

**ORIGINAL RESEARCH****Calcium serum concentration among pregnant women in a tertiary hospital and its satellite hospital in Medan, Indonesia****Muhammad Agung Khoiri**<sup>ID</sup>\*, **Sarma N Lumbanraja**<sup>ID</sup>, **Duddy Aldiansyah**<sup>ID</sup>, **M. Fidel Ganis Siregar**<sup>ID</sup>, **Makmur Sitepu**<sup>ID</sup>, **M. Rhiza Tala**<sup>ID</sup>

Department of Obstetric and Gynecology, North Sumatra University, Medan, Indonesia

**ABSTRACT**

**Objectives:** This study aimed to evaluate serum calcium concentration in pregnant women who made prenatal appointments to Obstetric and Gynecologic Outpatient Clinics at Adam Malik General Hospital, Medan, Indonesia, and its satellite hospitals.

**Materials and Methods:** This study was a descriptive study with a case series approach. The case series of the study included 35 pregnant women in their second or third trimester chosen by consecutive sampling method.

**Results:** The mean calcium serum level of pregnant women in the second and third trimester was  $9.12 \pm 0.49$  mg/dl and  $8.97 \pm 0.26$  mg/dl, respectively. The mean calcium level of pregnant women aged <20, 20-35, and >35 years old were  $9.0 \pm 0.28$  mg/dl,  $9.07 \pm 0.44$  mg/dl, and  $8.96 \pm 0.06$  mg/dl, respectively.

**Conclusion:** This study found that the mean calcium serum level in pregnant women who made prenatal appointments at Haji Adam Malik General Hospital, Medan, Indonesia, was normal.

**Keywords:** Calcium; pregnancy; second trimester; third trimester; maternal health

\***Correspondence:** Muhamad Agung Khoiri, Jl. Perjuangan Komp. Anthurium No. 18 Setia Budi, Medan, Indonesia. E-mail: muhammadagungkhoiri717@gmail.com

**ABSTRAK**

**Tujuan:** Mengetahui gambaran konsentrasi kalsium serum pada wanita hamil yang dirawat di Rumah Sakit Umum Pusat Haji Adam Malik, Medan, Indonesia, dan RS Jejaring.

**Bahan dan Metode:** Penelitian ini merupakan penelitian deskriptif observasional dengan pendekatan case series, dimana kasus serial dalam penelitian ini adalah 35 wanita hamil pada trimester dua dan tiga yang dipilih secara consecutive sampling.

**Hasil:** Dijumpai rerata kadar kalsium darah pada usia kehamilan trimester 2 adalah  $9,12 \pm 0,49$  mg/dl dan pada usia kehamilan trimester 3 adalah  $8,97 \pm 0,26$  mg/dl. Kadar kalsium rerata pada subjek penelitian usia <20 tahun, 20-35 tahun dan >35 tahun adalah  $9,0 \pm 0,28$  mg/dl,  $9,07 \pm 0,44$  mg/dl, dan  $8,96 \pm 0,06$  mg/dl, berturut.

**Simpulan:** Penelitian ini menemukan rerata kadar kalsium ibu hamil yang mengikuti kontrol kehamilan di poliklinik RSUP Haji Adam Malik Medan, Indonesia, adalah masih dalam rentang normal.

**Kata kunci:** Kalsium; kehamilan; trimester dua; trimester tiga; kesehatan ibu

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## INTRODUCTION

In 2010, it was estimated that up to 287,000 women died during pregnancy and childbirth, with the majority of deaths attributed to maternal health issues. Gestational hypertension disease accounted for 2-8% of complications in pregnancy and attributed to low birth weight, preterm birth, and maternal mortality.<sup>1</sup> Pregnancy-related hypocalcaemia is still a common laboratory and clinical finding. Throughout pregnancy, a number of hormonal changes contribute to the relatively constant serum calcium levels. Despite the fact that several studies have found that ionized serum concentrations are rarely altered throughout pregnancy and lactation, if appropriate replenishment is not promoted, these concentrations are typically kept steady at the expense of the maternal skeletal storage. Balk et al. and Cormick et al. both conducted systematic reviews, and they both found that women in low- and middle-income countries are much more likely to have inadequate calcium intake and consequently low serum calcium concentrations.<sup>2,3</sup>

Meanwhile in Indonesia, pregnant women with low calcium level are still prominent. Ana Nurjannah's study in Palembang city from 2019 found that 66.7%; 40% and 41.7% of pregnant women in first, second and third trimester had hypocalcemia, respectively.<sup>4</sup> Other study conducted by Devi Kurniasari in Bandar Lampung showed that as many as 60% of pregnant women with preeclampsia had lower calcium level compared with 33% normal pregnant women.<sup>5</sup> Study in Makassar also found low calcium level in first and second trimester pregnant women as low as  $7.79 \pm 0.44$  and  $7.64 \pm 0.36$  mg/dL, respectively.<sup>6</sup>

Pregnant women's average intake of vitamin D and calcium was 1.1 g and 433.3 mg, respectively, according to a study by Bardosono et al. involving 143 healthy first-trimester pregnant women living in Jakarta. This intake was 100 percent and 97.9 % below the recommended daily allowances for both nutrients.<sup>7</sup> Aji et al. and Sari et al. did additional research in North Sumatra and West Sumatra, and their findings revealed that more than 80% of participants had insufficient vitamin D intake, with an average intake of vitamin D ranging between 5.24 and 7.29 g/day.<sup>8,9</sup> According to a systematic review from three studies by Hartriyanti et al., pregnant women's average calcium consumption was between 45% and 80% below the estimated average requirement (EAR). Intakes of calcium averaged 536.23 mg, 614.41 mg, and 360 mg in these studies, respectively.<sup>10</sup>

In some studies, a relationship between hypocalcemia and high blood pressure has been discovered. Calcium

intake has been found to be inversely related to the occurrence of gestational hypertension in some studies. Low calcium intake during pregnancy may stimulate parathyroid hormone secretion, resulting in an increase in intracellular calcium and, as a result, uterine smooth muscle contractibility. This chain of events could result in preterm birth, spontaneous abortion, or renin release from the kidney, which causes vasoconstriction and sodium and fluid retention. These physiological changes are capable of developing gestational hypertension and preeclampsia. According to studies, low serum calcium levels were found in women who already had preeclampsia, and calcium supplementation could reduce the risk of preeclampsia as well as maternal mortality and morbidity.<sup>11</sup>

Low calcium intake during pregnancy has been linked to a calcium metabolic disorder in the pregnant women, which may affect fetal development. Calcium supplementation in preeclampsia prevention was found to increase fetal birth weight and reduce the prevalence of neonatal intensive care, compared to the untreated group.<sup>12</sup>

Early detection of pregnant women's calcium levels can have an impact on the prevention of complications above. Based on the data on the description of calcium levels that has been done previously, we conducted a study aimed to evaluate maternal serum calcium level concentration among pregnant women in Obstetrics and Gynecology outpatient clinic in Haji Adam Malik General Hospital Medan and satellite hospitals in Medan. Haji Adam Malik General Hospital was chosen because of its status as tertiary health facility and main referring hospital in Sumatera Island that may represent pregnancy in variable conditions.

## MATERIALS AND METHODS

### Subjects and design of the study

This study was a descriptive study with a case series approach. Research was conducted in Obstetric and Gynecologic Outpatient Clinic of Haji Adam Malik General Hospital Medan, North Sumatra, Indonesia. The study population was healthy pregnant women who took antenatal care at hospital in their first or second trimester. The inclusion criteria are pregnant women who were in their first or second trimester and aged 18-40 years old. In contrast, pregnant women with thyroid and parathyroid disorder, impaired liver function, or renal disorder were excluded from this study. Samples were chosen by non-probability sampling with consecutive sampling techniques, which describes a process of conducting research including all the people

who meet the inclusion criteria and are conveniently available, as part of the sample. The researchers conduct research one after the other until they reach a required number of subjects. Sample was obtained by using descriptive categorical sample size formula which results in 35 minimal samples.

### Serum calcium level examination

We assess the serum calcium level by using CPC Photometric method. As much as 3 mL of blood sample were placed in an Eppendorf tube and was centrifuged at 4000 rpm for 10 minutes. The serum was then homogenized by vortex and placed in the home temperature area (18-30°C) for 1 minute. Lastly, the reading of the absorbance test and absorbance standard was done to reagent blank in wavelength of 570 (578) nm.

### Statistical analysis

Data collected were descriptively analyzed and presented in the distribution of frequency. Mean value and standard deviation were determined for numerical scale variables, e.g., serum calcium level.

### Ethical clearance

The Ethical Committee Commission of Healthy Study in Medical Faculty of North Sumatra University/ Adam Malik General Hospital Medan related to health study practice has approved this study with Ethical Clearance Letter no. 646/KEP/USU/2020

## RESULTS AND DISCUSSION

This study involved 35 pregnant women, dominated by women aged 20-35 years old (80%) and pregnant women in the second trimester (57.1%). The majority of the subjects were primigravida (54.3%) (Table 1).

Table 1. Study subjects' characteristics

	Subjects of Pregnant Women (n, %)
Age, n (%)	
< 20 years	2 (5.7)
20 – 35 years	28 (80)
> 35 years	5 (14.2)
Gestational Age, n (%)	
1 <sup>st</sup> Trimester	20 (57.1)
2 <sup>nd</sup> Trimester	15 (42.9)
Parity, n (%)	
Primigravida	19 (54.3)
Multigravida	16 (45.7)
Level of Education, n (%)	
Elementary School	2 (5.7)
Junior High School	3 (8.6)
Senior High School	25 (71.4)
Graduated	5 (14.3)

Mean calcium serum levels found in pregnant women in the second and third trimesters were  $9.12 \pm 0.49$  mg/dl and  $8.97 \pm 0.26$  mg/dl, respectively. Mean calcium serum level in subjects age < 20 years old, 20 -35 years old and > 35 years old were  $9.0 \pm 0.28$  mg/dl,  $9.07 \pm 0.44$  mg/dl, and  $8.96 \pm 0.06$  mg/dl, respectively. Analysis was done between pregnancy age and serum's calcium level with  $p > 0.05$  ( $P = 0.246$ ). Based on this analysis there was no significant relationship between pregnancy age and serum calcium level (Table 2).

Table 2. Mean serum calcium level based on pregnancy age

Trimester	Serum Calcium Level(mg/dl)				p value
	Mean	SD	Minimum	Maximum	
2 <sup>nd</sup> Trimester (n=20)	9.12	0.49	7.60	9.90	.246
3 <sup>rd</sup> Trimester (n=15)	8.97	0.26	8.50	9.40	

Table 3. Mean serum calcium level based on subject's age

Age	Serum Calcium Level (mg/dl)				p value
	Mean	SD	Minimum	Maximum	
<20 years old	9	0.28	8.80	9.20	
20-35 years old	9.07	0.44	7.60	9.90	.732
>35 years old	8.96	0.06	8.80	9.20	

Table 4. Mean serum calcium level based on parity

Parity	Serum Calcium Level (mg/dl)				p value
	Mean	SD	Minimum	Maximum	
Primigravida	9	0.58	7.60	9.90	.645
Multigravida	9.07	0.31	8.50	9.60	

Table 5. Mean serum calcium level based on education level

Education	Serum Calcium Level (mg/dl)			p value
	Mean	Minimum	Maximum	
Elementary	9.1	8.9	9.3	.488
Junior high	9.03	8.6	9.3	
Senior high	9.02	7.6	9.8	
Associate degree	9	8.8	9.2	
Bachelor degree	9.3	8.9	9.9	

Analysis of age and serum's calcium level from 35 women in this study shows no significant relationship with  $p > 0.05$  (0.732). Mean calcium level found in under 20 years group, 20-35 years, and above 35 years are 9.00, 9.07, and 8.96, respectively (Table 3). Mean calcium found in primigravida is 9.00 and in multigravida is 9.07. Analysis of parity and serum's calcium level from 35 women in this study shows no significant relationship with  $p > 0.05$  (0.645) (Table 4). Mean calcium found in pregnant women based on their education level are 9.1, 9.03, 9.02, 9, 9.3 for elementary education, junior high school, senior high school, associate degree, and bachelor degree, respectively. Analysis was done and there was no significant relationship between calcium serum level and education level in pregnant women with  $p > 0.05$  ( $P = 0.488$ ) (Table 5).

Nutritional status, maternal and neonatal health are important indicators of the burden of any disease. The most prevalent mineral in the body, calcium is crucial for many different biochemical processes, including bone formation, muscle contraction, and hormone and enzyme activity. In three different forms, ionic, protein-bound, and complexed, calcium in extracellular fluid maintains its physiologic equilibrium.<sup>13</sup> Hypocalcaemia in pregnancy remains a major health issue, particularly in the developing world where daily calcium intakes are suboptimal. This electrolyte imbalance can lead to severe maternofetal and childhood consequences.<sup>14</sup>

In our study, the mean serum calcium level found among pregnant normocalcemia women was 9.12 mg/dL and 8.97 mg/dL for pregnant women in first and second trimester, respectively. This result was in line with the study of Aqbar et al.<sup>15</sup> who conducted a study involving 34 pregnant women in third trimester. This study found a normal calcium serum level average of 8.89 mg/dL. This result was also in line with Indonesian

study performed by Setiarsih et al. which found that the mean levels of serum calcium were 8.94 mg/dL in the group of pregnant women and 9.74 mg/dL in the non-pregnant group. These values are within the normal range of 8.1-10.4 mg/dL. There was a significant difference in serum calcium levels between the pregnant and non-pregnant groups ( $P = 0.047$ ) and the average value of serum calcium levels was lower in the pregnant group.<sup>22</sup> Our study also found that only one pregnant woman had low calcium level (7.81 mg/dL). While it is difficult to ascertain the risk factor for such cases, diet and exercise might be a contributing factor that cause the mother's low calcium level.

Furthermore, we discovered that mean serum calcium levels were higher in the second trimester than the third trimester, which was similar to Zapata et al.'s study in 2004.<sup>16</sup> When compared to younger pregnancy (10–12 weeks of gestation), almost all nearly term or older pregnancy (34–36 weeks of gestation) had lower serum calcium levels. This is believed to be the result of a twofold increase in intestinal calcium absorption as a maternal physiological adaptation to meet the fetal calcium requirement. Calcitriol levels can double during pregnancy, as previously stated, and this increase in calcitriol causes an increase in intestinal calcium absorption. However, an animal study found that the increase in intestinal calcium absorption occurred before the rise in free calcitriol levels, and that calcitriol and vitamin D receptors were not involved in the increase in intestinal calcium absorption during pregnancy. Other factors such as placental lactogen and prolactin were found to stimulate that increase in intestinal calcium absorption.<sup>16</sup>

In this study, maternal calcium level was found to be lowest in pregnant women older than 35 years old. According to Nordin (2018), healthy postmenopausal women accounted for 30% of the decrease in calcium

absorption until the age of 75. In addition, this late decrease was not associated with 25(OH)D or 1,25(OH)2D concentration. The reduced in gastrointestinal responses against 1,25(OH)2D also seemed to cause the decrease in calcium absorption in elder women.<sup>17</sup> Wulandari et al. conducted a cross-sectional study in 53 Indonesia pregnant women across couples of ethnicities and found that Madurese women with mean ages of 34.20±5.58 years old had the least calcium serum level of 7.7 mg/dL, compared to Chinese women with the mean age of 28.20 ±2.16 and had calcium serum level of 9.0 mg/dL (P = .000).

Ajong et al. found hypocalcemia predominated in pregnant women aged 21-25. However, it turns out that the percentage of hypocalcemia in pregnant women aged 31-49 years is also quite high (54.63%).<sup>14</sup> Our study also contradicted Katung et al., who stated that hypocalcemic pregnant women primarily found in the age range of 20 – 34 years old with the mean age of 26.6 years old.<sup>18</sup> It is well known that parathyroid hormone levels rise with age. This increase is estimated to reduce renal function, calcium absorption efficiency, and the 25-hydroxyvitamin D [25(OH)D] concentration that subsequently cause loss of bone mass in postmenopausal women. The level of 25(OH)D is the primary determinant of parathyroid serum level; it also causes the increase in calcium ion level, and causes the decrease in body weight. Studies found that changes in calcium ion level, body weight, and age would affect the parathyroid serum level only if the 25(OH)D serum level is lower than 80 nmol/liter.<sup>17</sup>

Low calcium serum levels could cause some pregnancy complications, including preeclampsia, lower birth weight, preterm labor, and neonatal death. Previous studies found that women with low-birth-weight fetuses had a lower mean serum calcium level. Calcium has been shown to reduce the contractility of uterine smooth muscle. A healthy calcium level during pregnancy may help to prevent preterm labor and low-birth-weight newborns.<sup>19,20</sup> An adequate maternal nutrition is associated with normal fetal development. Deficiency in maternal nutrition could deteriorate fetal brain development, leading to embryonic malformation and increased congenital defect incidence. Calcium is an essential micronutrient as the reduced maternal calcium reserve could affect maternal bone quality, reduce bone density, and increase bone resorption. Pregnancy in the third trimester was the most consequent trimester. Pregnant women in this state no longer produce calcium, so that calcium needs to be taken exogenously. Fetal nutrition during pregnancy solely depends on maternal nutrition so a good intake of calcium in this condition is crucial to prevent maternal calcium reserve consumption.<sup>2</sup>

## CONCLUSION

This study found that the mean calcium serum level in pregnant women from Adam Malik General Hospital outpatient clinic involved in the study was normal. There was no significant relationship between serum calcium level with age (P = 0.732), parity (P = 0.645), education level (0.488), and pregnancy age (P = 0.246)

## DISCLOSURES

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### Conflict of interest

The authors report no conflicts of interest in this work.

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### Author Contribution

All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting, and approval for publication of this manuscript.

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