Egyptian Journal of Medical Research

Print ISSN: 2682-4396 / Online ISSN: 2682-440X

Original article

The Relation between serum calcium levels and Atonic Postpartum Hemorrhage

Sayed.M.Sayed , Abeer Mabrouk Bakry, Ashraf Samir Faheem

Obstetrics and Gynecology department, Faculty of Medicine, Beni-Suef University, Egypt.

Article Info

Article history:

Received 11 January 2023

Accepted 7 February 2023

Corresponding Author:

Abeer Mabrouk Bakry

amabrouk2211@gmail.com

Keywords:

Serum calcium

PPH

uterine atony.

Abstract

Objective : The goal of this study is to find a link between the amount of calcium in the blood and how stiff the uterus is and how much blood is lost in women who are in the first and second stages of labour. **Methods :** Study design is cross sectional study in department of Obstetrics & Gynaecology Beni-suif University Hospital, Duration of study is from July 2021 till November 2021. Number of subjects studied: 180 women, with intrapartum estimation of serum calcium level and relationship to atonic primary PPH after vaginal delivery or caesarian delivery. Atonicity is characterised by a soft, swollen uterus and a lack of muscle tone. **Results :** 180 clients in total were looked at. 45 women who had a calcium level in their blood that was less than 8 mg% developed uterine atonicity. Only five of the women who had a serum calcium level of more than 8 mg% had uterine atonicity.

Conclusions: Our results showed that, reduced calcium level is strongly linked to uterine atony and is therefore a risk factor for it.

1. Introduction:

Postpartum haemorrhage (PPH), which is the most common cause of obstetric bleeding, is an emergency that can happen after a vaginal or caesarean delivery. Obstetric haemorrhage is one of the five main causes of maternal death in both high-income and low-income countries [1]. It is also one of the main causes of maternal illness. There is a lot of reason to think that the rate of PPH is going up around the world. The main reason for this rise is that uterine atony is becoming more common [2].

PPH can be mild (500–1000 ml of blood loss) or severe (more than 1000 ml blood loss). PPH has also been put into two groups: primary PPH, which happens within 24 hours of giving birth and is caused by uterine atony in more than 80% of cases, and secondary PPH, which happens 24 hours to 12 weeks after giving birth [3].

Having the right amount of calcium is very important for the uterine muscle to contract. When serum calcium levels are low, muscles don't work as well. It has been shown that myometrial contraction can be increased by increasing calcium levels in the body or by optimising physiological calcium levels in the case of augmented prolonged labour, which increases the risk of weak uterine contractions and PPH[4].

Total calcium in the serum should be between 8.0 and 10.2 mg%, or 2.2 and 2.5 mmol/L. About half of this total is ionised calcium, which is usually between 4.5 and 5.6 mg% (1.05 and 1.3 mmol/L) [1]. The total calcium level in the blood may not be a good indicator of the ionised calcium level. The physiological state is based on how much ionised calcium is in the body. Because of this, measuring the ionised calcium is better for making clinical decisions [5].

Calcium does what it does by getting the muscle proteins to work and making the uterus contract. Intravenous calcium gluconate can make the uterus contract and helps prevent and treat PPH by making the uterus stronger. Patients with PPH due to an atonic uterus who didn't respond

to the usual oxytocics did well with intravenous calcium gluconate, which made the uterus harden and made the PPH go away [6]. It was thought that the higher calcium levels in the blood could have helped start labour, which happens when the smooth muscles in the uterus contract enough. A low serum calcium level can affect how well the smooth muscles of the uterus contract, which can lead to an atonic uterus and PPH [7]. So, this study is being done to find out if there is a link between PPH and serum calcium levels in a tertiary care hospital.

2. Aim of the work:

The goal of this study is to look at how uterine atony and primary postpartum haemorrhage are related to serum calcium levels.

❖ **Subjects and Methods Study Design:**

Observational prospective study.

❖ **Study Site:**

The study was done at Beni-Suef University hospital's Department of Obstetrics and Gynecology.

❖ **Study period:**

The study was conducted from July 2021 till November 2021.

❖ **Study Population:**

The study population were recruited when they are admitted for delivery, they were asked by verbal consent to participate in the study after been evaluated to ensure fulfilling inclusion and exclusion criteria.

Sample size:

G*Power Version 3.1.9.2 [computer software] (Franz Faul, Kiel, Germany) was used to figure out how many samples were needed for a chi-square test with an alpha error probability of 0.05, a power of 0.95, a medium effect size (w = 0.3), and 1 degree of freedom. Based on the above assumptions, the number of people who should be in the sample is 145. Using the 25% dropout rate, the smallest possible sample size is 180 patients.

❖ **Inclusion criteria:**

1. Age: 20 – 40 years.
2. Both vaginal and caesarian deliveries.
3. Spontaneous labor onset.
4. Term pregnancies based upon the date of last day of last menstrual period, confirmed by ultrasonographic scan.

❖ **Exclusion criteria:**

There are things that make it hard for the uterus to contract.

1. Grand multipara (≥5).
2. Placenta previa.
3. Retained placenta.
4. Macrosomia.
5. Anemia

6. More than one pregnancy.
7. Traumatic postpartum hemorrhage.
8. Abnormal labour (precipitate labour, prolonged labour, obstructive labour).
9. Polyhydramnios.
10. Abruptio placenta.
11. Gestational diabetes, preeclampsia, chronic renal or liver diseases,
12. Uterine anomalies.
13. Bleeding disorders.
14. Ante- or intra-partum hemorrhage.
15. Women who require general anesthesia.
16. Chorioamnionitis.
17. Women taking drugs like nifedipine and magnesium sulphate, which may have an effect on myometrium contractility, are at an increased risk of having a miscarriage.

❖ **Study Procedure:**

All participants will be subjected to:

☒ **Full history taking** including:

✓ Personal, past, family and surgical history.

✓ Previous medical treatment.

☒ Obstetric history (parity, methods of previous deliveries)

☒ **Careful physical examination** to ensure fulfilling both inclusion and exclusion criteria, including: general abdominal and pelvic examination.

☒ **Trans-abdominal ultrasonography:** The ultrasound equipment used was (Toshiba Xario 200) with 6 - 9 MHz . To ensure date of pregnancy, viability and any abnormalities.

☒ **Laboratory investigations:** will include :

- Routine investigations including: kidney function, liver function, random blood sugar and complete blood count, One hour before surgery, the hematocrit will be measured, and 24 hours after surgery, the hematocrit will be checked.
- Serum Calcium levels: 5 ml of blood samples (The same sample was taken for routine investigations) was collected from each woman in labour and collected from each woman one hour before cesarean section , allowed to clot, and centrifuged. The total and ionised calcium content of the serum was finally measured by (Beckman Coulter AU 480).

☒ After the baby is born, the third stage of labour will be "actively managed" by giving the mother 10 I.U. of intramuscular oxytocin within 1 minute of the birth and delivering the

placenta by pulling on the cord in a controlled way. The birth weight of the baby and how it was born will be written down. Over the next 24 hours, the participants will be watched for signs of primary PPH.

PPH is defined as the loss of 500 ml or more of blood from the genital tract within 24 hours after vaginal delivery and 1000 ml or more after CS. PPH can be classified into minor PPH (500 to 1000 ml) and major PPH (more than 1000ml).[8] .

After the uterine incision, a nurse was in charge of collecting blood and amniotic fluid in two separate suction sets. She was also in charge of weighing surgical towels before and after the operation and writing down the number and difference in weight of the towels. (before and after CS), (We calculated 1gm of weight difference equal to 1ml blood loss),and amount of blood in suction unit was recorded.

The amount of postpartum blood loss in the first 24 hours after delivery was estimated by the usual clinical visual assessment, the number and weight of soaked pads, the drop in haemoglobin level (preoperative hematocrit will be measured one hour before surgery, and postpartum hematocrit will be measured 24 hours after surgery), and any blood transfusions that were given.

Loss of tone in the uterine muscle or the inability of the myometrium to contract after the placenta has been delivered, along with bleeding from the placental site, are signs of uterine atony.

❖ **Outcomes:**

The primary outcome measure is to identify the relation between serum calcium levels (total and ionized) and primary postpartum haemorrhage due to uterine atony.

Normal Range of serum calcium (David A. Goldstein1990):

Total Calcium ranges from 8.5 to 10.5 mg/dl (4.3 to 5.3 mEq/L or 2.2 to 2.7 mmol/L)

Ionized Calcium ranges from 4.5-5.6 mg/dL or 1.05-1.3 mmol/L.

The secondary outcomes are:

✓ Relation of maternal serum calcium to fetal outcome (APGR at 1and 5minutes,NICU admission and neonatal death) and maternal outcome .

✓ Relation between serum calcium level and mode of delivery (e.g . in primipara) .

❖ **Ethical Considerations**

✓ Approval by the institution's ethics committee; Approval No:FMBSUREC/06072021/Bakry

✓ verbal consent from each person.

Informed consent is given after the purpose of the study is explained to people who might take part. Participants can choose whether or not to take part, and we tell them that their choice won't affect the quality of care they get.

❖ **The statistical Analysis:**

When it makes sense, data will be described statistically in terms of mean standard deviation (SD), frequencies (number of cases), and relative frequencies (percentages).

The Kolmogorov-Smirnov test is used to figure out if the continuous variables in the demographic data are spread out in a normal way. The independent-samples t test (when the data showed a normal distribution) and the Mann-Whitney U test (when the data did not show a normal distribution) were used to compare numerical variables between the study groups.

Chi square (2) test is used to compare categorical data, and Fisher's Exact Test is used when sample sizes are small.

A probability value (P value .05) is used to decide if something is statistically important.

The Statistics Package for Social Science will be used to process and analyse the data that is collected (version 22; SPSS Inc).

3. Results:

Table (1): Mean age of the studied cases:

	N	Minimum	Maximum	Mean	Std. Deviation
Age	180	18.0	40.0	27.333	4.7871

This study includes 180 females with a minimum age 18 yrs., and a maximum age of 40 yrs. The mean age of the studied females was 27.33 ± 4,78

Table (2): Relation between serum calcium level and mode of delivery

	serum Ca ≤ 8.5mg/dl Frequency (%)	Serum Cal ≥ 8.5mg/dl Frequency (%)	Test of significance	P-value
Vaginal Delivery	26 (32.9 %)	42 (41.6 %)	Chi square (χ^2) test $\chi2(1, N= 180) = 1.42$	0.234
Cesarean Section	53 (67.1%)	59 (58.4%)		

This table shows that there is no statistical significance of the mode of delivery between patients with normal and low Ca level

Table (3): Distribution of the PPH cases according to the type

Cases No. 180	Count	Column N %
No PPH	130	72.2%
Minor PPH	40	22.2%
major PPH	10	5.6%

This table showed that the number of patients who were presented by No PPH were 130 cases while those who presented by minor PPH were 40 cases and those who were presented with major PPH were only 10 cases

Table (4): Distribution of the studied cases according to the PPH and Ca level:

Groups	No PPH		Minor PPH		Major PPH	
	No.	%	No.	%	No.	%
serum Ca less than 8.5mg/dl	**34**	**43%**	**35**	**44.3%**	**10**	**12.7%**
Serum Cal more than 8.5mg/dl	**96**	**95%**	**5**	**5%**	**0**	**0%**

This table shows that 34 (43%) of the cases presented with no PPH, 35 (44.3%) of the cases presented with minor PPH and 10 (12.7%) of the cases presented by major PPH showed Ca level less than 8.8 gm/dl.

Table (5): Association between Ca level and postpartum hemorrhage:

PPH	N	Mean of serum Calcium	Std. Deviation	P-value
No PPH	130	8.60	0.87	0.001*
Minor PPH	40	7.77	0.012	
Major PPH	10	6.66	0.5	

*. The mean difference is significant at the 0.05 level.

This table showed that serum calcium levels in cases with No PPH were higher than cases with PPH, and cases with minor PPH showed lower level of Ca than cases with no PPH and cases with major PPH showed lower Ca level than cases with no PPH and P-value was (0.001).

Table (6): Relation between maternal Serum calcium level and fetal outcome.

Groups / Variables	serum Ca ≤ 8.5mg/dl Mean (SD) or Frequency (%)	Serum Cal ≥ 8.5mg/dl Mean (SD) Or Frequency (%)	Test of significance	P-value
Birth weight, g	2867(486)	2870 (443)	Independent-samples Mann-Whitney U test	0.88
Apgar Score	7.5 (1.68)	8.2 (0.89)	Independent-samples Mann-Whitney U test	0.023
NICU admission	17(21.5%)	5(5%)	Chi square (χ^2) test $\chi2(1, N= 180) = 11.34$	0.001
Neonatal LOS	9 (5.39)	8.4(5.4)	Independent-samples Mann-Whitney U test	0.94

This table showed that :-

There is statistical significance between maternal serum calcium level and fetal outcome regarding Apgar score and percentage of NICU admission (P_value 0.023 _ 0.001).

There is no statistical significance between maternal serum calcium level and fetal outcome regarding Birth weight and Neonatal LOS (P_value 0.88 _ 0.94).

- LOS (length of stay).

Table (7): Relation between maternal serum calcium level and neonatal complication

	serum Ca ≤ 8.5mg/dl Frequency (%)	**Serum Cal ≥ 8.5mg/dl Frequency (%)**	**Test of significance**	**P-value**
RDS	7 (8.9%)	3 (3%)	Chi square (χ^2) test $\chi 2(1, N= 180) = 12.41$	0.053
NEC	1 (1.3%)	0		
IVH	1 (1.3%)	0		
Early sepsis	5 (6.3%)	1(1%)		
Convulsion	2 (2.5%)	1 (1%)		
Neonatal jaundice	1 (1.3%)	0		

This table showed that there is no statistical significance between maternal serum calcium level and neonatal complication .

- RDS (Respiratory Distress Syndrome)
- NEC (Necrotizing enterocolitis)
- IVH (Intraventricular Hemorrhage).

4. Discussion:

This study includes 180 females with a minimum age 18 yrs., and a maximum age of 40 yrs. The mean age of the studied females was 27.33 ± 4,78. Most of studied cases (57) shows parity of one followed by 55 cases showed parity of 2 and 41 cases showed parity of 3. Most of cases 112 (62.2) underwent Cesarean section while 68 (37.8) underwent vaginal delivery.

Based on our study, 45 of the 180 women who had serum calcium of less than 8.5% had uterine atonicity (35patients developed minor PPH and 10 patients developed major PPH). Only 5 of the women whose serum calcium was more than 8.5% did not have uterine atonicity. This means that uterine atony is more common when serum calcium is less than 8.5 mg% than when serum calcium is more than 8.5 mg%, which is statistically significant (Pvalue at the level of 0.05).

Epstien et al. [9] found that, out of 436 patients, 68 (15.6%) had severe PPH, 74 (17%) had Hypocalcaemia (Ca2 4.65mg/dl, and 20 (4.6%) had Ca24.01mg/dl. At the time of the PPH diagnosis, 51% of patients were in the severe bleeding group with hypocalcemia, while 10.6% were in the non-severe PPH group (P<0.001). 35 (47.3%) of the 74 women who had hypocalcaemia when they were diagnosed with PPH went on to develop severe PPH. This was compared to 33 (9.1%) of the 362 women who had normal Ca2 (P<0.001).

The results of this study are very similar to the results of a number of other studies. Premalahta HL et alstudy .'s of 200 women showed that. 100 women whose serum calcium was more than 8 mg% and 100 clients whose serum calcium was less than 8 mg%. 24 women who had a calcium level in their blood that was less than 8 mg% developed uterine atonicity. Only one of the women who had a serum calcium level of more than 8 mg% had uterine atonicity. Chi square test X2=0.04(<0.05). This means that uterine atony is more common when serum calcium is less than 8 mg% than when serum calcium is more than 8 mg%. This is statistically significant. Premalahta HL et al [10]

Our study's results are also the same as those of Oguaka et al. [11],

Ten of the 16 women with primary PPH were caused by uterine atony. The average serum ionised calcium level of the people who didn't have primary PPH was higher (4.4–5.4 mg/dl) than that of the people who did have primary PPH caused by uterine atony (2.62–5.41 mg/dl). In this study, the atony could have been caused by the fact that the pregnant women with primary PPH from uterine atony had lower levels of calcium in their blood. That was how the

number of women with primary PPH from uterine atony and those who didn't have it was split up by their serum calcium level. The average calcium level in the blood of the 124 (92.53%) women who did not have a postpartum haemorrhage was 4–5mg/dl. In contrast, the average calcium level in the blood of the 10 (7.46%) women who had PPH due to uterine atony was 2.62–5.41mg/dl. There was a statistically significant difference between the levels (0.05).

In the present study, there is no statistical significance of the mode of delivery between patients with normal calcium level(42 patient with vaginal delivery and59 with cesarean section) and low calcium level (26 with vaginal delivery and 53 with cesarean secion) (P_value 0.234)

In contrast, Oguaka et al. [11] found that out of 140 patients, 16 women with spontaneous vaginal delivery had primary PPH, 10 of which were caused by uterine atony. The mean serum ionised calcium level of the participants without primary PPH was higher (4.4–5.4 mg/dl) than that of the participants with primary PPH from uterine atony (2.62–5.41 mg/dl).

In our study, there is statistical significance between maternal serum calcium level and fetal outcome regarding the Apgar score and percentage of NICU admission (P_value 0.023_0.001),there is no statistical significance between maternal serum calcium level and fetal outcome regarding the Birth weight and Neonatal LOS (P_value 0.88_0.94) and also there is no significance between maternal serum calcium level and Neonatal complication (P_value 0.053).

Kant et al. [12] found that the prevalence of hypocalcemia among a sample of 696 patients was 24%; the mean serum calcium level was lower in pregnant women who gave birth to babies with low birth weights compared to women whose babies were born at a healthy weight. This distinction was clearly discernible from the numbers. The mean serum calcium level did not differ substantially across the other pregnancy outcomes, The prevalence of preeclampsia was 12.6% in both the hypocalcaemic and normocalcaemic groups. Preterm birth was more common among those with hypocalcemia (21.93%) than those with normal calcium levels (17.0%), although the difference was not statistically significant (p-value – 0.23). There was no statistically significant difference between the hypocalcaemic and normocalcaemic groups, despite the fact that the prevalence of low birth weight was higher in the hypocalcaemic group (24.78%) than in the normocalcaemic group (17.0%). (pvalue – 0.06). Similar

results were found when comparing the prevalence of newborn death in the hypocalcaemic and normocalcaemic groups (p-value – 0.25).

5. Conclusions and Recommendations

Based on our findings, low calcium level can be considered a risk factor for uterine atony. The prevention of PPH and the reduction of maternal morbidity and mortality necessitates the estimation of serum calcium in all patients admitted in labour, and the administration of intravenous calcium gluconate to those with serum calcium less than 8 mg% during the second stage of labour or prior to LSCS. We also recommend further assessment in larger sample sizes to confirm our results.

6. References:

1. Adinma J .,Okafor C., Udigwe G. et al (2019):Serum calcium in primary postpartum hemorrhage, EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH ejpmr, ,6(10), 53-58.
2. Callaghan Wn, Kuklina EV, Berg CJ (2010): Trends in Post partumhaemorrhage: United States, 1994-2006. Am J ObstetGynecol ; 202:353-356.
3. Neb H, Zacharowski K, Meybohm P (2017): Strategies to reduce blood product utilization on obstetric practice. Curr.Opin.Anaesthesiol ; 30: 294-299.
4. Sheema and Suhail Rafiq (2018): A Study of Relationship between Serum Calcium levels and the Occurrence and Severity of Post-Partum Hemorrhage, International Journal of Science and Research (IJSR), Volume 8 Issue 2,727-729.
5. Bansal T, Sarla H. (2013) Hyperventilation causing symptomatic hypocalcaemia during labour in a parturient, Egyptian Journal of Anaesthesia; 29: 333-335.
6. Yu H, Ling Y.(2009) Calcium supplementation before cesarean section in prevention and treatment for postpartum hemorrhage due to uterine inertia. Journal of Hainan Medical College. ;15(6):646-7
7. Reddi Rani and Jasmina Begum (2017): Recent Advances in the Management of Major Postpartum Haemorrhage. Journal of Clinical and Diagnostic Research: JCDR ; 11(2): QE01-QE05.
8. Green-top Guideline No. 52, 2016 : Mavrides E, Allard S, Chandraharan E, Collins P, Green L, Hunt BJ, Riris S, Thomson AJ on behalf of the Royal College of Obstetricians and Gynaecologists. Prevention and management of postpartum haemorrhage. BJOG ;124:e106–e149

9. Epstein, D., Solomon, N., Korytny, A., Marcusohn, E., Freund, Y., Avrahami, R., Neuberger, A., Raz, A. and Miller, A., (2021). Association between ionised calcium and severity of postpartum haemorrhage: a retrospective cohort study. British Journal of Anaesthesia, 126(5), pp.1022-1028.
10. HL, P., & Krishnegowda, R. (2016). Prospective study of association of uterine atonicity and serum calcium levels. International Journal Of Reproduction, Contraception, Obstetrics And Gynecology, 2221-2223. https://doi.org/10.18203/2320-1770.ijrcog20162097 .
11. Oguaka, Victor & Adinma, Joseph & Okafor, Charles & Udigwe, Gerald & Adinma-Obiajulu, ND & Edet, Mark. (2019). Serum calcium in primary postpartum hemorrhage.European journal of pharmaceutical and medical research. 6. 53-58.
12. Kant S, Haldar P, Gupta A, Lohiya A (2019). Serum calcium level among pregnant women and its association with pre-eclampsia and delivery outcomes: A cross-sectional study from North India. Nepal J Epidemiol;9(4); 795-803.