**Obstetrics & Gynaecology** 



## THE ASSOCIATION IN SERUM VITAMIN D3 LEVELS IN PATIENTS WITH EARLY PREGNANCY LOSS

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**ABSTRACT** AIM: To find out the association between vitamin D levels in normal pregnancy and pregnancy loss in the first trimester. **METHODOLOGY:** -The present study was a hospital based comparative study conducted in 40 pregnant (7-9 weeks) women having pregnancy loss (Group I) and 40 pregnant (7-9 weeks) women having normal pregnancy coming to department of Obstetrics and Gynaccology, SMS medical college and associated hospitals, Jaipur, Rajasthan. **RESULTS:** The mean Vitamin D3 level in pregnancy loss cases was 17.77±6.56 ng/ml and in normal pregnancy group was 24.85±7.55 ng/ml. So the results showed that the mean Vitamin D3 level was significantly higher in normal pregnancy group compare to early pregnancy loss cases. **CONCLUSION:** Present study concluded that vitamin D has a significant role during pregnancy started from early implantation and decidulization phase till late pregnancy.

## KEYWORDS : Vitamin D

## INTRODUCTION

Miscarriage is defined as the spontaneous loss of pregnancy before the fetus reaches viability. The term therefore includes all pregnancy losses from the time of conception until 24 weeks of gestation.<sup>1</sup>

Spontaneous pregnancy loss is seen in approximately 10-15% of clinically observed pregnancies. When pregnancy loss occurs before completion of 12 weeks gestation, it is defined as early pregnancy loss (spontaneous abortion)<sup>3</sup> and as the majority of spontaneous pregnancy loss happens early (before 12 weeks gestation), a thorough study of the pathophysiology behind this adverse pregnancy outcome is of great importance. Pregnancy loss has an important emotional impact on women and their partners and leads to feelings of guilt, shame, isolation which intensify with each loss.<sup>2</sup>

In pregnancy there is suppression of Th1 and natural killer (NK) cells and change in the Th1 /Th2 balance which prevent pregnancy rejection by suppression of cellular immunity but humoral immunity remains intact.<sup>4</sup>

Vitamin D deficiency is common during pregnancy and has become one of the most important health problems worldwide.<sup>5,6</sup> The vitamin D receptor and 1*a*-hydroxylase (related to vitamin D metabolism) are expressed in reproductive tissues such as the human placenta, endometrium, and ovaries. Therefore, vitamin D seems to be an important hormone that is involved in the modulation of physiological processes associated with reproduction.<sup>7,8</sup>

Vitamin D act as an immune modulator, and help prevent pregnancy loss by facilitating maternal immune tolerance during pregnancy.<sup>9,10</sup>

However, the exact effects of vitamin D on pregnancy outcome remain unclear. Normal pregnancies depend on synchronized immune-endocrine crosstalk at the maternal-fetal interface.<sup>11</sup>

Hence, the aim of this study is to see the correlation of serum vitamin D levels and early pregnancy losses.

## AIM

To find out the association between vitamin D levels in normal pregnancy and pregnancy loss in the first trimester.

# METHODOLOGY

The hospital based comparative study was carried in Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur for a duration extending from June 2019 to August 2020.

## STUDY POPULATION:

Pregnant Women carrying singleton fetus at 7–9-week of gestation by first day of the last menstrual period were included in study population after taking written informed consent and were divided into two groups.

**GROUP 1**(n= 40) - Pregnant women having pregnancy loss at 7-9 weeks of gestation.

**GROUP 2**(n=40) - Pregnant women at 7-9 weeks of gestation having normal pregnancy.

#### **Exclusion Criteria:**

Women diagnosed with thyroid dysfunction, uterine anomalies, autoimmune disorders, medical disorders of pregnancy and multifetal gestation were excluded from the study.

#### **METHODLOGY:**

The approval from institutional ethical committee was taken. After applying inclusion and exclusion criteria the women were divided into two groups. The detail history, general and systemic examination was done for each patient.

Blood samples from women were collected after fasting state of 8 hours in plain labelled vials at 7–9 weeks of gestational age and sent to institutional laboratory for evaluation. Samples were centrifuged for 10 min at 3000 r.p.m. at room temperature. Quantification of serum 25(OH) D was performed using commercial ELISA kits. Reports were collected with name and details mentioned on it.

All information and reports were recorded on a pre designed Performa and were entered in Microsoft excel sheet to prepare master chart.

#### Data Entry And Statistical Analysis:

The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analyzed and statistically evaluated using SPSS-PC-21 version.

Quantitative data was expressed in mean, standard deviation and difference between two comparable groups were tested by student's t-test (unpaired) or Mann Whitney 'U' test. Qualitative data were expressed in percentage. Statistical differences between the proportions were tested by chi square test or Fisher's exact test. 'P' value less than 0.05 was considered statistically significant.

### RESULTS

A total of 80 women were enrolled in the study and divided into two groups. The groups were matched for demographic profile.

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TABLE 1: Demogrphic profile of the study subjects.				
	Group I (n=40)	Group II (n=40)	P value	
	Mean±SD	Mean±SD	]	
Mean age in years	22.08±2.65	21.95±2.35	0.82	
TSH level (µU/ml)	2.37±1.11	2.02±0.87	0.09	
Table 2: Vitamin D level comparison between both groups				
	Group I (n=40)	Group II (n=40)	P value	
	M ICD	M ICD	1	

**Mean±SD Mean±SD** Vitamin D3 (ng/ml) 17.77±6.56 24.85±7.55 < 0.001 Range 7 0-31 0 9.0-36.0

The above table shows the comparison of mean vitamin D between pregnancy loss cases and normal pregnancy cases. The mean Vitamin  $D_3$  level in pregnancy loss cases was 17.77±6.56 ng/ml and in normal pregnancy group was 24.85±7.55 ng/ml. So the results showed that the mean Vitamin D, level was significantly higher in normal pregnancy group compare to early pregnancy loss cases.



Figure 1: Vitamin D level comparison between both groups

#### DISCUSSION

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The relationship of vitamin D on skeletal system and calcium metabolism are well understood. While it's effect on cardiovascular system, immune system and reproductive system are not well improved. There is a relationship between immunity system and vitamin D.12 It was found that T cell, B cell have vitamin D receptor and can produce 1,25, di-hydroxy cholecalciferol the active form of vitamin D.16Vitamin D deficiency lead to high level of natural killer cells and changes the balance of Th1/Th2 during pregnancy and hence, vitamin D could act as an immune regulator during implantation and play an important role in regulation of reproductive function.4

Table 2 shows the comparison of mean vitamin D between pregnancy loss cases and normal pregnancy cases. The mean Vitamin D<sub>3</sub> level in pregnancy loss cases was 17.77±6.56 ng/ml and in normal pregnancy group was 24.85±7.55 ng/ml. So the results showed that the mean Vitamin D<sub>3</sub> level was significantly higher in normal pregnancy group compare to early pregnancy loss cases.

In study by Ashwaq Kadhim Mohammed et al<sup>15</sup>, Assessment of mean maternal serum vitamin D concentration in women with abortions revealed that the mean was 21.48±11.82 (ng/ml) and the range was from 5 to 50 (ng/ml). The number of women with low serum Vitamin D (<20 ng/ml) were 25 (approximately 60%) and highly negative correlation was obtained between number of abortions and maternal serum Vitamin D (r=-0.717, p<0.001).

Zhang H et al14 reported in a meta-analysis that a low vitamin D concentration is not significantly associated with an increased risk of spontaneous pregnancy loss. However, an extremely low vitamin D concentration (<20 ng/mL) was associated with an increased risk of spontaneous pregnancy loss in the first trimester. This meta-analysis also concluded that the maternal vitamin D level might be related to spontaneous pregnancy loss in the first trimester, but not in the second, with a serum vitamin D concentration of less than 20 ng/mL increasing the risk of early spontaneous pregnancy loss by a factor of 2.24. This finding indicates that severe maternal vitamin D deficiency may be a modifiable risk factor in early embryonic development. Therefore, it is essential that maternity and child care institutions highlight the need for vitamin D supplementation in early pregnancy.

In study by Lebriz HA et al<sup>13</sup>, serum vitamin D levels for normal pregnancy group was 47.64 ± 3.2 (95% CI: 44.4-50.8 ng/ml), 27.3 ±

1.2 (95% CI: 26.1-28.5 ng/ml) for the group of early pregnancy loss and  $11.6 \pm 4.2$  (95% CI: 7.9 - 15.6 ng/ml) for the non-gravid women with history of 1 or more first trimester pregnancy loss. There was a strong correlation between vitamin D levels and early pregnancy loss (odds ratio (OR): 1.70, 95% CI: 1.2-2.3, p < 0.001).

In study by Hou W et al<sup>12</sup>, mean vitamin D concentration was  $49.32 \pm$ 11.65 µg/l (95% confidence interval (CI): 44.97-53.67 µg/l) for the normal pregnant group,  $34.49 \pm 15.60 \,\mu g/l \,(95\% \,\text{CI}: 28.66-40.31 \,\mu g/l)$ for the Pregnancy loss group. Anderson LB et al also reported that Concentrations of 25(OH)D, 50 nmol/L were associated with a.2-fold increased adjusted HR for miscarriage (HR: 2.50; 95% CI: 1.10, 5.69). Concentrations of vitamin D were not associated with an increased risk of second-trimester miscarriage.

#### CONCLUSION

Present study concluded that vitamin D has a significant role during pregnancy started from early implantation and decidualization phase till late pregnancy. So, it is advised to use vitamin D as screening in child bearing women in preconception period, and to supplement vitamin D to prevent vitamin D deficiency linked first trimester pregnancy loss in future pregnancy.

#### REFERENCES

- Royal College Obstetricians and Gynaecologists (RCOG). Recurrent Miscarriage, Investigation and Treatment of Couples (Green-top Guideline No. 17). 2011 Available at :https://www.rcog.org.uk/en/guidelines-research-services/ guidelines/gtg17 /#:~:text=Miscarriage %20is% 20defined% 20as%20the,until% 2024%20weeks %20of% 20gestation.
- Bardos J, Hercz D, Friedenthal J, Missmer SA, Williams Z. A national survey on public 2 perceptions of miscarriage. Obstet Gynecol. 2015;125(6):1313 1320. Yinping H. Spontaneous abortion. In: Yue J, editor. Obstetrics and Gynecology. 7th ed.
- 3 Beijing: People's Health Publishing House; 2008. p. 83-6.
- 4. Szekeres-Bartho J. Immunological relationship between the mother and the fetus. Intern Rev immunol. 2002;21(6):471-95. Javaid MK, Crozier SR, Harvey NC, Gale CR, Dennison EM, Boucher BJ et al. Maternal
- 5. vitamin D status during pregnancy and childhood bone mass at age 9 years: A longitudinal study. Lancet. 2006;367:36-43.
- 6 Christesen HT, Falkenberg T, Lamont RF, Jorgensen JS. The impact of vitamin D on pregnancy: A systematic review. Acta Obstet Gynecol Scand. 2012;91:1357–67. Muscogiuri G, Altieri B, de Angelis C, Palomba S, Pivonello R, Colao A et al. Shedding 7.
- new light on female fertility: The role of vitamin D. Rev Endocr Metab Disord. 2017; 18(3):273-283. 8.
- Yayla Abide Ç, Kurek Eken M, Turan I, Özkaya E, Pekin O, Karateke A. Association between maternal circulating 25 hydroxyvitamin D concentration and placental volume in the first trimester. J Matern Fetal Neonatal Med. 2017; 30(24):2944-50. 9.
- Hewison M. Vitamin D and immune function: autocrine, paracrine or endocrine? Scand J Clin Lab Invest Supplementum. 2012;243:92-102. 10 Lagishetty V, Liu NQ, Hewison M. Vitamin D metabolism and innate immunity. Mol Cell Endocrinol. 2011;347:97–105.
- 11. Nair RR, Verma P, Singh K. Immuneendocrine crosstalk during pregnancy. Gen Comp
- Endocrinol. 2016: 242:18-23. Hou W, Yan XT, Bai CM, Zhang XW, Hui LY, Yu XW. Decreased serum vitamin D levels
- in early spontaneous pregnancy loss. Eur J Clin Nutr. 2016 Sep;70(9):1004-8. Lebriz HA, Yeliz A, Oktay O. Is There an Association Between Early Pregnancy Losses
- and Low 25-Hydroxy Vitamin D Levels?. POJ Gyn Obst Res. 2017;1(1):1-5. Zhang H, Huang Z, Xiao L, Jiang X, Chen D, Wei Y. Meta-analysis of the effect of the 14. maternal vitamin D level on the risk of spontaneous pregnancy loss. Int J Gyna Obstet. 2017 Sep;138(3):242-9.
- Kadhim MA, Alqani VHA. Association between maternal serum vitamin d and early pregnancy spontaneous abortion in Iraqi women. Asian J Pharm Clin Res 2018;11(2):432-4.
- 16 Adorini L, Penna G. Control of autoimmune disease by the vitamin D endocrine system. Nat Clin. Pract Rheumatol. 2008;4(8):404-12.

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