of Vitamin D deficiency was noted in our study population. Pregnant women should be screened routinely for Vitamin D levels, particularly those with previous history of preterm births to avoid them in subsequent pregnancies. Vitamin D deficiency was significantly associated with poor socioeconomic status, increasing age and gestational age less than 30 weeks.

**KEYWORDS:** Vitamin D deficiency, preterm labor, gestational age.

## INTRODUCTION

Preterm term labour is the leading cause of morbidity and mortality worldwide. Of all early neonatal deaths (deaths within the first 7 days of life) that are not related to congenital malformations, 28% are due to preterm birth.<sup>[1]</sup> Preterm birth rates have been reported to range from 5% to 7% of live births in some developed countries, but are estimated to be substantially higher in developing countries.<sup>[2]</sup> The global prevalence of preterm birth is 9.6%.<sup>[3]</sup> The rate of preterm birth in Pakistan is 15.7% whereas it is 6.6% in Australia.<sup>[4]</sup>

Preterm labour is the spontaneous occurrence of regular uterine contractions leading to cervical changes and initiating the labour after 24<sup>+0</sup> weeks and prior to 36<sup>+6</sup> weeks calculated by LMP. Labour is the process by which regular painful uterine contractions bring about effacement and dilatation of the cervix and descent of the presenting part ultimately leading to expulsion of the fetus and the placenta from mother.

Vitamin D has immunomodulatory and anti-inflammatory effects by regulating the production and function of cytokines and neutrophil degranulation products, that prevents microbial invasion, hence has a protective effect on SPB risk.<sup>[5-7]</sup> Vitamin D is involved in cell-mediated immunity by reducing the production of inflammatory cytokines such as IL-1, 6 and TNF  $\alpha$  that are involved in spontaneous preterm birth.<sup>[5,9-10,14]</sup> Several studies point to the fact that vitamin D is involved in the regulation of acquired and innate immune responses at the fetal-maternal interface across gestation.<sup>[5,11,15]</sup> Vitamin D might reduce the risk of spontaneous preterm birth also by maintaining myometrial quiescence.<sup>[12,13]</sup>

Baker et al conducted a nested case-control study which showed prevalence of first-trimester maternal vitamin D deficiency [25(OH) D < 50 nmol/L] was comparable among women who subsequently delivered preterm compared with controls (7.5% versus 6.7%, p=0.90).<sup>[16]</sup>

Asano S et al at Fujita Health University, Toyoake, Aichi, Japan carried out a study which shows, Mothers with threatened premature delivery had significantly lower 25-OHD levels ( $11.2 \pm 3.2$  ng/ml) than those in mothers with normal delivery ( $15.6 \pm 5.1$  ng/ml).<sup>[17]</sup>

In spite of several randomized controlled trials and meta-analysis, there is lack of evidence that how frequently vitamin D deficiency is associated with preterm labour. The purpose of our study was to evaluate the frequency of vitamin D deficiency in preterm labour in our general population.

## MATERIALS AND METHODS

Patients coming to the Outpatient and Emergency Department of Obstetrics and Gynaecology, Fatima Memorial Hospital Lahore fulfilling the inclusion were enrolled in the study. All pregnant women with singleton pregnancy with gestational age more than 23<sup>+6</sup> weeks and less than 36<sup>+6</sup> weeks calculated from the first day of last menstrual period were included in our study while patients having cervical incompetence in patients having history of 2<sup>nd</sup> trimester miscarriages or cervical cerclage, multiple pregnancy, placental abruption, fetal distress, women with medical disorders like diabetes, hypertension, bleeding disorders and anemia were excluded. Induction was done after evaluating the Vitamin D levels in patients with preterm labour under supervision of consultant gynaecologist having more than 5 years post fellowship experience. Vitamin D levels was confirmed after receiving laboratory reports of vitamin D levels of the patients. Outcome variable i.e. vitamin D deficiency (less than 30 ng/dl) was noted in the proforma along with demography of the patients by the researcher. Data were entered and analysis was done

by using SPSS software. Descriptive statistics was used to calculate mean and standard deviation of age and gestational age of the patients. Frequencies and percentages were calculated for vitamin D deficiency. Effect modifier like age, gestational age and parity were controlled by stratification and effect of these was seen on outcome through Chi-square test. p- Value  $\leq 0.05$  was taken as significant.

## RESULTS

In this study, a total of 167 pregnant women fulfilling inclusion and exclusion criteria of this study were registered from the department of Obstetrics and Gynecology of Fatima Memorial Hospital, Lahore. Mean age of our study cases was  $28.48 \pm 3.58$  years (with minimum age was 22 years and maximum age was 35 years). Our study results have indicated that majority of our study cases i.e. 64.7 % were less than 30 years of age. Mean parity was  $3.95 \pm 1.15$  (with minimum parity was 2 and maximum parity was 6) while our study results have indicated that majority of our study cases i.e. 65.3 % were having parity equal or less than 4. Mean gestational age of our study cases was  $30.29 \pm 3.02$  weeks (with minimum gestational age was 26 weeks while maximum gestational age was 35 weeks). Our study results have indicated that 54.5 % had their gestational age between 23-30 weeks. Majority of our study cases i.e. 105 (62.9%) had poor socioeconomic status, while 62 (37.1%) were from middle class while none of them were from rich class. Mean vitamin D level was  $40.86 \pm 8.51$  ng/dl (with minimum vitamin D level was 22 ng/dl and maximum vitamin D level was 56 ng/dl). Vitamin D deficiency was seen in 27 (16.2%) of our study cases.

**Table 1: Stratification of Vitamin D deficiency with regards to age. (n=167).**

Age groups (In Years)	Vitamin D deficiency		P – value
	Yes (n = 27)	No (n = 140)	
20 – 30 Years (n = 108)	10	98	0.002
More than 30 Years (n = 59)	17	42	
Total	167		

**Table 2: Stratification of Vitamin D deficiency with regards to parity. (n=167).**

Parity	Vitamin D deficiency		P – value
	Yes (n = 27)	No (n = 140)	
Equal or less than 4 (n = 109)	18	91	1.00
More than 4 (n = 58)	09	49	
Total	167		

**Table 3: Stratification of Vitamin D deficiency with regards to gestational age. (n=167).**

Gestational age (In weeks)	Vitamin D deficiency		P – value
	Yes (n = 27)	No (n = 140)	
23 – 30 weeks (n = 91)	26	65	0.000
More than 30 weeks (n = 76)	01	75	
Total	167		

**Table 4: Stratification of Vitamin D deficiency with regards to socioeconomic status. (n=167).**

Socioeconomic status	Vitamin D deficiency		P – value
	Yes (n = 27)	No (n = 140)	
Poor (n =105)	22	83	0.031
Middle income (n = 62)	05	57	
Total	167		

**Table 5: Stratification of Vitamin D level with regards to age. (n=167).**

Age groups (In Years)	Vitamin D level		P – value
	Mean	Standard deviation	
20 – 30 Years (n = 108)	41.79	7.69	0.057
More than 30 Years (n = 59)	39.17	9.68	

## DISCUSSION

In this study, a total of 167 pregnant women fulfilling inclusion and exclusion criteria of this study were registered from the department of Obstetrics and Gynecology of Fatima Memorial Hospital, Lahore. Mean age of our study cases was  $28.48 \pm 3.58$  years (with minimum age was 22 years and maximum age was 35 years). Our study results have indicated that majority of our study cases i.e. 64.7 % were less than 30 years of age. Thorp et al,<sup>[18]</sup> reported mean age  $26.8 \pm 5.5$  years which is close to our study results. Pratumvinit et al<sup>19</sup> reported  $28.9 \pm 6.4$  mean age, which is similar to that of our study results. Similar results have been reported by Bodnar et al.<sup>[20]</sup>

Mean gestational age of our study cases was  $30.29 \pm 3.02$  weeks (with minimum gestational age was 26 weeks while maximum gestational age was 35 weeks). Our study results have indicated that 54.5 % had their gestational age between 23-30 weeks. Similar results have been reported by Thorp et al.<sup>[18]</sup> and Bodnar et al.<sup>[20]</sup>

Poor dietary intake is an important risk factor for vitamin D deficiency and which is associated with socioeconomic status of the family and majority of our study cases i.e. 105 (62.9%) had poor socioeconomic status, while 62 (37.1%) were from middle class while none of them were from rich class. Vitamin D deficiency was significantly more seen in patients with poor socioeconomic status (p=0.031).

Mean vitamin D level was  $40.86 \pm 8.51$  ng/dl (with minimum vitamin D level was 22 ng/dl and maximum vitamin D level was 56 ng/dl). Thorp et al,<sup>[18]</sup> reported

relatively higher mean values of vitamin D levels to be 67 ng/dl. Vitamin D deficiency was seen in 27 (16.2%) of our study cases. Pratumvinit et al,<sup>[19]</sup> reported 34 % vitamin D deficiency with preterm labor from Thailand. Thorp et al,<sup>[26]</sup> reported 22 % vitamin D deficiency associated with preterm labor. Bodnar et al,<sup>[20]</sup> reported 11.3 % vitamin D deficiency in pregnant women undergoing preterm labor, which is close to our study results.

## CONCLUSION

High frequency of Vitamin D deficiency was noted in our study among pregnant women undergoing preterm labour. Pregnant women should be screened routinely for Vitamin D levels, particularly those with previous history of preterm births to avoid these births in subsequent pregnancies. Vitamin D deficiency was significantly associated with poor socio-economic status, increasing age and gestational age less than 30 weeks. More studies are suggested in this field which would analyze the impact of confounding factors as well as socio-demographic distribution on Vitamin D deficiency in our population.

## REFERENCES

1. Lawn JE, Wilczynska-Ketende K, Cousins SN. Estimating the causes of 4 million neonatal deaths in the year 2000. *Int J Epidemiology*, 2006; 35: 706-18.
2. Lawn JE, Cousins SN, Darmstadt GL, Bhutto ZA, Martine's J, Paul V, et al., et al. 1 year after The Lancet Neonatal Survival Series — was the call for action heard? *Lancet*, 2006; 367: 1541-7.

3. Beck S, Wojdyla D, Say L, Betray AP, Merialdi M, Requejo JH, et al.: The world wide incidence of preterm birth: a systematic review on maternal mortality and morbidity. *Bull World Health Organ*, 2010; 88: 31-8.
4. Lawn JE, Gravett MG, Nunes TN, Nunes TM, Robens CE, Stanton C; GAPPS Review Group. Global report on preterm birth and still birth (1 of 7): definitions, description of the burden and opportunities to improve data. *BMC Pregnancy Childbirth*, 2010; 10(Suppl 1): 1471-2393.
5. Liu PT, Stenger S, Li H, Wenzel L, Tan BH, Krutzik SR, et al. Toll-like receptor triggering of a vitamin D mediated human antimicrobial response. *Science*, 2006; 311(5768): 1770-1773.
6. Nizet V, Ohtake T, Lauth X, Trowbridge J, Rudisill J, Dorschner RA, et al. Innate antimicrobial peptide protects the skin from invasive bacterial infection. *Nature*, 2001; 414(6862): 454-457.
7. Chesney RW: Vitamin D and The Magic Mountain: the anti-infectious role of the vitamin. *JPediatr*, 2010; 156(5): 698-703.
8. Muller K, Diamant M, Bendtzen K. Inhibition of production and function of interleukin-6 by 1,25-dihydroxyvitamin D<sub>3</sub>. *Immunol Lett.*, 1991; 28(2): 115-120.
9. Helming L, Bose J, Ehrchen J, Schiebe S, Frahm T, Geffers R, et al. 1 $\alpha$ ,25-Dihydroxyvitamin D<sub>3</sub> is a potent suppressor of interferon gamma-mediated macrophage activation. *Blood*, 2005; 106(13): 4351-4358.
10. Bouillon R, Carmeliet G, Verlinden L, van Etten E, Verstuyf A, Luderer HF, et al. Vitamin D and human health: lessons from vitamin D receptor null mice. *Endocr Rev.*, 2008; 29(6): 726-776.
11. Liu N, Kaplan AT, Low J, Nguyen L, Liu GY, Equils O, et al. Vitamin D induces innate antibacterial responses in human trophoblasts via an intracrine pathway. *BiolReprod*, 2009; 80(3): 398-406.
12. Delorme AC, Danan JL, Acker MG, Ripoche MA, Mathieu H. In rat uterus 17 beta-estradiol stimulates a calcium-binding protein similar to the duodenal vitamin D-dependent calcium-binding protein. *Endocrinology*, 1983; 113(4): 1340-1347.
13. Tribe RM. Regulation of human myometrial contractility during pregnancy and labour: are calcium homeostatic pathways important? *Ext Physiol*, 2001; 86(2): 247-254.
14. Morley R, Carlin JB, Pasco JA, Work JD. Maternal 25-hydroxyvitamin D and parathyroid hormone concentrations and offspring birth size. *J Clin Endocrinol Metab.*, 2006; 91(3): 906-912.
15. Kovacs CS. Vitamin D in pregnancy and lactation: maternal, fetal, and neonatal outcomes from human and animal studies. *Am J Clin Nutr*, 2008; 88(2): 520S-528.
16. Baker AM, Haeri S, Camargo CA Jr, Stuebe AM, Boggess KA. A nested case control study of first-trimester maternal vitamin D status and risk for spontaneous birth. *AM Perinatal*, 2011; 28(9): 667-72.
17. Shibata M, Suzuki A, Skeat, Sekiguchi S, Asano S, Udagawa Y, et al. High prevalence of hypervitaminosis D in pregnant Japanese women with threatened premature delivery. *J Bone Metab*, 2011; 29(5): 615-20.
18. Thorp JM, Camargo CA, McGee PL, Harper M, Klebanoff MA, Sorokin Y, et al. Vitamin D status and recurrent preterm birth: a nested case-control study in high-risk women. *BJOG*, 2012; 119(13): 1617-23.
19. 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 Jul 6; 10(7): e0131126.
20. Bodnar LM, Rouse DJ, Momirova V, Peaceman AM, Sciscione A, Spong CY, et al. Maternal 25-hydroxyvitamin D and preterm birth in twin gestations. *Obstet Gynecol*, 2013; 122(1): 91-8.