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**Research**

# Prospective Study To Determine Association Between Maternal Serum Calcium Levels And Uterine Atonicity In A Tertiary Care Hospital

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## Abstract

Post partum hemorrhage accounts for 38% of maternal deaths. The main cause is atonicity of uterus. PPH can be classified as primary (within 24hours after delivery) and secondary (24 hours to 12 weeks) after delivery. Most cases of postpartum bleeding occur within 4 hours after delivery. Optimum levels of calcium are important for contraction of uterine musculature. Low levels of serum calcium results in reduced contraction. Reduced serum calcium level may affect contractility of uterine smooth muscle, hence may result in atonic uterus and PPH.

**AIMS AND OBJECTIVES:** Study the association between maternal serum calcium levels and development of uterine atonicity in a tertiary care hospital.

**MATERIALS AND METHODS:** This is a prospective case control study conducted in department of obstetrics and gynecology, KAPV Government medical college, Tiruchirappalli.

156 antenatal mothers in first and second stage of labour were tested for serum calcium levels.

**RESULTS AND OBSERVATION:** In this study, mothers with serum calcium less than 9mg/dl, 36.7% had PPH, and those who had levels more than 9mg/dl , only 7.8% developed PPH.

**CONCLUSION:** Serum calcium levels were found to have statistically significant association with PPH implying that participants having low serum calcium levels have increased chances of atonic PPH.

**Keywords:** PPH, uterine atonicity, serum calcium, labour

## INTRODUCTION

Post partum hemorrhage accounts for 38% of all maternal deaths. There is a strong evidence to believe that the rate of PPH is increasing worldwide. The main reason for this increase is the growing frequency of uterine atony. [1]

PPH can be classified as minor (500 – 1000 ml blood loss) and major (more than 1000ml blood loss). PPH has also been classified as primary PPH (within 24 hours after delivery) and secondary PPH (24 hours to 12 weeks after delivery). Most cases of postpartum bleeding occur within 4 hours after delivery.

52% of maternal deaths are attributable to three leading causes- hemorrhage, sepsis, hypertensive disorders. WHO statistics suggest that 25% of maternal deaths are due to PPH.

Every year about 14 million women around the world suffer from PPH resulting in 70,000 maternal deaths globally. Incidence of PPH in India is reported as 2%-4% after vaginal delivery and 6% following LSCS, with uterine atony being the cause in about 50% cases [2, pp. 1-2]. In our institution the prevalence of PPH being 1.5- 2 %

PPH also holds alternative definitions like a fall in > 10 % of predelivery hematocrit and volume of blood loss which requires blood transfusion as given in Cochrane database of systemic reviews -2009 [3].

The excitation-contraction coupling of uterine smooth muscle is also very similar to that of other smooth muscle in general, with intracellular increase in calcium ($Ca^{2+}$) leading to contraction. [4]

The mechanism of calcium absorption involves binding of calcium to a specific protein (calcium-binding protein) whose synthesis is stimulated by active forms of vitamin D (1,25-dihydroxyvitamin D). Maternal serum 1, 25(OH)2D levels increase twofold during pregnancy, allowing the intestinal absorption of calcium also to double. Serum 25-hydroxy vitamin D (inactive form of vitamin D) levels do not change during pregnancy, but an increase in 1-a- hydroxylase and additional synthesis in the placenta allows for an increase in the conversion of 25-hydroxy vitamin D to 1, 25(OH)2D. [5]

The principal maternal adjustment during pregnancy is increasing parathyroid hormone and PTHrP secretion which maintains the serum ionic calcium level within its characteristically narrow physiologic range in the face of extracellular fluid volume expansion, renal function increase and placental calcium transfer. However, even with these high rates of absorption, maternal and fetal needs may not be met in women with chronically low calcium consumption (<500 mg/day). [5]

Calcium exerts its effect by activating the muscle proteins and causing effective uterine contraction. Serum calcium status regulated by vitamin D plays a role in smooth muscle contraction in early labor. It was speculated that the higher serum calcium levels played a role in the mechanism of initiation of labor which is the result of adequate uterine smooth muscle contraction. Reduced serum calcium level may affect the contractility of uterine smooth muscle hence, may result in atonic uterus and PPH. So present study is conducted to determine the relationship of serum calcium levels with PPH in a tertiary care hospital.

**AIMS / OBJECTIVES**

To study the association between maternal serum calcium levels and development of uterine atonicity in a tertiary care hospital - Govt K.A.P.V Medical College, Trichy.

## MATERIALS AND METHODS

**Methodology**

This is a prospective case control study conducted in the department of obstetrics and gynecology, Govt K.A.P.V Government Medical College, Tiruchirappalli.

156 antenatal mothers who are in first and second stage of labour, admitted in Govt K.A.P.V Medical College were tested for serum calcium levels. After fulfilling inclusion and exclusion criteria 100 mothers were included in the study.

Blood sample collected for serum calcium
Group A - patients with serum calcium more than 9 mg%
Group B – patients with serum calcium less than 9 mg%
In both the group uterine tone will be assessed.

**Inclusion criteria**

- Primi, second & third gravida
- Vaginal deliveries
- Term pregnancies.

**Exclusion criteria**

- Multiple pregnancy
- Placenta previa
- Retained placenta
- Anemia
- Traumatic PPH
- Poly hydramnios
- Gestational diabetes
- Abruptio placenta
- Bleeding disorder
- Patients on anticoagulants

**STUDY DESIGN:** Prospective case control study
**SAMPLE SIZE:** 100
**STUDY PLACE:** KAPV Government medical college and hospital, Tiruchirappalli

**STATISTICAL ANALYSIS**

Plan SPSS software Written informed consent was taken from all the subjects and approval from the institutional ethical committee was obtained. Chi – square test was applied to compare the occurrence of PPH in both the groups. Serum calcium levels and occurrence of PPH were correlated.

## RESULTS

**Socioeconomic status**
In our study population, 19 % belonged to SES II, 47% belonged to SES III and 34% belonged to SES IV.

**Table 1: SES of the study population**

| SES | Frequency (N) | Percentage (%) |
|---|---|---|
| II | 19 | 19 |
| III | 47 | 47 |
| IV | 34 | 34 |

**Parity**
42 of them were Primi and 43 belonged to G2 and the remaining were of G3.

**Table 2: Parity Status of the study population**

| Parity | Frequency (N) | Percentage (%) |
|---|---|---|
| G2A1 | 11 | 11 |
| G2P1L1 | 32 | 32 |
| G3A2 | 3 | 3 |
| G3P1L1A1 | 10 | 10 |
| G3P2L2 | 2 | 2 |
| Primi | 42 | 42 |

**Gestational age**
The gestational age of the study population is listed below which shows that 31 of them had GA of 37 weeks, 48 of them had GA of 38 weeks while there were 16 and 5 patients in 39 weeks and 40 weeks respectively.

**Table 3: Gestational Age of the study population**

| Gestational Age | Frequency (N) | Percentage (%) |
|---|---|---|
| 37 weeks | 31 | 31 |
| 38 weeks | 48 | 48 |
| 39 weeks | 16 | 16 |
| 40 weeks | 5 | 5 |

**Onset of labour**
89 of them spontaneous labour and out of the remaining who had induced labour, 5 of them were induced because they were postdated. 3 of them were induced because of IUGR and 3 of them were induced because of oligohydramnios.

**Table 4: Onset of Labour of the study population**

| Onset of Labour | Frequency (N) | Percentage (%) |
|---|---|---|
| Induced (postdated) | 5 | 5 |
| Induced (IUGR) | 3 | 3 |
| Induced (oligohydramnios) | 3 | 3 |
| Spontaneous | 89 | 89 |

**Mode of delivery**

In our study, 89 of them had vaginal delivery and 11 of them had instrumental delivery

**Table 5: Mode of Delivery of the study population**

| Mode of Delivery | Frequency (N) | Percentage (%) |
|---|---|---|
| Instrumental | 11 | 11 |
| Vaginal | 89 | 89 |

**Post partum hemorrhage**

In our study, 22 of them had post partum hemorrhage and 78 of them had no hemorrhage

**Table 6: PPH complication of the study population**

| PPH | Frequency (N) | Percentage (%) |
|---|---|---|
| No | 78 | 78 |
| Yes | 22 | 22 |

**Mode of delivery and PPH**

The mode of delivery and PPH were studied which showed that those who had vaginal delivery 18 of them had PPH, and those who had instrumental delivery 4 of them had PPH.

**Table 7: Mode of delivery and PPH**

| Mode of delivery | PPH | Frequency (N) | Percentage (%) |
|---|---|---|---|
| Vaginal | Yes | 18 | 20% |
| Instrumental | Yes | 4 | 36% |

**Serum calcium levels and post partum hemorrhage**

The Serum calcium levels and PPH were studied which showed that those who have serum calcium levels <9mg/dl, 36.7% had PPH and those who had serum calcium levels >9mg/dl only 7.8% developed PPH

**Table 8: Serum calcium levels and PPH**

| Serum Calcium Levels (mg/dl) | PPH | Frequency (N) | Percentage (%) |
|---|---|---|---|
| < 9 | No | 31 | 63.3 |
| | Yes | 18 | 36.7 |
| >9 | No | 47 | 92.1 |
| | Yes | 4 | 7.8 |

**Serum calcium levels and blood transfusion**

The Serum calcium levels and Blood transfusion were studied which showed that those who have serum calcium levels <9 mg/dl, 12.2% had blood transfusion and those who had serum calcium levels >9mg/dl no one required blood transfusion.

**Table 9: Serum calcium levels and Blood transfusion**

| Serum Calcium Levels (mg/dl) | Blood T ransfusion | Frequency (N) | Percentage (%) |
|---|---|---|---|
| < 9 | No | 43 | 87.8 |
| | Yes | 6 | 12.2 |
| >9 | No | 51 | 100 |
| | Yes | 0 | 0 |

**Serum calcium levels and post partum hemorrhage**

In our study population, those with Serum calcium levels <8mg/dl, 5 patients developed PPH among those with 8-8.5 mg/dl range, 12 patients developed PPH.

**Table 10: Serum calcium levels and Post partum hemorrhage**

| Serum Calcium Levels (mg/dl) | PPH | Frequency (N) | Percentage (%) |
|---|---|---|---|
| < 8 | No | 0 | 0 |
| | Yes | 5 | 100 |
| 8-8.5 | No | 5 | 29.4 |
| | Yes | 12 | 70.6 |
| 8.5-9 | No | 26 | 96.3 |
| | Yes | 1 | 3.7 |
| >9 | No | 47 | 92.2 |
| | Yes | 4 | 7.8 |

**Serum calcium levels and blood transfusion**

In our study population, those with Serum calcium levels <8 mg/dl, 4 patients had blood transfusion and among those with 8-8.5 mg/dl range, 2 patients required blood transfusion

**Table 11: Serum calcium levels and Blood transfusion**

| Serum Calcium Levels (mg/dl) | Blood Transfusion | Frequency (N) | Percentage (%) |
|---|---|---|---|
| < 8 | No | 1 | 20 |
| | Yes | 4 | 80 |
| 8-8.5 | No | 15 | 88.2 |
| | Yes | 2 | 11.8 |
| 8.5-9 | No | 27 | 100 |
| | Yes | 0 | 0 |
| >9 | No | 51 | 100 |
| | Yes | 0 | 0 |

**BMI category and PPH**

In BMI categories and PPH, those who had normal BMI, 14 patients developed PPH and those who were in the overweight and obese categories there were 4 patients in each category

**Table 12: BMI category and PPH**

| BMI | PPH | Frequency (N) | Percentage (%) |
|---|---|---|---|
| < 18.5 | No | 0 | 0 |
| | Yes | 0 | 0 |
| 18.5-24.9 | No | 61 | 81.3 |
| | Yes | 14 | 18.7 |
| 25-29.9 | No | 16 | 80 |
| | Yes | 4 | 20 |
| >30 | No | 1 | 20 |
| | Yes | 4 | 80 |

**BMI category and blood transfusion**

In BMI categories and PPH, those who had normal BMI, 4 patients had blood transfusion and those who were in the overweight and obese categories there were 1 patient in each category who required blood transfusion.

**Table 13: BMI category and Blood transfusion**

| BMI | Blood Transfusion | Frequency (N) | Percentage (%) |
|---|---|---|---|
| < 18.5 | No | 0 | 0 |
| | Yes | 0 | 0 |
| 18.5-24.9 | No | 71 | 94.6 |
| | Yes | 4 | 5.4 |
| 25-29.9 | No | 19 | 95 |
| | Yes | 1 | 5 |

| | | | |
|---|---|---|---|
| >30 | No | 4 | 80 |
| | Yes | 1 | 20 |

**Independent't test**

Variables like Age, BMI and Serum calcium were checked for association with Post partum hemorrhage and it was found that BMI and Serum Calcium levels were found to have statistically significant association with PPH implying that persons with higher BMI had increased chances of PPH and those with low serum calcium levels also have increased chances of PPH as the p value <0.05.

**Table 14: Association of Age, BMI and Serum calcium with PPH**

| Variables | PPH | N | Mean | Std. Deviation | p value |
|---|---|---|---|---|---|
| Age | Yes | 22 | 25 | 4.231 | 0.563 |
| | No | 78 | 24.49 | 3.486 | |
| BMI | Yes | 22 | 24.93 | 3.704 | **0.042** |
| | No | 78 | 22.99 | 2.506 | |
| Serum Calcium | Yes | 22 | 7.46 | 0.699 | **<0.001** |
| | No | 78 | 8.56 | 0.837 | |

**CHI square test**

Socioeconomic status, Parity, Gestational age, Onset of labour and Mode of delivery were seen for association with PPH and it was found that onset of labour is statistically significant with PPH, as patients with induced labour had PPH with a p value of <0.05.

**Table 15: Association of Socioeconomic status, Parity, Gestational age, Onset of labour and Mode of delivery with PPH**

| Variables | Sub variable | PPH | | p value |
|---|---|---|---|---|
| | | No | Yes | |
| SES | II | 17 (89.5%) | 2 (10.5%) | 0.397 |
| | III | 35 (74.5%) | 12 (25.5%) | |
| | IV | 26 (76.5%) | 8 (23.5%) | |
| Parity | Multigravida | 47 (81%) | 11 (19%) | 0.466 |
| | Primi | 31 (73.8%) | 11 (26.2%) | |
| Gestational Age | 37 weeks | 28 (90.3%) | 3 (9.7%) | 0.009 |
| | 38 weeks | 33 (68.8%) | 15 (31.3%) | |
| | 39 weeks | 15 (93.8%) | 1 (6.3%) | |
| | 40 weeks | 2 (40%) | 3 (60%) | |
| Onset of labour | Induced | 3 (27.3%) | 8 (72.7%) | **<0.001** |
| | Spontaneous | 75 (84.3%) | 14 (15.7%) | |
| Mode of Delivery | Instrumental | 7 (63.6%) | 4 (36.4%) | 0.252 |
| | Vaginal | 71 (79.8%) | 18 (20.2%) | |

*A significant association was there between PPH and blood transfusion as those with PPH had blood transfusion with a p value of <0.05.*

**Table 16: Association of PPH with Blood transfusion**

| Variables | Blood transfusion | | P value |
|---|---|---|---|
| PPH | No | Yes | |
| | 16 (72.7%) | 6 (27.3%) | <0.001 |

## DISCUSSION

In this study we have compared the levels of serum calcium and uterine atony and PPH, a life threatening condition and a single most preventable cause of maternal death.

Postpartum hemorrhage (PPH) is defined as blood loss of more than 500ml during normal vaginal delivery and loss of more than 1000ml following cesarean section. PPH is the most common and serious obstetric risk factor resulting in increased morbidity and mortality.

Uterine atony is one of the commonest cause of the postpartum hemorrhage leading to maternal morbidity and mortality. The oxytocic drug increases the uterine tone by increasing intracellular calcium. [20].

The fundamental process involved in myometrial contraction is actin-myosin interaction. Myosin is the principal protein in muscle contraction and the process is dependent on calcium.

Calcium ions entering into the myometrial cells initiates a cascade of events, culminating in myometrial contractions. Calcium interacts with calmodulin to activate myosin light chain kinase which in turn phosphorylates the light chains of myosin.

This leads to exposure of actin myosin binding site and phosphorylated myosin interacts with actin to bring about muscle contraction.

- In the present study, relationship between serum calcium level and uterine atony was studied, in that 49 patients were taken as study group, who had serum calcium level less than 9 mg/dl among 100 patients.
- In the present study, 47% participants belong to socioeconomic class III, 34% belong to socioeconomic class IV, 19% belong to socioeconomic class II.
- In my study population, 42 of them were primi gravida, 43 were second gravida and 15 were third gravida.
- The gestational age of study population were distributed as follows; 31 of them were within 37-38weeks, 48 of them were within 38-39 weeks, 16 of them were within 39-40 weeks and 5 of them were more than 40 weeks .
- In my study population, 89 of them were on spontaneous labour and 11 of them were induced.
- Also 89 of them had normal vaginal delivery and others went in for instrumental delivery.
- In the present study, 22 of them had Post partum hemorrhage and 78 of them had no Hemorrhage .
- In the present study, 89 participants had normal vaginal delivery of which 18 of them developed PPH (20%), 11 participants had instrumental delivery of which 4 of them developed PPH (30%).
- The serum calcium levels and PPH were studied which showed that, among participants those who had serum calcium levels less than 9 mg/dl , 18 participants (36.7%) developed PPH and 4 of them who had serum calcium level > 9mg/dl developed PPH (7.8%).
- In my study population, those with serum calcium levels <8mg/dl ,5 patients developed PPH in which 4 of them needed blood transfusion; those with serum calcium levels between 8-8.5 mg/dl range 12(70.6%) patients developed PPH in which 2 of needed blood transfusion ,those with serum calcium levels in the range of 8.5-9 mg/dl one(3.7%) participant developed PPH and those with serum calcium level >9mg/dl 4(7.8%) of them developed PPH.
- In my study, serum calcium levels were checked for association with postpartum hemorrhage and it was found that serum calcium levels were found to have statistically significant association with PPH implying that participants having low serum calcium levels have increased chances of atonic PPH as the P value is <0.05(<0.001).
- In the current study, we are of the opinion that all subjects admitted in first and second stage of labour should be tested for serum calcium levels and if less than 8.5 mg/dl should anticipate uterine atonicity.

## CONCLUSION

Results of the current study suggests that low calcium level (8.5 mg/dl) is strongly associated with increased occurrence of PPH hence, is a risk factor for PPH. Our study also concludes that major PPH is more likely associated with serum calcium level less than 8 mg/dl. Our findings suggest that all patients admitted in first and second stage of labor should have estimation of serum calcium level, less than 9 gm/dl are at risk and less than 8 gm/dl are at higher risk to develop uterine atonicity and PPH. Based on the hypothesis of the present study ;CALBLOC- Calcium chloride for prevention of blood loss during intrapartum in cesarean delivery- A Randomized double blind trial to establish the effect of 1 gram intravenous calcium chloride upon quantitative blood loss and uterine tone during cesarean delivery is being conducted .

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