

## Study of Association of PPH due to Uterine Atonicity and Serum Calcium levels

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### ABSTRACT

**Background:** Uterine atonicity stands out as a primary and leading factor contributing to maternal morbidity and mortality. Postpartum hemorrhage (PPH) resulting from uterine atony poses a life-threatening risk. Oxytocic drugs, by elevating intracellular calcium, enhance uterine tonicity, with optimal calcium levels playing a crucial role in facilitating effective uterine contractions. The study aimed to explore the relationship between the concentration of calcium in the bloodstream and the occurrence of PPH associated with inadequate uterine contractions admitted during the 1st and 2nd stages of labour at a tertiary care facility such as the Combined Military Hospital in Dhaka. The study likely involved analyzing data to identify any patterns or connections between serum calcium levels and the incidence of uterine atony-related PPH.

**Methods:** The study follows a randomizing controlled trial (RCT) design within the Department of Obstetrics and Gynecology at Combined Military Hospital, Dhaka. The study duration spans from January 2016 to January 2019, involving a total of 306 subjects. Group A includes those with serum calcium levels between 8-10.4 mg/dl without uterine atonicity, while Group B comprises individuals with serum calcium levels below 8 mg/dl experiencing uterine atonicity, either post cesarean or vaginal delivery. Atonicity features include a soft, distended uterus with a lack of muscle tone.

**Results:** A total of 306 patients were included in the study, with 153 having serum calcium levels exceeding 8 mg/dl and another 153 having levels below 8 mg/dl. Among women with serum calcium levels below 8 mg/dl, 37 patients experienced uterine atonicity. In contrast, it was observed that among women with serum calcium levels exceeding 8 mg/dl, only one patient experienced uterine atonicity. This highlights a potential association between higher serum calcium levels and a reduced likelihood of developing uterine atony in the studied population.

**Conclusions:** The study findings indicate a strong association between low calcium levels and reduced uterine tonicity, establishing low calcium as a significant risk factor for uterine atony.

**Keywords:** Serum calcium, Uterine atony, PPH

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## INTRODUCTION

Uterine atonicity refers to the insufficient contraction of myometrial cells in the corpus uteri in response to the endogenous oxytocin released during delivery. Postpartum hemorrhage (PPH) can ensue due to the unique absence of musculature in spiral arteries, relying on uterine contractions to mechanically compress them for hemostasis. Uterine atony stands as the primary cause of PPH, significantly contributing to maternal morbidity and mortality.<sup>1,2</sup>

PPH is an abrupt and unpredictable factor leading to maternal mortality, affecting two-thirds of women without known risk factors mentioned in exclusion criteria. Oxytocic drugs enhance uterine tone by increasing intracellular calcium, activating muscle proteins to induce effective uterine contractions.<sup>3-5</sup> Intravenous calcium gluconate emerges as a crucial intervention, promoting uterine contraction and playing a vital role in preventing and treating PPH by augmenting uterine tonicity.<sup>6</sup>

Patients with PPH from an atonic uterus unresponsive to conventional oxytocics have shown positive responses to intravenous calcium gluconate, resulting in increased tonicity, marked uterine hardening, reduced bleeding, and PPH control.<sup>7</sup> The regulation of serum calcium status by vitamin D influences smooth muscle function during early labour. Elevated serum calcium levels have been observed in pregnant women delivering vaginally compared to non-labouring term women undergoing cesarean section.<sup>8</sup>

Calcium supplementation before either cesarean section or vaginal delivery has been employed to prevent and treat PPH arising from uterine atonicity.<sup>9</sup> Speculation suggests that higher serum calcium levels play a role in

initiating labor through adequate uterine smooth muscle contractions.<sup>10</sup> The current study aims to investigate the association between serum calcium levels and PPH due to uterine atonicity in a tertiary care hospital setting.

## MATERIALS AND METHODS

**Study Type:** This study was a randomizing controlled trial (RCT) conducted within the Department of Obstetrics and Gynecology at Combined Military Hospital Dhaka, starting from January 2016 to January 2019.

**Actual Enrollment:** A total of 306 subjects were included in this study.

**Allocation:** Randomized

**Intervention Model:** Parallel Assignment

**Intervention Model Description:** Patients participating in the study are randomized using permuted block randomization. Group A received a single dose of either 1 gm of calcium gluconate (administered as 10 ml of a 10% calcium gluconate solution) diluted with 10 ml of distilled water, given intravenously over a 20-minute period and group B received a placebo. This administration occurs at the time of either post vaginal delivery or cesarean section.

Following the administration of either calcium gluconate or placebo, the contractility and tonicity of the uterus are assessed. The evaluation reveals that the uterus exhibits contraction, and there is a noticeable decrease in blood loss. This suggests a positive impact on uterine function, indicating improved tonicity and a reduction in hemorrhagic complications.

Blood samples are collected for serum calcium assessment during the 1st and 2nd stages of labor in cases of vaginal delivery and during

cesarean delivery. Group A comprises patients with serum calcium levels exceeding 8 mg/dl (consisting of 153 patients), while Group B includes patients with serum calcium levels below 8 mg/dl (also comprising 153 patients).

Upon satisfying the inclusion and exclusion criteria, the clinical assessment of uterine tone is conducted in both groups.

#### **Inclusion criteria:**

1st and 2nd gravida, gestational age 37-41 weeks, single-tone pregnancy, both vaginal and caesarian deliveries and women who gave informed written consent were inclusion criteria.

#### **Exclusion criteria:**

Women who refused to give informed written consent, women who require general anesthesia and factors which interfere with the ability of the uterus to contract, such as multiparity, placenta previa, retained placenta, big baby, anemia, hypotension, traumatic PPH, multiple pregnancies, prolonged labour, polyhydramnios, abruptio placenta, mismanagement of labour, gestational diabetes, uterine anomalies, bleeding disorders, chorioamnionitis, previous history of postpartum bleeding, emergency LUCS in labour, women on medications that could affect myometrium contractility, such as nifedipine, labetalol or magnesium sulphate were exclusion criteria.

The study investigated the connection involving serum calcium levels and the occurrence of uterine atonicity. Cases of uterine atonicity were identified based on specific criteria, characterized by a soft, distended uterus with a lack of muscle tone. These cases were observed following the expulsion of the placenta, whether post cesarean operations or vaginal deliveries. Prior to their participation, approval from the institutional ethical committee was obtained.

To assess the incidence of atonicity in both groups, the chi-square test was employed. Furthermore, the study aimed to explore the interrelation between serum calcium levels and the occurrence of atonicity, shedding light on any potential connections between calcium concentration and the development of uterine atonicity.

All participants underwent a comprehensive assessment involving the following components:

A) Detailed medical history including personal history, menstrual history, past and obstetric history, encompassing parity, methods of previous deliveries, and the gestational age of previous miscarriages.

B) Physical examination: After gathering medical history and ensuring adherence to both inclusion and exclusion criteria, a clinical examination was conducted, covering general abdominal and pelvic assessments.

C) Ultrasound examination: This was performed to ascertain the date of pregnancy, viability, and detect any abnormalities.

D) Laboratory investigations: Prior to intervention: Routine investigations, including kidney function, liver function, fasting and postprandial blood sugar, and a complete blood picture. After intervention: Estimation of Hb% was carried out.

E) All patients received 5 IU syntocinone in the third stage of labor after delivery of the baby.

F) Intervention: The first group received calcium gluconate as calcium, while the second group received a placebo for preventing postpartum hemorrhage (PPH).

#### **Assessment of PPH and Uterine Tonicity:**

The assessment of uterine tone in this study followed a structured protocol:

Uterine tone was examined before drug administration, immediately after the delivery of the placenta, and subsequently at five-minute intervals. A 5-point scale was used to rate uterine tone, with 0 indicating a soft boggy uterus and 4 indicating a rock-hard tetanic uterus. Despite the ideal preference for internal probes, they were unavailable for this measurement. A complete blood count was performed twice, once just before delivery and again 24 hours after delivery. The estimation of blood loss began after the suctioning of amniotic fluid, discarding it from the measurement. Post the delivery of the placenta, the volume of blood loss was assessed by weight, involving the subtraction of the dry weight of absorbing materials (pads, sponges, etc.) from the weight of blood-containing materials. The conversion factor of 1 gm weight =1 ml was applied to quantify the blood volume.

It's noteworthy that the study received approval from the Ethics Board of Combined Military Hospital, ensuring adherence to ethical standards and guidelines.

#### Data management and statistical analysis:

The gathered data underwent a meticulous process, including revision, coding, tabulation, and entry into a computer using IBM SPSS Version 25.0. The presentation of data and subsequent analysis were tailored to the specific type of data acquired for each parameter.

#### i. Descriptive Statistics:

- For parametric numerical data, the mean, standard deviation( $\pm$ SD), and range were calculated.
- For non-numerical data, frequency and percentage were determined.

#### ii. Analytical Statistics:

The Fisher's Exact test was utilized to examine the association between two qualitative variables.

## RESULTS

This study was a randomizing controlled trial (RCT) conducted in the Department of Obstetrics and Gynecology at Combined Military Hospital Dhaka, during the period of January 2016 to January 2019. Out of total of 306 patients, 153 had serum calcium levels exceeding 8 mg/dl, and the remaining 153 had levels below 8 mg/dl.

**Table-I:** Distribution of the respondents by socio-demographic characteristics (n=306)

Characteristics		Frequency	Percent
Age group in years	< 20	18	5.88
	21-25	112	36.60
	26-30	126	41.18
	31-35	38	12.42
	36-40	12	3.92
Educational Qualification	SSC or equivalent	68	22.22
	HSC or equivalent	114	37.25
	Graduate or equivalent	106	34.65
	Post graduate or above	18	5.88
Occupational status	Student	42	13.73
	Housewife	187	61.11
	Service	77	25.16
Monthly family income (Tk.)	10000-20000	17	5.55
	21000-50000	143	46.73
	51000-80000	123	40.20
	81000-100000	23	7.52

Table-I depicts that maximum respondents i.e. 126(41.18%) were in the age group 26-30 years. In respect of educational qualification highest number (114, 37.25%) were HSC or equivalent qualified. Maximum respondents (187, 61.11%) were housewives and monthly family income of maximum respondents were Tk. 21000-50000.

**Table-II:** Distribution of the respondents by parity (n=306)

Parity	Frequency	Percent
Primi para	109	35.62
Multi para	197	68.38

**Table-III:** Serum calcium level and number of patients with uterine atonicity (n=306)

Group	Serum Ca level (mg/dl)	Uterine Tonicity		Total n(%)	Significance
		Absent n(%)	Present n(%)		
Group A	8-10.4	01(0.66)	152(99.34)	153(100)	Fisher's Exact Test= 38.4 & p<0.001
Group B	<8	37(24.18)	116(75.82)	153(100)	

Table-III shows that uterine atony was more when serum calcium was <8 mg/dl, compared to serum calcium level >8 mg/dl which was statistically significant (p<0.001).

**Table-IV:** Serum Ca level and number of the patients with PPH (n=306)

Group	Serum Ca level (mg/dl)	PPH		Total n(%)	Significance
		Present n(%)	Absent n(%)		
Group A	8-10.4	01(0.66)	152(99.34)	153(100)	Fisher's Exact Test= 38.4 & p<0.001
Group B	<8	37(24.18)	116(75.82)	153(100)	

Table-IV reveals that PPH was more when serum calcium was <8 mg/dl, compared to serum calcium level >8 mg/dl which was statistically significant (p<0.001).

## DISCUSSION

In this study, a comparison of serum calcium levels with uterine atony and postpartum hemorrhage (PPH), a life-threatening condition were done that may necessitate emergency hysterectomy. The study findings suggest that maintaining an optimum serum calcium level is crucial for effective uterine contractions, and low serum calcium levels may lead to varying degrees of atonic uterus and PPH. Out of the 37 patients with serum calcium levels below 8 mg/dl, uterine atony and PPH developed. Among them, 29 subjects were treated with oxytocics and compression sutures, while 8 patients, unresponsive to routine oxytocics, received IV calcium gluconate (10 ml in 500 ml Ringer Lactate). This intervention resulted in a

firmer and harder uterus, effectively controlling PPH.

The present study proposes that all labour-admitted subjects should undergo testing for serum calcium levels. If the levels are less than 8 mg/dl, anticipating atonicity and infusing IV calcium gluconate could be crucial in preventing PPH. Although not statistically significant, participants with hypotonic uterine contractions displayed mean serum ionized calcium in the sub-physiologic range (hypocalcemia), while those with adequate uterine contractions exhibited levels within the physiologic range (eucalcemia). Similar findings were reported by independent researchers Wattimury et al and Adilia et al, who observed significantly lower mean serum calcium levels in individuals with hypotonic uterine contractions compared to those with adequate contractions.<sup>14,15</sup> It's worth noting that none of these studies utilized intrauterine pressure catheters, considered the gold standard for determining uterine contractility. Further studies are recommended to establish a correlation between serum calcium and atonicity.

Uterotonic drugs such as oxytocin and prostaglandins enhance uterine smooth muscle contraction by increasing intracellular calcium levels.<sup>11,12</sup> Current treatment options for severe hemorrhage due to uterine atony involve uterotonic agents, compression sutures, intrauterine balloon tamponade, pelvic devascularization techniques, vascular occlusion, and, in cases of persistent bleeding, aggressive procedures like abdominal hysterectomy.<sup>13</sup> This study suggests the need for more investigations to explore whether serum calcium levels contribute to atonic uterus and if IV calcium gluconate administration can enhance uterine tone, potentially preventing PPH and avoiding the need for aggressive procedures such as



hysterectomy. Reports associating nifedipine, MgSO<sub>4</sub>, and calcium channel blockers with uterine atony indicate that low serum calcium may indeed play a role in this condition.<sup>4,13</sup>

## CONCLUSION

The study findings indicate a strong association between low calcium levels and uterine atonicity, highlighting low calcium as a significant risk factor for this condition. Consequently, it is recommended that all patients admitted in labor should undergo for serum calcium level estimation. For those with serum calcium levels less than 8 mg/dl, the study suggests the administration of IV calcium gluconate in the second stage of labor or before undergoing lower segment cesarean section (LSCS). This proactive measure aims to prevent postpartum hemorrhage (PPH) and the need for aggressive interventions such as hysterectomy. Implementing this strategy has the potential to reduce maternal morbidity and mortality interconnected with uterine atony.

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**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethical Committee

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