

Hypocalcemia In Pregnancy: Diagnosis Challenges In Low Resource Settings.

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Abstract

Background: Hypocalcemia is when a total serum calcium concentration is less than 8.8mg/dl or an ionized calcium level is less than 4.7 mg/dl with normal plasma protein. Hypocalcemia in pregnancy is a major health issue particularly in developing countries where daily calcium intakes are suboptimal, and there is paucity of data in reporting this condition.

Case presentation: A case of 21 years old woman gravida 3 para2, who presented to us with general body weakness and spasticity, stiffness and pain on hands and lower limbs for three weeks. She was amenorrhea of 32 weeks and 2 days. She has history of confining herself indoor for one year, history of poor feeding habits since she became pregnant. Upon evaluation, a diagnosis of hypocalcemia was reached. She was treated with intravenous calcium gluconate, calcitriol and magnesium sulfate during the acute phase, then oral calcivit tablet. She improved drastically, and she was later discharged with instruction of attending antenatal clinic at our hospital, but She didn't turn up for follow up antenatal care after discharged, instead she was taken by her mother, who took care until she gave birth at Mara Hospital a healthy baby 3.4kg. and there were no complications.

Conclusion: Hypocalcemia is under reported and presentation of hypocalcemia may be confused with other cause of tetanic muscle cramps such as eclampsia, epilepsy, and tetanus. This is contributed by low or poor diet and increased demand during pregnancy as gestation advances. It is important to emphasize the need for balanced diet during pregnancy and supply of micronutrients. This remains vital to the metabolic needs of the woman and her baby during antenatal period.

Keywords: hypocalcemia, pregnancy, calcium

Introduction:

Calcium is an element which is used for optimal function in the body vital processes such as muscle contraction, cardiac function, transmission of nerve impulses, blood clotting, membrane stability, bone structure and intracellular signaling [1]. Calcium is also important cofactor for hormonal secretion in endocrine organs [2].

Normal serum calcium concentration is maintained within the very narrow range of 8.5-10.5mg/dl (2.12mmol/l to 2.26mmol/l). Sources of calcium includes milk, cheese and other dairy foods, green leafy vegetables, soya beans, micronutrients supplements [3]. The 7-dehydrocholesterol in the skin absorbs UV Radiation from the sun and is converted to pre vitamin D3 which in turn isomerizes into vitamin D3 1-25 dihydroxyvitamin D [4]. This plays an important role

in regulating calcium and phosphate metabolism for maintenance of metabolic function and skeletal health. Thus, deficiency in diet rich in calcium and limited exposure to sun rays ultimately lead to impaired calcium metabolism and hypocalcemia [5]. In humans, more than 99 % of calcium is stored as hydroxyapatite in bones and the rest 5-6g is in the intracellular and extracellular compartments with only 1.3 g located extracellularly [4]. Half of plasma calcium is in a free or ionized state, and only this ionized calcium is metabolically active and affects body functions [6]. Of the remaining plasma calcium 40 % is transported partly bound to plasma proteins, and the rest is bound to small anions such as phosphate, carbonate, citrate, lactate and sulfate [3].

Case presentation

We present a case of a 21-year-old woman from Nyamongolo Mwanza, a referral case from Sekou Touré Regional Hospital in Mwanza city, Tanzania, Gravida 3, Para 2 with 2 living children. Her last normal menstrual period was 28/12/2019, and expected date of delivery was 4/10/2020, presented with a complaint of general body

weakness for three weeks, muscle pain and stiffness on upper and lower limbs for one week. This was preceded by history of muscle cramps, which were felt occasionally at night several months ago. The symptoms were of gradual onset progressing with time. There was no specific periodicity, aggravating factors or relieving factors. The

complaints were not accompanied with fever, headache and convulsions. But there was history of constipation which was not associated with abdominal distension pain or vomiting. She denied history of heartbeat awareness, lower limbs swelling. She also denied history of pain on passing urine or increased frequency of urination, no history of vaginal bleeding or leakage of fluid per vagina; she perceived fetal movement normally. During the course of this illness, she attended to a nearby primary health facility where she was treated as a case of malaria and urinary tract infection (UTIs) without any improvement. She attended once antenatal clinic at six months pregnant approximately 2-months ago, where she was examined in which her blood pressure was 110/68mmHg, body weight was 50kg, urine for protein was negative, HIV and Syphilis were negative, she was blood group O Rhesus positive, while her hemoglobin level was not measured.

Her past obstetric history was unremarkable; however, she had a short pregnancy interval in which she had vaginal birth in 2016, 2018 and in 2019. Both her past gynecological history and past medical/surgical history were unremarkable. She is married but staying with her sister-in-law due to her pregnancy state, she is not taking alcohol, not smoking cigarette. For the past one year, for unknown reasons she has decided to stay indoor not going outside, and since she become pregnant, she has developed a habit of not eating enough, instead she just take juice and few slice of bread.

During admission, physical examination revealed a middle-aged woman, underweight, with a body mass index of 16.5kg /m² alert, pale, not dysphonic, not icteric, not cyanosed not dehydrated, weak, conscious looks depressed. Vital signs- temperature 36.4⁰C, Blood pressure-115/68mmHg, Pulse rate- 98B/min, respiratory rate 21 cycles per minute, Saturation of oxygen (SPO₂)-98 % on room air. Local examination -upper limbs both hands from the wrist joints are spastic, especially on the fingers with hyper flexed and restricted range of movement and painful on trying movement. Pulse was well-felt and normal warmth. Both passive and active movement of Lower limbs-normal except pain on the calf muscles.

Per abdomen-height of fundus 26cm, longitudinal lie, cephalic presentation fetal heart rate was 140beats/minute; there was no palpable contractions, no area of tenderness. Other systems there were no significant findings. A physical test done where Trousseau's sign was positive, Chvostek's sign is equivocal.

Investigations done Full Blood Picture-WBC total was normal, RED BLOOD CELLS (erythrocytes)- 2.52×10⁶mm³(low), HB- 7.5g/dl (low), HEMATOCRIT -22.6 % (low)

Discussion

Hypocalcemia is defined as total serum calcium level of lower than 8.2mg/dl (2.05mmol/l), or an ionized calcium level of lower than 4.4mg/dl (1.1mmol/l) [7]. Calcium is the fifth most prevalent element in the body [8]. The recommended dietary allowance (RDA) for

Renal function-Serum Urea-7.60mmol/l (Normal)- (0.00-8.30), SERUM CREATININE-134μmol/l (High)-(44-80)

Serum electrolyte- SODIUM-135.80mmol/l (Low)-(136-145), POTASSIUM – 2.97mmol/l(Low)-(3.50-5.10) SERUM CHLORIDE-100.24mmol/L (Normal) SERUM CALCIUM. -1.43 mmol/l (Low) (2.15- 2.55), SERUM MAGNESIUM -0.51mmol/l-(Low) (0.66-1.07).

Ultrasound done -showed single tone intra uterine fetus at 32+2 days in breech, estimated fetal weight 2.0 kg, EDD 21/09/2020, No Fetal Abnormality Detected.

Management plan:

Patient was then kept on calcium gluconate 10gm slowly intravenous in 5 % dextrose run slowly for 10 to 20 minutes twice a day for 3 days, intravenous magnesium sulfate 10 % in intravenous infusion 2gm, for 10 to 20min, followed by 1gm in 100ml fluid per hour. Also, calcivit tablets was given orally 1 tablet twice a day, and Ferrous sulphate and folic acid 200/5mg twice a day for 60 days, blood transfusion 1 unit was given also. In the ward she was improving and on day six control investigations were done and the following were result- Full Blood Picture after 3 units given, Hemoglobin became 7.3g/dl, Calcium 1.93mmol/l (Low), Urea 5.32mmol/l, Serum creatinine 125μmol/l (High), Potassium- 2.53mmol/l, Chloride. 94.33mmol/l, Alkaline phosphate (ALP) – 101mmol (Normal)

Thyroid function tests were further performed and the results were as follows:

Tri-iodothyronine (T₃) 1.66ng/ml (0.60-2.10)

Total Thyroxine (T₄) 12.6ng/dl (5.0-13.0)

Thyroid Stimulating Hormone (TSH) 2.66U/L (0.32-5.20). Day six post-admission, the patient was calm and had no complaint, she requested for hospital discharge. She was discharged home on day ten, with more oral calcium supplements and given appointment for follow up after one week. Unfortunately, she went home and she travelled to Mara region to her mother so as she can be taken care closely. She then attended to Mara Regional hospital where she had a vaginal birth to a 3.4 kg healthy baby boy. There were no complications thereafter for the mother and the baby.

calcium is between 800mg to 1000mg per day for a male adult and 1000mg to 1200mg for female adult. During pregnancy, dietary allowance of calcium increases by 300 % (9). The Fetus retains 2530g of calcium mostly in the third trimester of pregnancy [10].

In developing countries where daily calcium intakes are suboptimal, hypocalcemia in pregnancy is common, making it a major public health issue [11]. Considerable strain on maternal calcium homeostasis occurs during period of pregnancy and lactation cycle. Adaptive mechanisms mostly involve increased intestinal calcium absorption, renal calcium conservation and changes in bone metabolism. These adaptations are mediated through changes in the secretion of various calciotropic hormones [1,25(OH) 2 D3, parathormone, and calcitonin]. In all of these adaptive mechanisms, vitamin D is involved directly or indirectly [12].

Though there is underreporting of hypocalcemia in pregnancy in the literature, it occurs commonly in cases of hypoparathyroidism and in mothers with severe dietary inadequacy [5,13]. A study in India found the prevalence of hypocalcemia in pregnant women to be 66.4 %; all being asymptomatic. The mean daily dietary calcium intake and corrected serum calcium level for the group were 325 ± 198 mg and 8.1 ± 1.5 mg/dL, respectively. The daily dietary calcium intake being less than the recommended dietary allowances was a most probable cause of the hypocalcemia [5]. In our case, the patient changed her behavior and confine herself in door, taking very little food which was juice and bread and sometimes not eating at all, become weak and she lost weight due to poor eating, also not exposed to sun light which also has a role in calcium metabolism. She was not receiving any calcium supplement during antenatal visits.

Clinical presentation depends on the severity, speed of development, the rate of decline of serum calcium, and duration of the hypocalcemia varying from an asymptomatic biochemical abnormality to a life-threatening disorder [7]. Mild hypocalcemia is common, and most patients will have no symptoms while many have vague muscular aches and pains [5]. In our case, the patient reported muscular aches before development of muscle spasms and muscle cramps. Many do not realize they are deficient until problems occur. Inflating a blood pressure cuff above systolic pressure for up to three minutes and looking for a carpopedal spasm positively revealed trousseau's sign which is diagnostic of calcium deficiency [5]. The sign can be established to a patient during physical examination with pain on the wrist joint.

Moreover, Chvostek's sign can be prompted by tapping the facial nerve below the zygoma (about 1–2 inches anterior to the ear). An ipsilateral contraction of the facial muscle (i.e., twitching first at the angle of the mouth) is a positive sign. Chvostek's sign can be elicited in up to 25 % of individuals with normal levels of serum calcium, thus it is a sensitive but not specific sign of hypocalcemia [14]. This was not observed in our patient. Our patient also presented with tetany muscle stiffness and myalgias as both hands from the wrist joint were spastic, especially fingers, which were hyper- flexed and causing her not being able to perform normal movement, (restricted movement and painful on attempt to movement).

Measuring the total ionized serum calcium level makes absolute diagnosis of hypocalcemia. The ionized calcium which is difficult to measure independently of the total calcium, Ionized calcium remains the gold standard for assessing calcium status because it measures the biologically active (or free) calcium [3,15,16]. However, due to the costs and complexity in performing the test, ionized calcium is not performed routinely. It is important to note that the affinity of calcium for albumin is increased in the presence of alkalosis. Thus, respiratory alkalosis may cause an acute decrease in ionized calcium [16–18]. The first step in the evaluation of hypocalcemia is to know serum calcium concentration. If the patient has a low ionized calcium or serum total calcium (corrected for albumin in patients with hypoalbuminemia), further evaluation to identify the cause is indicated [19].

In this patient we used total serum calcium level obtained plus other electrolyte derangement supported by signs and symptoms to reach the diagnosis. Serum calcium, serum magnesium, sodium and potassium were all found low. Unfortunately, parathyroid hormone (PTH) and vit D could not be assessed. Serum alkaline phosphate was normal serum creatinine was also elevated. Our patient had no history of any neck surgery or other known chronic illness. However, for the past one year she seems decided to remain indoor most of the time and she had reduced food intake. This can be sign of depression, which might also be a sign of hypocalcemia. According to the World Health Organization (WHO), chronic insufficient calcium intake before or during pregnancy is associated with a significantly increased likelihood of hypocalcemia in pregnancy [20]. In pregnancy and lactation, there is an increase in calcium demand [21].

The treatment of hypocalcemia depends on its severity and the underlying cause. The severity of symptoms (paresthesia's, carpopedal spasm, tetany, seizures) and signs (Chvostek's or Trousseau's signs, bradycardia, impaired cardiac contractility, and prolongation of the QT interval) depends upon the absolute level of calcium, as well as the rate of decrease [22]. Maternal treatment includes calcitriol dihydrotachysterol or large vitamin D doses of 50,000 to 150,000u/d; calcium gluconate or calcium lactate in doses of 3 to 5g/day, and a low phosphate diet. The goal during pregnancy is to maintain a corrected level in the low normal range [23].

If there are symptoms of prolonged QT interval due to hypocalcemia, recommended treatment is intravenous 10 % calcium (1 or 2 g of calcium gluconate equivalent to 90 or 180 mg elemental calcium, in 50 mL of 5 % dextrose or normal saline) run over 10 to 20 minutes [24]. Calcium should be continued until the patient can receive an effective regimen of oral calcium and vitamin D. For patients with hypoparathyroidism, calcitriol (in a dose of 0.25 to 0.5 mcg twice daily) and oral calcium (1 to 4 g of elemental calcium carbonate daily in divided doses) should be initiated as soon as possible [24].

Our patients had also hypomagnesemia; it is as such recommended to correct hypomagnesemia. This will make correction of hypocalcemia

easier if the hypocalcemia is magnesium related [25]. Therefore, if the serum magnesium concentration is low, 2 g (16 mEq) of magnesium sulfate should be infused as a 10 % solution over 10 to 20 minutes, followed by 1 gram (8 mEq) in 100 mL of fluid per hour [26]. Magnesium repletion should be continued as long as the serum magnesium concentration is less than 0.8 mEq/L (1 mg/dL or 0.4 mmol/L). Care must be taken for those patients with renal insufficiency. Our patient had features of impaired renal function as serum creatinine was elevated which could be contributed to low calcium. She received calcium gluconate as well as magnesium

Conclusion

Hypocalcemia is under-reported and presentation of hypocalcemia may be confused with other cause of tetanic muscle cramps such as eclampsia, epilepsy, and tetanus. This is contributed by low and poor diet in calcium levels and increased demand during pregnancy as pregnancy advances. It is important to emphasize the need for balanced diet during pregnancy and routinely micronutrients supplementation during ANC. This remains vital to the metabolic needs of the pregnant woman and her baby during antenatal period.

Patient's perspective: The care provided was timely with full explanation of the diagnosis and prognosis was explained to the patient and plan of follow up made.

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- Port OF, Teaching H (2017) Prevalence of Hypocalcaemia and sulfate, and serial monitoring of renal function and levels of serum magnesium and calcium. She improved after a period of 10 days of treatment and was discharged home with an appointment of weekly attendance to antenatal clinic.
- As a culture of most of women in our setting, when a pregnant woman reaches near term would like to move to mother-in-law or her mother so as to be taken care during those last week's/days of pregnancy and delivery. However, during follow-up via phone she reported to have given birth to a baby boy 3.2kg 2-months after hospital discharge. There were no complications, and they are all doing well.

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