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Original Research Article

Prospective Evaluation of Serum Calcium in Atonic PPH: The Kashmir Experience

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Abstract

Background: Postpartum haemorrhage (PPH) is a leading cause of maternal mortality; uterine atony accounts for most cases. Uterine contractility is calcium-dependent, and hypocalcaemia may predispose to atony. Regional data from Kashmir are limited.

Objective: To evaluate the association between maternal serum calcium and atonic PPH in a tertiary-care setting in Kashmir.

Methods: Consecutive women ≥28 weeks were enrolled at delivery, corrected serum calcium was sampled intrapartum or within 30 minutes postpartum before resuscitation. Atonic PPH was defined as cumulative blood loss ≥1000 mL within 24 hours or any blood loss with hypovolaemia after excluding trauma/retained tissue. Associations were tested with multivariable logistic regression; discrimination was assessed by ROC analysis.

Results: Among 1,584 women, 396 (25.0%) had hypocalcaemia (<8.5 mg/dL). Atonic PPH occurred in 120 (7.6%) overall and was more frequent with hypocalcaemia than normocalcaemia (12.1% vs 6.1%). Each 1.0 mg/dL decrease in calcium increased odds of atony by 35%. Corrected calcium showed fair discrimination; the optimal cut-off was 8.55 mg/dL (sensitivity 62%, specificity 66%, PPV 13%, NPV 96%). Hypocalcaemia was associated with higher blood loss (median 680 vs 520 mL, p<0.001), greater need for escalation beyond oxytocin (28.0% vs 18.0%, p<0.001) and uterine-sparing procedures (6.8% vs 2.9%, p<0.001), more transfusion (9.1% vs 5.0%, p=0.004), more HDU/ICU admission (4.5% vs 2.1%, p=0.01), and longer stay (3 vs 2 days, p<0.001).

Conclusion: Hypocalcaemia is common and independently linked to atonic PPH and worse clinical course. A corrected calcium threshold near 8.55 mg/dL may aid intrapartum risk triage.

Keywords: Postpartum Haemorrhage; Uterine Atony; Serum Calcium; Hypocalcaemia; Kashmir.

Introduction

Postpartum haemorrhage (PPH) remains a major obstetric emergency and a leading cause of maternal mortality worldwide. The World Health Organization estimates that nearly 14 million women experience PPH annually, resulting in ~70,000 maternal deaths; in India, PPH contributes about 19.9% of maternal deaths, with a 2–4% incidence after vaginal birth [1,2].

Atonic PPH due to inadequate uterine contraction accounts for the majority of cases, frequently cited around 75–90% [3]. Definitions have evolved to improve clinical specificity. While primary/early PPH has long been described as blood loss ≥500 mL after vaginal birth or ≥1000 mL after caesarean delivery, the American College of Obstetricians and Gynecologists revised this in 2017 to "cumulative blood loss ≥1000 mL or bleeding associated with signs/symptoms of hypovolemia within 24 hours of birth regardless of route," to reduce misclassification (ACOG, 2017) [4]. Physiologically, immediate postpartum haemostasis depends on effective myometrial contraction to compress the placental bed. Oxytocin the first-line uterotonic acts via myometrial oxytocin receptors to raise intracellular Ca^{2+}, triggering contraction; importantly, spontaneous uterine activity relies more on extracellular (serum) calcium.

Thus, optimal serum calcium is critical for uterine contractility, and hypocalcaemia can blunt contraction and increase the risk of uterine atony and PPH [5-8]. Ionized calcium is the biologically active fraction and the preferred measure for clinical decision-making [9,10]. Accumulating clinical data support an association between lower maternal calcium levels and atonic PPH. In a prospective case-control study from Karnataka,

women with serum calcium <8 mg/dL had markedly higher uterine atony (24/100) than those ≥8 mg/dL (1/100) (χ^2 significant) [11-13]. Similarly, an Egyptian prospective study found uterine atony in 45 women with calcium <8 mg% versus only 5 women with calcium ≥8 mg% and demonstrated a step-down in serum calcium from "no PPH" to "minor" to "major" PPH [14,15]. In a large single-centre observational cohort from Jaipur (n=250 term primigravidas), serum calcium <8.5 mg/dL was significantly associated with PPH overall and with atonic PPH specifically; lower calcium also tracked with greater PPH severity and worse immediate neonatal outcomes (Apgar, NICU admission) ($p \leq 0.01$) [16-21].

Notably for the regional context, a Srinagar study (GMC, Kashmir) reported PPH in 12/50 women with calcium <8.5 mg/dL versus 1/50 with ≥8.5 mg/dL, and more major PPH in the low-calcium group—underscoring a potential signal in North Indian populations [22-24].

Beyond uterine tone, calcium is an essential coagulation co-factor. In a retrospective cohort of 436 women with PPH, hypocalcaemia at diagnosis was substantially more common in severe PPH (51.5% vs 10.6%; P<0.001). In multivariable analysis, ionized Ca^{2+} and fibrinogen were the only independent predictors of severity; each 0.1 mmol/L decrease in Ca^{2+} nearly doubled the odds of severe PPH (OR 1.97, 95% CI 1.25–3.10). Adding Ca^{2+} to fibrinogen improved discrimination for severe PPH (AUC 0.90) [25-27].

Objectives

1. To assess the association between maternal serum calcium levels and atonic postpartum hemorrhage (PPH) in a prospective Kashmiri cohort.
2. To estimate the prevalence of hypocalcaemia among delivering women and compare it between atonic PPH cases and non-atony controls.
3. To examine whether lower serum calcium correlates with greater PPH severity (blood loss, transfusion, additional interventions).
4. To identify a serum calcium cut-off that best predicts risk of atonic PPH in this population.

Material and Methods

This prospective observational study was conducted in the labour wards and operating theatres of a tertiary-care teaching hospital in Kashmir, India. Consecutive eligible women delivering at ≥28 weeks' gestation were enrolled in real time and followed for 24 hours postpartum using a standardized case-record form.

Inclusion Criteria

- Pregnant women at ≥28 weeks' gestation delivering at the study centre during the study period.
- Availability of a serum calcium measurement within the prespecified intrapartum or immediate postpartum window.
- Ability to quantify postpartum blood loss by calibrated drape and gravimetric methods.
- Provision of written informed consent.

Exclusion criteria

- Multifetal gestation.
- Placenta previa or placenta accreta spectrum.
- Known coagulation disorders or chronic kidney, parathyroid, or hepatic disease.
- Calcium/vitamin-D therapy exceeding routine antenatal supplementation.
- Magnesium sulfate administration within 12 hours before delivery for the primary analysis set.
- Genital tract trauma or retained placental tissue as the primary source of bleeding.
- Incomplete clinical or laboratory data for key variables.

A single sample (serum calcium) was obtained in late labour (≤2 hour's pre-birth) or within 30 minutes after delivery, and always before transfusion or massive haemorrhage activation. Total calcium was measured on an automated analyser with simultaneous albumin; corrected calcium (mg/dL) was calculated as measured calcium + 0.8 × (4.0 − albumin). Ionized calcium, when available on blood-gas, was used in sensitivity analyses. Hypocalcaemia was defined a priori as corrected calcium <8.5 mg/dL, with alternative ROC-derived thresholds explored secondarily.

The primary outcome was atonic postpartum haemorrhage (PPH) clinically diagnosed uterine atony with cumulative blood loss ≥1000 mL within 24 hours or any blood loss with hypovolaemic signs, after excluding trauma and retained tissue. Secondary outcomes were PPH severity (500–999 vs ≥1000 mL), cumulative uterotonic dose and escalation, additional uterine-sparing interventions, transfusion (including massive transfusion), and maternal morbidity (HDU/ICU admission, length of stay). Blood loss was quantified by calibrated drapes and gravimetry (1 g = 1 mL); at caesarean, suction volumes were combined with swab weights, subtracting amniotic fluid. Prespecified covariates included age, BMI, parity, gestational age, anaemia, hypertensive disorders, intrapartum fever/chorioamnionitis, induction/au gmentation, labour duration, magnesium sulfate exposure, and mode of delivery.

Result

Table 1: Baseline characteristics of the cohort by serum calcium status

Characteristic	Overall (N=1,584)	Hypocalcaemia <8.5 mg/dL (n=396)	Normocalcaemia ≥8.5 mg/dL (n=1,188)	p value
Maternal age, years (mean ± SD)	27.5 ± 4.8	27.2 ± 4.9	27.6 ± 4.8	0.18
BMI, kg/m² (mean ± SD)	24.2 ± 3.6	24.1 ± 3.7	24.2 ± 3.6	0.64
Primiparity, n (%)	830 (52.4)	214 (54.0)	616 (51.9)	0.41
Gestational age at delivery, weeks (mean ± SD)	38.2 ± 1.6	38.1 ± 1.7	38.2 ± 1.6	0.09
Anaemia (Hb <11 g/dL), n (%)	555 (35.1)	182 (46.0)	373 (31.4)	<0.001
Hypertensive disorders of pregnancy, n (%)	159 (10.0)	48 (12.1)	111 (9.3)	0.08
Induction/augmentation of labour, n (%)	626 (39.5)	162 (40.9)	464 (39.0)	0.51
Mode of delivery Vaginal, n (%)	1,153 (72.8)	286 (72.2)	867 (73.0)	0.77
Mode of delivery Caesarean, n (%)	431 (27.2)	110 (27.8)	321 (27.0)	0.77
Intrapartum fever/ chorioamnionitis, n (%)	67 (4.2)	20 (5.1)	47 (4.0)	0.36
Magnesium sulfate exposure, n (%)	79 (5.0)	24 (6.1)	55 (4.6)	0.23

The mean maternal age was 27.5 ± 4.8 years, with no significant difference between the hypocalcaemia and normocalcaemia groups (27.2 ± 4.9 vs 27.6 ± 4.8 years, p=0.18). Similarly, mean BMI was comparable (24.1 ± 3.7 vs 24.2 ± 3.6 kg/m², p=0.64). The proportion of primiparous women was slightly higher in the hypocalcaemia group (54.0%) compared to the normocalcaemia group (51.9%), though not statistically significant (p=0.41). Mean gestational age at delivery was also similar (38.1 ± 1.7 vs 38.2 ± 1.6 weeks, p=0.09). Anaemia (Hb <11 g/dL) was significantly more prevalent among hypocalcaemic women (46.0%) compared to normocalcaemic women (31.4%, p<0.001). Hypertensive disorders of pregnancy showed a higher proportion in the hypocalcaemia group (12.1% vs 9.3%), but this difference did not reach statistical significance (p=0.08). Induction or augmentation of labour occurred in 40.9% of hypocalcaemic and 39.0% of normocalcaemic women (p=0.51). Mode of delivery was similar between groups, with vaginal delivery rates of 72.2% vs 73.0% and caesarean delivery rates of 27.8% vs 27.0% (both p=0.77). Intrapartum fever or chorioamnionitis occurred in 5.1% of hypocalcaemic women and 4.0% of normocalcaemic women (p=0.36). Magnesium sulfate exposure was slightly more frequent among hypocalcaemic women (6.1% vs 4.6%), but the difference was not statistically significant (p=0.23). In summary, baseline demographic and obstetric characteristics were largely similar across groups, except for anaemia, which was significantly more common among women with hypocalcaemia.

Table 2: Discrimination of corrected calcium for atonic PPH and optimal cut-off

Metric	Value (95% CI)
AUC (ROC) for corrected calcium	0.68 (0.64–0.73)
Optimal cut-off (Youden index), mg/dL	8.55
Sensitivity at cut-off, %	62
Specificity at cut-off, %	66
PPV, %	13
NPV, %	96

Table 3: Secondary outcomes by calcium status

Outcome	Hypocalcaemia (n=396)	Normocalcaemia (n=1,188)	p value
Cumulative blood loss, mL—median (IQR)	680 (520–920)	520 (420–720)	p<0.001
Escalation beyond oxytocin, n (%)	111 (28.0)	214 (18.0)	p<0.001
Additional uterine-sparing intervention†, n (%)	27 (6.8)	34 (2.9)	p<0.001
Any blood product transfusion, n (%)	36 (9.1)	59 (5.0)	p=0.004
Massive transfusion‡, n (%)	7 (1.8)	8 (0.7)	p=0.06
HDU/ICU admission, n (%)	18 (4.5)	25 (2.1)	p=0.01
Length of stay, days—median (IQR)	3 (2–4)	2 (2–3)	p<0.001

†Balloon tamponade, compression sutures, devascularization procedures. ‡≥4 PRBC within 1 h or ≥10 within 24 h.

Table 3 presents maternal outcomes in relation to serum calcium status. Women with hypocalcaemia experienced significantly greater cumulative blood loss compared to those with normocalcaemia (median 680 mL [IQR 520–920] vs 520 mL [IQR 420–720], p<0.001). Escalation beyond first-line oxytocin was more frequent in the hypocalcaemia group (28.0% vs 18.0%, p<0.001), as was the need for additional uterine-sparing interventions such as balloon tamponade, compression sutures, or devascularisation (6.8% vs 2.9%, p<0.001). Transfusion requirements were also higher among hypocalcaemic women, with 9.1% requiring any blood product compared to 5.0% of normocalcaemic women (p=0.004). Massive transfusion was observed in 1.8% of hypocalcaemic versus 0.7% of normocalcaemic participants, a difference that approached but did not reach statistical significance (p=0.06). Maternal morbidity, as reflected by HDU/ICU admission, was significantly greater in the hypocalcaemia group (4.5% vs 2.1%, p=0.01). Length of hospital stay was also prolonged, with hypocalcaemic women staying a median of 3 days (IQR 2–4) compared to 2 days (IQR 2–3) among normocalcaemic women (p<0.001).

Discussion

In this prospective Kashmiri cohort (N=1,584), hypocalcaemia (<8.5 mg/dL) was common (25.0%) and independently associated with atonic PPH: 12.1% vs 6.1% in normo-calcaemic women (adjusted OR 1.92, 95% CI 1.29–2.85). Discrimination was modest (AUC 0.68), and a threshold of 8.55 mg/dL balanced sensitivity (62%) and specificity (66%). Clinically, hypocalcaemia tracked with higher blood loss, greater escalation beyond oxytocin, more uterine-sparing procedures, more transfusion, higher HDU/ICU admission, and longer stay.

Our findings align with and extend prior regional and international evidence. A study reported PPH in 12/50 women with calcium <8.5 mg/dL versus 1/50 with ≥8.5 mg/dL, and more major PPH in the low-calcium group an effect direction and crude magnitude consistent with our adjusted association in a much larger sample (Sheema, Rafiq S, 2019) [20].

Clinically, hypocalcaemia tracked with higher blood loss, greater escalation beyond oxytocin, more uterine-sparing procedures, more transfusion, higher HDU/ICU admission, and longer stay. Our findings are consistent with and extend prior regional and international evidence. A case control study reported PPH in 12/50 women with calcium <8.5 mg/dL versus 1/50 with ≥8.5 mg/dL, and more major PPH in the low-calcium group an effect direction and crude magnitude consistent with our adjusted association in a much larger sample (Sheema, Rafiq S, 2019) [20].

Mechanistically, our observation that lower calcium tracks with escalation of therapy and transfusion fits external data that link ionised calcium to bleeding severity. In a 436-patient cohort, Epstein D et al., (2022) [29] showed hypocalcaemia at PPH diagnosis in 51.5% of severe cases vs 10.6% in non-severe, and each 0.1 mmol/L fall in Ca^{2+} nearly doubled the odds of severe PPH; adding Ca^{2+} to fibrinogen improved model AUC to 0.90. Beyond association, interventional signals though not definitive support biological plausibility. A study by Oguaka VN et al., (2019) [30] synthesised prior observations that women with low postpartum calcium had higher PPH risk and reported lower ionised calcium among atony-PPH cases (mean 1.0 ± 0.35 mmol/L), while older studies noted improved uterine tone and bleeding reduction after intravenous calcium gluconate in refractory atony. In parallel, an Egyptian analysis recommended screening labouring women and considering IV calcium when serum levels are <8 mg%, echoing our threshold-based risk stratification.

Taken together, the consistency across settings Srinagar's [20] high crude risk at low calcium, Jaipur's [21] severity gradient (mean 7.47 mg/dL in major PPH), our adjusted Kashmiri estimates (aOR 1.92), and the international ionised-calcium literature on haemostatic severity supports a coherent pathophysiological narrative: suboptimal maternal calcium compromises myometrial contractility and may worsen coagulopathy, raising the likelihood and intensity of atony-related haemorrhage.

Strengths of our study include prospective design, standardized timing of sampling before major resuscitation, objective blood-loss quantification, and adjusted modelling. Limitations are: use of total-corrected rather than ionised calcium in the primary analysis (though the direction is corroborated by ionised-calcium studies), single-centre design, and only fair discrimination of calcium alone (AUC 0.68). These echo Epstein et al.'s [29] conclusion that calcium is informative but best combined with other predictors (e.g., fibrinogen).

Conclusion

In this large prospective cohort, hypocalcaemia (<8.5 mg/dL) was common and independently related to atonic PPH, with higher odds of atony (aOR 1.92) and worse clinical course greater blood loss, more escalation beyond oxytocin, more procedures and transfusions, and longer stay.

Practically, incorporating a timely calcium measurement into intrapartum risk assessment and

focusing vigilance when corrected calcium is <8.5 mg/dL may aid early identification and targeted management of women at risk of atony-related haemorrhage in our setting.

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