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ASSOCIATION OF HYPOVITAMINOSIS D WITH PRE-TERM LABOR IN FEMALES PRESENTING FOR NORMAL DELIVERY IN A TERTIARY CARE HOSPITAL

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Abstract:

Background: *Pre-term delivery is defined as delivery of fetus before completed 37weeks of gestation, according to ultrasonography and last menstrual period. Maternal deficiency of vitamin D, as indicated by low levels of 25-Hydroxyvitamin D [25(OH)D], during pregnancy is considered to be a health problem of unusual significance, across the globe. Increased interest has been developed these days to find out the relationship between low vitamin D status and its outcome on pregnancy.*

Objective: *To measure the association between hypovitaminosis D with pre-term labor in females presenting for normal delivery in a tertiary care hospital.*

Methodology: *Total 630 patients fulfilling the required criteria were taken up for study from labor ward of Lady Atchison Hospital Lahore. Informed consent was obtained & patient's demographic information recorded. Females were decided into two groups; one group for Cases and the other for Controls as mentioned in inclusion criteria. The females undergone delivery. Blood samples were drawn and were delivered to laboratory of the hospital. Reports were assessed for vit D levels. Hypovitaminosis D was labeled.*

Results: *The age(mean) of women undergoing preterm and term delivery was 30.22±5.88 and 29.40±5.74 years. Mean levels of vitamin D in women with preterm and term delivery was 67.01±26.56 and 89.75±34.71. Among women in whom hypovitaminosis was seen 124(72.5%) women had preterm and 47(27.5%) women had term delivery. As per p-value significant association was seen statistically between hypovitaminosis and mode of delivery. Odds ratio 0f 3.70 is showing that women having hypovitaminosis they have a significantly 3.70 times more chances of preterm delivery as compared to that of women who did not have hypovitaminosis.*

Conclusion: *Results obtained by this study show a strong association and high risk for women with hypovitaminosis D to undergo a preterm delivery.*

Keywords: *Hypovitaminosis D, Preterm delivery, Tertiary care hospital.*

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INTRODUCTION:

Vit D has multiple functions that are important both for growth and development.1 25- hydroxyvitamin D [25(OH)D] is the metabolite of vit D and is a best marker used nowadays to study vit D status. Cohorts of pregnant women in the USA were studied and the levels serum 25(OH)D were measured in them, it has been found that women from different ethnic groups living at various latitudes were having a low vitamin D status, regardless of the exact definition used [1]. There is a high prevalence of maternal vit D deficiency occurring during pregnancy and at delivery which have been demonstrated in different ethnic populations living at varying latitudes.1 Low levels of vitamin D , have been described in pregnant women in different countries. Presence of adequate vitamin D in mother's body during pregnancy is not only important for maternal health but also for infant health. During pregnancy a lack of adequate amount of vitamin D, results in poor mineralization of fetal and bones. Poor vit D status has also been linked with an increased risk of lower birth weight, diabetes (type I) and asthma in the baby. There are evidences of increased risk of pre-eclampsia in women undergoing pregnancy having poor status of Vitamin D [2].

Further investigation of the relationships between pre term birth and low levels of 25(OH)D and its sequelae is thus warranted [3] Baker, et al., in 2010; conducted a case control study and found that the hypovitaminosis D prevalence rate among females undergoing preterm labour was 19% which was obviously higher than females undergoing delivery at term (11%, p-value<0.01) [4]. But after that in another study Baker, et al., found that the hypovitaminosis D prevalence rate among females undergoing preterm labour was 7.5% which was slightly higher than females undergoing delivery at term (6.7%), however, the difference was insignificant (p-value=0.90) [5]. Rationale of this study is to measure the association between preterm delivery and hypovitaminosis D in females presenting for normal delivery in a tertiary care hospital. In above mentioned articles, it was noticed that different studies have contradiction. On the basis of above mentioned contradictory evidences, we are unable to say whether hypovitaminosis D may be cause of preterm delivery. With this study we want to assess that whether hypovitaminosis D is a real risk and cause of preterm delivery, so that in future hypovitaminosis D can be diagnosed and cured at initial stages and the preterm birth risk can also be prevented [6].

MATERIALS AND METHODS:

The cause of preterm birth is often not known. Risk factors include diabetes, high blood pressure, being pregnant with more than one baby, being either obese or underweight, a number of vaginal infections, tobacco smoking, and psychological stress, among others. It is recommended that labor not be medically induced before 39 weeks unless required for other medical reasons. The same recommendation applies to cesarean section. Medical reasons for early delivery include preeclampsia. In those at risk, the hormone progesterone, if taken during pregnancy, may prevent preterm birth. Evidence does not support the usefulness of bed rest. It is estimated that at least 75% of preterm infants would survive with appropriate treatment. In women who might deliver between 24 and 34 weeks corticosteroids improve outcomes. A number of medications including nifedipine may delay delivery so that a mother can be moved to where more medical care is available and the corticosteroids have a greater chance to work. Once the baby is born care includes keeping the baby warm through skin to skin contact, supporting breastfeeding, treating infections, and supporting breathing [21].

About 45–50% of preterm births worldwide are estimated to be idiopathic, 30% are related to preterm prelabour rupture of membranes (PPROM) and another 15–20% are ascribed to medically indicated or elective preterm deliveries. Its impact on public health has resulted in broad attention to this topic in scientific research. Preterm birth was recently ranked in the top 10 causes of global burden of disease, justifying its reduction to become a main goal of the global community. Treatment of threatened preterm birth has limited effectiveness; as antenatal administration of corticosteroids is the only intervention proven to improve neonatal outcome. Since prevention seems to be more effective than treatment, the medical world is searching for tools to identify women at risk for spontaneous preterm birth [22].

Study Design: It is a Case control study.
Setting: Unit V, Department of Obstetrics and Gynecology, Lady Aitchison hospital Lahore.
Duration Size: 6 months after synopsis approval.
Sample Size: Sample size of 630 cases; 315 cases in each group is calculated with 80% power of test, 5% level of significance and hypovitaminosis D prevalence is = 19% in preterm and 11% in term delivery in females presenting in a tertiary care hospital.

Sampling Technique: Non Probability, Purposive Sampling.

Sample Selection

Inclusion Criteria: Females of age 20-40 years with

- parity<6
- presenting for delivery with labour pains (>10 pains in 30 minutes)
- cervical opening >3cm.

Cases: Females undergoing preterm delivery (gestational age<37weeks on ultrasound).

Controls: Females undergoing term delivery (gestational age>37weeks on ultrasound).

Exclusion Criteria:

- Multiple pregnancy (on ultrasound)
- Non-cephalic or malpresentation (on Ultrasound)
- Fetus having congenital anomalies (on ultrasound)
- Females with PIH (BP>140/90mmHg), DM (GTT>40mg/dl), preeclampsia (PIH with +1 protein urea on dipstick method) or eclampsia (convulsions).

Methodology

After approval from ethical committee, 630 females fulfilling the above mentioned criteria were taken up for study from labor ward of Lady Aitchison Hospital Lahore. Informed consent was taken and patient related information i.e. name, age, gestational age and contact were recorded. Two groups of females were made, one group of cases and the other of controls, as mentioned in inclusion criteria. Then females undergone delivery. Blood samples were drawn from females and were sent to the laboratory of the hospital. Vitamin D levels were measured. Hypovitaminosis D was labeled. Proforma were filled and the reports were attached to it.

Data Analysis:

Data entry was made and analysed through SPSS 17. Quantitative variable like age and gestational age was calculated by mean standard deviation. Qualitative variable like parity and hypovitaminosis D was presented as frequency and percentage. Odds Ratio was calculated to measure the association of hypovitaminosis D with that of preterm delivery. OR>1 was considered as risk for preterm delivery and was taken as significant.

Results

✓ The mean of the ages of women who had preterm and term delivery was 30.22±5.88 and 29.40±5.74 years. In both cases and controls minimum and maximum age of women was 20 and 40 years. **(Table-1)**

✓ In preterm group the gravidity status of women was as follows: 55(17.5%) women had G-1, 106(33.7%) women with G-2, 69(21.9%) women with G-3, 47(14.9%) women with G-4 and 38(12.1%) women with G-5. In women undergoing term delivery the gravid status is as follows: 63(20%) women had G-1, 110(34.9%) women with G-2, 66(21.0%) women with G-3, 45(14.3%) women with G-4 and 31(9.8%) women with G-5. **(Table-2)**

✓ In preterm group the parity status of women was as follows: Parity-0= 60(19%) women, Parity-1= 110(34.9%) women, Parity-2= 73(23.2%) women, Parity-3= 43(13.7%) women and Parity-4= 29(9.2%) women. While women in term group among them parity status was as follows: Parity-0= 63(20%) women, Parity-1= 120(38.1%) women, Parity-2= 71(22.5%) women, Parity-3= 43(13.7%) women and Parity-4= 18(5.7%) women. **(Table-3)**

✓ In preterm group 36(5.71%) women had abortion and in term group 38(6.03%) women had abortion. **(Figure-1)**

✓ The mean gestational age in women undergoing preterm delivery was 35.40±1.12 weeks and those undergoing term delivery were having 39.02±0.82 weeks as a mean gestational age. In women with preterm delivery the maximum and minimum gestational age was 34 and 37 weeks while in women who had term delivery the minimum and maximum gestational age was 38 and 40 weeks. **(Table-4)**

✓ In women undergoing preterm and term delivery the mean vit D level was 67.01±26.56 and 89.75±34.71. In preterm group women minimum and maximum vit D level was 30 and 120 while in term group it was 30 and 150 respectively. **(Table-5)**

✓ 124(19.68%) women suffered from hypovitaminosis in preterm group and only 47(7.46%) women had hypovitaminosis in term group.**(Figure-2)**

✓ Among Women having hypovitaminosis ,124(72.5%) women had preterm and 47(27.5%) women had term delivery. As per p-value statistically significant association was seen between hypovitaminosis and mode of delivery. Odds ratio 0f 3.70 showed that women who had hypovitaminosis they had significantly 3.70 times more chances of preterm delivery as compared women having normal vit D levels. **(Table-6)**

Table-1: Descriptive statistics of Age of women

	Preterm	Term
N	**315**	**315**
Mean	30.22	29.40
SD	5.881	5.747
Minimum	20	20
Maximum	40	40

Table-2: Gravid status of women

Gravida	Preterm		Term	
1	55	17.5%	63	20.0%
2	106	33.7%	110	34.9%
3	69	21.9%	66	21.0%
4	47	14.9%	45	14.3%
5	38	12.1%	31	9.8%
Total	**315**		**315**	

Table-3: Parity Status of women

Parity	Preterm		Term	
0	60	19.0%	63	20.0%
1	110	34.9%	120	38.1%
2	73	23.2%	71	22.5%
3	43	13.7%	43	13.7%
4	29	9.2%	18	5.7%
Total	**315**		**315**	

Table-4: Gestational age of women

	Preterm	Term
N	**315**	**315**
Mean	35.40	39.02
SD	1.125	.821
Minimum	34	38
Maximum	37	40

Table-5: Vitamin D level in women

	Preterm	Term
N	**315**	**315**
Mean	67.01	89.75
SD	26.562	34.713
Minimum	30	30
Maximum	120	150

Table-6: Association of hypovitaminosis D with preterm delivery

Delivery	Hypovitaminosis D		Total
	Yes	No	
Preterm	124(72.5%)	191(41.6%)	**315**
Term	47(27.5%)	268(58.4%)	**315**
Total	**171**	**459**	**630**

Chi-Square Test= 47.59
p-value= 0.000
Odds Ratio= 3.70 (2.52-5.43)

DISCUSSION:

Low vitamin D levels in maternal blood is commonly seen during pregnancy and is considered an important problem with respect to community's health prospective. Vit D deficiency is highly prevalent and its deficiency has been seen in a significant proportion of women who are undergoing through pregnancy [7],with its prevalence varying by sun exposure and ethnicity [8]. There is an increasing trend nowadays to study relationship between low vit D status and its adverse outcomes during pregnancy [9],including preeclampsia, [10, 11] small-for-gestational age (SGA) [12], gestational diabetes mellitus (GDM) and preterm birth [12, 13].

An interesting area of study that has recently been given significant importance is the role of vit D and its active metabolite, 1,25(OH)2 vit D. Increased inflammatory cytokines production, such as TNF α (tumor necrosis factor-α), has been observed in pregnancies that are complicated by vit D deficiency.

Furthermore, activity of T-regulatory cells is also stimulated by 1,25(OH)2 D , which causes immune tolerance and helps in placental implantation[16]. These data provide evidence of probable role of vit D in the prevention of preterm birth with the help of its anti-inflammatory effects and immunomodulatory effects. In this study it was observed that mean vit D levels were low in women who had preterm delivery as compared to that of women having term delivery. i.e. Preterm delivery (Vitamin D level): 67.01 vs. term delivery (Vitamin D level): 89.75. There were total 171 women who had hypovitaminosis. Among these women 124(72.5%) had preterm delivery and 47(27.5%) women had term delivery. In terms of p-value a statistically significant association was seen between preterm delivery and hypovitaminosis. Odds ratio of 3.70 shows that women who had hypovitaminosis among them risk of preterm delivery is 3.70 times more than that of women having normal vitamin D levels. Shu-Qin Wei in his systematic review and meta analysis reported that the deficiency of vitamin D in maternal's blood may be related with an increased risk of preeclampsia, GDM, preterm birth and SGA. Women having 25-hydroxyvitamin D [25(OH)D] level < 50 nmol/l during pregnancy were kept under consideration and eventually concluded that these women have an increased risk of 1.58 for preterm birth [15]

Odds ratio was high for preterm delivery in women who had hypovitaminosis as compared to that of Shu-Qin Wei in his meta analysis . But this difference may be due to the difference analysis. As in meta analysis pooled analysis was done. Baker,et al., in 2010; conducted a case control study and found that the prevalence of hypovitaminosis D among females undergoing preterm labour was 19% which was significantly higher than females undergoing delivery at term (11%, p-value<0.01). [11] The frequency of hypovitaminosis among women who had preterm delivery was 39.36% as compared to the women who had term delivery. i.e. 14.92%. In this study the frequency of hypovitaminosis was twice the frequency reported by Baker,et al in his study. Arthur M. Baker in 2011; found that the prevalence of vit D deficiency [25(OH)D level less than 50 nmol/L] in expecting mothers during 1st trimester was comparable among women who delivered preterm baby compared with those who have undergone normal delivery. (7.5% versus 6.7%, p-value=0.90) [14]

The results obtained in this study contradicts with results reported by Arthur M. Baker. As Arthur M. Baker showed no significant difference for preterm delivery in women who eventually delivered preterm compared with those who delivered at term. According to JM Thorp, the preterm delivery is not associated with serum 25(OH)D concentration in a much significant way (OR 1.33; 95% CI 0.48–3.70 for lowest versus highest quartiles) [2].

While AW Shand in his study showed that there was no significant difference in the rates of pre-eclampsia, gestational hypertension, preterm birth or other adverse pregnancy outcomes by 25OHD concentration. [18] i.e. Preterm Birth: Serum 25OHD concentration <37.5: 18(31.0%) OR (0.97), Serum 25OHD concentration <50: 33(56.9%) OR(1.02) & Serum 25OHD concentration <75: 46 (79.3) OR(0.79). The results of this study also contradicts with results of JM Thorp and AW Shand. Both these studies showed no impact of hypovitaminosis for preterm delivery. As JM Thorp considered the results obtained from recurrent preterm birth that makes the design of the study done by JM Thorp different from that of this study. But somehow the results can be comparable for hypovitaminosis in relation to preterm birth. There is multiple etiological factors responsible for spontaneous preterm birth. Responsible factors are over-distention of uterus, abnormality in fetal endocrine system, and uterine infection and inflammation [19].

Vitamin D through its effects on inflammatory response and immunomodulation deficiency can alter spontaneous risk of preterm birth. There is increase in the production process of cytokines responsible for inflammation in women having low Vit D levels. Vit D causes reduction in the response to microbes by

decreasing the production of Interleukin-1, Interlukin-6 and Tumor necrosis factor-alpha by macrophages [20]. More elaborative research and comprehensive study is required to further determine the levels of vit D at different stages of gestation and their association with both maternal and infant outcomes.

CONCLUSION:

Results showed a strong association between women with hypovitaminosis D and preterm delivery. Further longitudinal studies are required for evidence and to establish a strong link between hypovitaminosis D and preterm birth. However, for the time being it is very important that gynecologists should consider vitamin D status as essential marker like other routine screening parameters for women during pregnancy for preventing the adverse outcomes of pregnancy.

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