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# Association between Maternal Vitamin D Levels during 3rd trimester Prolonged Labor and Tobacco Smoking

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## ABSTRACT

**Background:**At the time of childbirth, Vitamin D plays an essential role in uterine contractions. Failure of adequate levels of vitamin D may delay uterine contractions (uterine atony), that lead to a maternal life threatening condition called Postpartum hemorrhage. Exposure to cigarette smoke during pregnancy leads to several adverse effects on mother and child.

**Objective**: Tostudy the effect of cigarette smoking on Vitamin D levels during pregnancy and its fetal effects on uterine contractions leading to postpartum hemorrhage.

**Study design:** A retrospective Cohort Study

**Place & Duration of Study:** By the Departmentof Forensic Medicine Department, Khyber Medical College, Peshawar, at District Head Quarter Hospital, DD Khan Pakistan; from October 2020 to Mar 2021.

**Methodology:**In this study; 108 pregnant females were enrolled and 25(OH)D was measured at 36-38 weeks gestation in a cohort study at district headquarter hospital DG Khan (DHQH). Moreover, for data validity, secondary data collected from the record room of Obstetrics unit of DG Khan DHQH. The participants, divided into two equal groups i.e. with and without a previous history of exposure to tobacco smoking.The fasting blood samples collected along with tested serum calcium and 25(OH)D Levels.Finally, data was presented in form of tables.

**Result**:Vitamin D levels during $3^{rd}$ trimester was $9.28 \pm 2.19$ ng/mlin exposed and $25.75 \pm 5.26$ ng/ml in non-exposed group($p > 0.05$) in maternal serum. Our study indicated that smoking caused low level of vitamin D and insufficiency of vitamin D wasstrongly associated with uterine atony.

**Conclusion**: It was revealed that low vitamin D level showed strongly associated with uterine atony. Moreover, the low socioeconomic status showed significant association among the families both in urban and rural communities of DG Khan, Pakistan.

***Key words***: Vitamin D, Postpartum Hemorrhage, Tobacco Smoking, Pregnancy

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## INTRODUCTION

Uterine atony is an obstetrics complication occurs due to the failure of the uterus to contract after the delivery of the neonate. If left untreated, it may lead to continuous uterine bleeding which may results to life threatening condition called postpartum hemorrhage; sometimes even hysterectomy is imminent to save the life of the mother[1]. Uterine atony is one of the causes of maternal mortality due to postpartum hemorrhage. Studies have shown that Vitamin D prevent postpartum hemorrhage. Vitamin D deficiency during pregnancy may lead to gestational diabetes, preeclampsia, and preterm and low birth weight neonate.The most suitable way to find vitamin D levels in blood is the 25-hydroxy vitamin D blood test. Normal level of vitamin D is 20-50 ng/ml. Deficiency and insufficiency of Vitamin D <12.0 ng/mlwas found associated with atonic uterus[2].

A deficiency in vitamin D can result from inadequate exposure to sunlight, insufficient production in the skin, low calcium in diet, depletion of vitamin D and demineralization from bones due to exposure to smoke and health conditions such as GIT disorders, renal diseases, hepatitis and cancers[3]. Besides building teeth and bones, calcium also keeps blood and muscles moving and helps nerves in conduction of signals. A pregnant woman must take at least 1,000 mg of calcium every day which is equal to 8-10 glass of milk[1,3].Tobacco cigarette smoke contains more than 2,500 chemicals that are present in foil /paper such as tar, carbon monoxide and molybdenum sulfate. These are teratogenic and have direct effect on uterus even in small amount.[4] Cigarette smoking expedite the formation of free radicals in the body. These free radicals cause cellular damage leading to cancer as well as other diseases. Studies have shown that cigarette smoke exposure in active or passive smokers may cause reduced amounts of vitamin C and D in their bodies leading to tissue damage and depletion of bone minerals[5].

Vitamin D exerts its effect by binding to the vitamin D receptors present in many tissues and organs including the osteoblasts, brain,skin, skeletal as well as in smooth muscles[6]. It was reported that 3 out of 4 women who were severely vitamin D deficient underwentcaesarean section. Vitamin D receptorsare present in both skeletal and smooth muscles. Its deficiency is directly associated with proximal muscle weakness as well as with suboptimal muscle performance and strength[7]. Vitamin D also regulates the level of serum calcium in blood. Serum calcium helps in the rhythmic contractions of theuterine smooth muscles during

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labor[8].The normal range for blood calcium level is 8.6 to 10.3 mg/dl.The higher serum calcium levels was reported in pregnant women at the time of vaginal delivery as compared to term women who were not in labor and delivered by caesarean section. It was presumed that vitamin D deficiency causes decrease in serum calcium, thereby affecting the contractility of uterine smooth muscle, might result in atonic uterus and postpartum hemorrhage[9]. The scope of present study was to determine the factors that cause as the depletion of Vitamin D from serum and an association of low serum vitamin D level with uterine atony, among women in labor in DG Khan District Head Quarter Hospital, Pakistan.

## METHODOLOGY

After ethical approval, the Department of Forensic Medicine Khyber Medical College Peshawar, conducted a retrospective cohort study at Gynecology &Obstetrics Department District Head Quarter Hospital, of DG Khan from October 2020 to Mar 2021. In this study, 108 patients studied in which the total participants wereequally divided into two groups. All those with and without the history of active or passive smoking were listed as exposed and non-exposedgroup. Inclusion criteria were gestational age between 38–40 weeks and age between 16-40 years with history of use of tobacco in any form. Exclusion criteria were mothers having the above mentioned criteria but previous history of chronic illnesses like Tuberculosis disease, malignancies, hypertension, diabetes mellitus, Renal dysfunction disease, hepatitis or any chronic disease that affect calcium or vitamin D metabolism. A research tool Questionnaire was developed and participants were interviewed and evaluated by the researcher. The number of cigarette smoked and time of exposure were also recorded.

### Laboratory Investigations for Mother's Vitamin D Levels

A fasting blood sample was obtained from the mothers. The serums were evaluated for 25-hydroxy vitamin D by ELISA method. 20–150 ng/ml was normal, whereas 25OHD concentration less than 11-19 ng/ml considered as insufficient and concentration of 25-hydroxy vitamin D lower than 10 ng/ml was labeled as severe deficiency of vitamin D.

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### Analysis of Statistical Data

A statistical program SPSS 19 was used for data interpretation. T-Test used to compare quantitative measures and Chi-Square Test wasapplied to compare the frequency between the two groups. P value of <0.05 was considered as significant with chi-square test value of more than 3.84 for categorical data with 1 degree of freedom.

### Rate of Exposure to Cigarette Smoking

81.4% of the exposed mothers have history of passive smoking. 53.7% were active smoker. Exposure rate was 30-45 minutes daily. 95% cases have past history of smoke exposure. 76% mothers are from low socioeconomic status and living in a single small room. 30.3% have tuberculosis patient at home.

**Table No. 1 Serum Vitamin D Levels**

| Serum Vitamin D levels (25 OH vitamin D) | Concentration in Blood | Value |
|---|---|---|
| | >20ng/ml | Normal Standard |
| | 12-19ng/ml | Insufficient |

The test for 25-OH vitaminD was performed on Roche Elecsys 2010 Immunoassay Analyzer by using electro-chemo-luminescence immunoassay technique. The Ethical approval and informed consent from taken from all patients and Medical superintendent DHQH DG Khan. Chi square test was performed to analyze and check hypothesis that deficiency of vitamin D causes uterine atony. T-test was also used to compare mean level of vitamin D and blood loss (hemoglobin) in both groups. The data wasanalyzedand interpreted on SPSS version 20.

## RESULT

In age estimated analysis, comparison of women who never smoked with smoke exposed, the Relative risk (RR) ofdeveloping uterine atony was less than 10%. When we examined the intensity of smoking, greater numbers of cigarettessmoked per day were associated with increasing risksof decreased metabolism of vitamin D. Total 108 participants were studied for vitamin D levels. Out of 54 mothers with previous exposure to cigarette smoking,n=48 had 25

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OH vitamin D less than 12ng/ml. Among the non-exposed group (n=54) showed n= 47 serum 25 OH vitamin D more than 20ng/ml. In women with 25 OH vitamin D less than 12ng/ml have serum calcium <8 mg%, out of which 38 patients developed uterine atonicity. In women with25 OH vitamin D more than 20ng/ml, serum calcium > 8 mg% only one client developed uterine atonicity.

**Table No. 2. Frequency of Tobacco Smoking, Uterine Atony, Vitamin D < 12ng/ml&Serum Calcium <8 mg% among the n=108 respondents Visiting Gynecology & Obstetrics Department DHQ Hospital, DG Khan, Pakistan**

| Variables | Yes | No |
|---|---|---|
| | Frequency (%) | Frequency (%) |
| Tobacco Smoking | 54 (50.0) | 54 (50.0) |
| Uterine Atony | 40 (37.04) | 68 (62.96) |
| Vitamin D < 12ng/ml | 55 (50.92) | 53 (49.07) |
| Serum Calcium <8 mg% | 104 (96.29) | 4 (3.70) |

**Table No. 3. Association of Tobacco smoking with Uterine Atony, Vitamin D &Serum Calcium <8 mg% among the n=108 respondents Visiting Gynecology & Obstetrics Department DHQ Hospital, DG Khan, Pakistan**

| **Uterine Atony** | | | | |
|---|---|---|---|---|
| **Independent Variable** | **Response** | **Yes** | **No** | **Chi Square Value (P-Value)** |
| **Tobacco Smoking** | Yes | 38 | 16 | 51.45***** (<0.00001) |
| | No | 2 | 52 | |
| | | | | |
| **Vitamin D < 12ng/ml** | | | | |
| **Independent Variable** | **Response** | **Yes** | **No** | Chi Square Value (P-Value) |
| **Tobacco Smoking** | Yes | 48 | 6 | 62.28***** (<0.00001) |
| | No | 7 | 47 | |
| | | | | |

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| Serum Calcium <8 mg% | | | | |
|---|---|---|---|---|
| **Independent Variable** | **Response** | **Yes** | **No** | Chi Square Value (P-Value) |
| **Tobacco Smoking** | **Yes** | 51 | 3 | 1.0385** (0.308) |
| | **No** | 53 | 1 | |

* The Chi Square Test Values are more than the critical value (3.84); thus reject the null hypothesis.

** The Chi Square Test Value (1.0358) is less than the table value (3.84); thus will fail to reject the null hypothesis.

According to the methodology of our research study, it was observed that those who have 30-45 mins exposure to cigarette smoke daily have low serum VitaminD levels. Relative risk for uterine atony is more in smoke exposed patients. The level of Vitamin D was found adequate in a group of patients who were regularly using Calcium supplement and milk. Out of 20 cases of Atony with history of exposure of cigarette smoke during pregnancy it was observed that the ratio of normal Vaginal delivery (NVD) and cesarean section(C-S) was 1:1.1 (n=11 and 9). 13(65%) primary para patients have atony as compared to 7(35%)multipara(Table-2).

## DISCUSSION

From our study conducted, it was found that vitamin D deficiency has significant role in causation of uterine atony. Uterine atony due to vitamin D deficiency leading to diminished uterine contractility was responsible of 79% cases of postpartum hemorrhage reported in america[10]. In current study, we found that low serum vitamin D level was strongly associated with uterine atony. Uterotonic drugs such as, oxytocin and prostaglandins increase the contraction of uterine smooth muscle by increasing intracellular calcium level, but in the presence of free radicals in blood due to the deficiency of vit D the pharmacokinetics of the drugs such as oxytocin and prostaglandins was greatly affected[11]. Another study conducted by B. W. Hollis and C. L. Wagner suggested that the action of oxytocin and prostaglandins increases when levels of vitamin D and serum calcium were optimal in patient underwent labor[12]. This is similar to our findings suggested that vitamin D has an efficient role in uterine contractility. Lisa M Bodnar et al, have concluded in their study that low maternal serum 25(OH) D was associated with a risk of spontaneous preterm birth before 35 weeks[13]. In another study it was suggests that vitamin D level has something to do with the uterine muscle ability to contract and its deficiency

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may lead to atony[14, 15]. In our study, primiparity was not significantly associated with uterine atony as indicated in some studies.

Instead of routine treatment remedies, our study suggested that serum levels of vitamin D and calcium might be considered as a primary factor for uterine atony. Drugs such as Nifedipine, a calcium channel blocker are not recommended during delivery as they block calcium. Such drugs reported to be associated with uterine atony[16, 17]. Similarly, prostaglandins are uterotonic agents, which cause an increase in myometrial intracellular calcium levels leading to an increase in myosin light chain kinase activity and uterine contractility[18]. High maternal age has been considered as a risk factor for postpartum hemorrhage due to uterine atony however, a previous study did not find any significant association of high age with uterine atony and this is comparable to our findings[19, 20]. This study had some limitationsi.e. inclusionof pregnant women and lack of a control group of non-pregnant women, the low frequency of dietary intake of calcium and vitamin D supplements, and not including data on dietary intake and physical activity.

## CONCLUSION

Our results revealed that cigarette smoke exposure has a significant direct adverse effect on decrease levels of serum Calcium and Vitamin D in pregnant women. Tobacco smoke is also responsible for depletion of minerals and vitamin from bones. Low or insufficient levels of vitamin D level is strongly associated with uterine atony and hence is a risk factor for uterine atony. It is advised that obstetrics should consider vitamin D deficiency as a primary risk factor for uterine atony. Furthermore, it wasrecommended that oral supplement and injectable might be indicated as per deficiency of vitamin D.

**Conflict of Interest:** No conflict of interest

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