

Association of Cigarette Smoking Exposure in Pregnant patients and Uterine Atony

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Abstract

Background: Uterine atony, is one of the life-threatening emergency obstetrics complications that may be affected by vitamin D deficiency and cigarette smoking.

Objective: To study the cause effect relationship between cigarette smoking and postpartum hemorrhage due to uterine atony.

Methodology: A case-control study was conducted in District Headquarters Hospital, DG Khan, from March to August 2020, from the record room of the Obstetrics ward. A total of 236 patients were included in the study, where 56 were cases of uterine atony and 180 were controls who did not have uterine atony. History of exposure to cigarette smoking (active or passive smoking) was taken from the study subjects. All of the study subjects had a deficiency of serum vitamin D. Odds Ratio was calculated to determine an association between smoking and Uterine atony. Exclusion criteria; grand multipara, polyhydramnios, preeclampsia, chronic renal or liver diseases, bleeding disorders, retained products of conception, and patients having bleeding from cervix or vaginal tear. A p-value of less than 0.05 was taken as significant.

Results: A total of 236 study subjects were included in the study. Out of 56 patients with uterine atony, 20 (35.7%) have a history of smoking, as compared to 120 (66.6%) out of 180 study subjects in controls. The Odds Ratio was 0.27 which reflects that those who smoked (active or passive) during pregnancy have less chances of uterine atony and has a protective effect. (p=0.000)

Conclusion: It was concluded that smoking was inversely associated with uterine atony and has a protective effect.

Keywords: Smoking, Uterine atony, Postpartum hemorrhage, Pregnancy

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Introduction

Uterine atony is one of the life-threatening emergency obstetrics complications that occur due to failure of the uterus to contract rhythmically after the delivery of the newborn.¹ If left untreated, it may lead to continuous uterine bleeding which may result in a life-threatening condition called postpartum hemorrhage. Sometimes hysterectomy is eminent to save the life of the mother.² Uterine atony is one of the causes of maternal mortality due to postpartum hemorrhage. Studies have shown that Vitamin D prevents postpartum hemorrhage. Vitamin D deficiency during the third trimester may lead to gestational diabetes, preeclampsia, preterm and low birth weight neonate.^{3,4}

The most suitable way to determine vitamin D levels in blood is a 25-hydroxy vitamin D blood test. The normal level of vitamin D in serum is 20-50 ng/ml. Deficiency of insufficiency of Vitamin D levels below 12.0 ng/mL was found associated with atonic uterus.² There are many confounders

associated with vitamin D insufficiency in pregnancy. Deficiency in vitamin D can result from inadequate exposure to sunlight, insufficient production in the skin, low calcium in the 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 the conduction of signals. A pregnant woman must take at least 1000 mg of calcium every day equivalent to 8-10 glasses of milk.^{1,3}

Cigarette smoke contains more than 2500 toxic chemicals that are present either in foil paper such as tar, carbon monoxide, and molybdenum sulfate, or in tobacco. These carcinogenic substances cause mutation at the cellular level. Most of them are teratogenic and have a direct effect on the uterus even in small amounts.⁴ Cigarette smoking expedites the formation of free radicals in the body. These free radicals suppress the TP53 gene. TP 53 gene is a

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checkpoint for newly formed genes before the S phase during the cell cycle. Leading to damaged cell mosaicism leading to cancer as well as other diseases.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 Vitamin D receptors are 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 the uterine smooth muscles during labor.⁸ The normal range for blood calcium level is 8.7 to 10.2 mg/dL in non-pregnant women. Higher calcium intake is required for fetal development in pregnancy and lactation. It was speculated that vitamin D deficiency causes a decrease in serum calcium, thereby affecting the contractility of uterine smooth muscles, which may result in postpartum hemorrhage.⁹ The objective of the present study was to study the cause-effect relationship between cigarette smoking and postpartum hemorrhage due to uterine atony.

Methodology

This was a retrospective, case-control study, conducted in the Gynae and Obstetrics department of DG Khan District teaching. Hospital from March to August 2020. A total of 236 patients were included in the study, where 56 were cases of uterine atony and 180 were controls who did not have uterine atony. History of exposure to cigarette smoking (active or passive smoking) was taken from the study subjects. All of the study subjects had a deficiency of the serum vitamin D. Cases of uterine atony were taken where myometrium failed to contract after the delivery of the placenta. Hemoglobin was tested before and after delivery. Overall 250 ml of Blood is considered equivalent to 1.43g/dl of Hb. The bleeding associated with the placental site more than 500ml (Hb 2.8g/dl) after normal delivery and more than 1000ml (5.6g/dl) after cesarean section were taken as cutoff values. Controls (Group B) were similar to cases (Group A) except that they did not have developed uterine atony. Exclusion criteria for this study were patients with a history

of grand multipara, polyhydramnios, preeclampsia, chronic renal or liver diseases, bleeding disorders, retained products of conception, and patients having bleeding from cervix or vaginal tears.

Their blood samples were taken for serum vitamin D (25 OH vitamin D) levels. 25 OHD concentrations >20ng/ml were considered as Standard Normal. A Serum Vitamin D level of less than 19ng/ml was considered as deficient or insufficient level of Vitamin D.

The test for 25-OH vitamin D was performed on Roche Elecsys 2010 Immunoassay Analyzer by using the electrochemiluminescence immunoassay technique. Informed consent was obtained from all patients and ethical approval was taken from the Medical Superintendent of DHQ Teaching Hospital DG Khan (Ref. No. 15590-93/Teaching Hosp: Dated D.G.Khan, Dated: 23-03-2020). A chi-square test was performed to analyze and check the hypothesis that deficiency of vitamin D causes uterine atony. T-test was also used to compare the mean level of vitamin D and blood loss (hemoglobin) in both groups. The data was analyzed and interpreted on SPSS version 20.

Results

A total of 236 study subjects were included in the study, and out of the total, 56 patients had developed atonic uterine contractions. The calculated mean age was 27 ± 3 years, and mean gravida of 2.2 ± 1 . All of the study subjects have a deficiency of serum vitamin D, 16 ± 4 ng/ml. The mean value of serum vitamin D was 14 ± 2.3 ng/ml vs 13 ± 1.9 ng/ml in cases vs controls.

Table-I: Association of Cigarette Smoking with Uterine Atony.

Risk Factor/Exposure	Case (Uterine atony)	Control (without uterine atony)	Total	Odds Ratio	P value
Exposed to cigarette smoke	20 (35.7%)	120 (66.6%)	140 (59.3%)	0.27	0.000
Not exposed to cigarette smoke	36 (64.3%)	60 (33.3%)	96 (40.7%)		
Total	56 (100%)	180 (100%)	236 (100%)		

It was shown in Table-I that out of 56 patients of the uterine atony, 20 (35.7%) have a history of smoking, as compared to 120 (66.6%) out of 180 study

subjects in controls. The Odds Ratio shows that those who smoked (active or passive) during pregnancy have 0.27 times less chances of uterine atony than those who do not smoke, and this has a protective effect. ($p=0.000$)

Discussion

In this study, we have evaluated the association of cigarette smoking with uterine atony, among vitamin D deficiency mothers. Uterine atony due to vitamin D deficiency leading to diminished uterine contractility was responsible for 79% of cases of postpartum hemorrhage reported in America.¹⁰ In the current study, we found that smoking among mothers with low serum vitamin D levels was significantly negatively associated with uterine atony. Uterotonic drugs such as oxytocin and prostaglandins increase the contraction of uterine smooth muscle by increasing intracellular calcium levels, but in the presence of free radicals in blood due to the deficiency of vitamin D, the pharmacokinetics of the drugs such as oxytocin and prostaglandins was greatly affected.^{11,12,13,14}

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 are optimal in patients undergoing 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.¹⁵ In another study it was suggested that vitamin D level has something to do with the uterine muscle's ability to contract and its deficiency may lead to atony.¹⁴

Instead of routine treatment remedies, our study suggested that serum levels of vitamin D and calcium may 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 are reported to be associated with uterine atony.¹⁵ Similarly, prostaglandins are uterotonic agents that cause an increase in myometrial intracellular calcium levels leading to an increase in myosin light chain kinase activity and uterine contractility.¹⁶ High maternal age has been considered as a risk factor for postpartum

hemorrhage due to uterine atony however, Khan SM, Saeed M et al did not find any significant association of high age with uterine atony and this is comparable to our findings.¹⁷

In a study, the findings which have no clear reasons to be understood, included that the healthiest low-birth-weight infants were found in couples where the wife smoked and her husband did not smoke; the most vulnerable were produced by couples where the wife did not smoke and the husband smoked. However, they found that there are differences in mode-of-life characteristics between smokers and nonsmokers.¹⁷

The nonsmokers were obviously more likely to use contraceptive methods, to plan the baby, and less likely to drink coffee and hard liquor. Another difference was that of age at menarche, which was lower for smoking mothers. These paradoxical findings raise doubts and argue against the proposition that cigarette smoking acts as an exogenous factor that interferes with the intrauterine development of the fetus.¹⁸ Our study found a similar finding where smoker mothers had a negative association with uterine atony (OR, 0.27; $p=0.000$). This study had some limitations. The inclusion of pregnant women and the possibility of 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 inverse effect on uterine atony. Low or insufficient levels of vitamin D are strongly associated with uterine atony and hence are a risk factor for uterine atony. However, smoking weakly but negatively affected the uterine atony.

Authors Contribution: **SN:** Conception of work, Acquisition and Analysis of data and Drafting. **RZA:** Acquisition and Analysis of data, Interpretation of data and revising. **NS:** Design of work, Acquisition and Analysis of data and revising. **ARQ:** Interpretation of data and revising. **MAK:** Acquisition and Analysis of data and drafting. **SMY:** Design of work and drafting.

All authors critically revised and approve its final version.

Conflict of Interest: No conflict of interest among authors.

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