ORIGINAL ARTICLE

Prevalence of Hypocalcemia and its Association among Pregnant and Lactating Mothers

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ABSTRACT

Background: The aim of the study is to estimate incidence of Hypocalcemia (decreased in serum calcium level) in pregnancy and lactation despite the fact that supplementation with calcium is not practice in Pakistan. A finding of a comparatively large number of subjects seen with Hypocalcemia in pregnancy and subsequent births insist proceedings to determine the long term hazards their factor and further relationships.
Aim: To calculate the occurrence and recognize the incidence of Hypocalcemia along with females who presented in OPD clinic with complains of repeated bouts of Tetany (Carpopedal spasm) during their pregnancies and lactation period.
Methods: The overall number of pregnant females (n=400) compared with lactating females (n=400) present along with sign and symptoms of hypocalcemia were recorded, serum calcium, phosphorus, vitamin D, and parathyroid hormone, analysis were done using standard laboratory techniques. Statistical analysis was done by using appropriate new version of SPSS software.
Results: There were 118 out of 400 pregnant having sign and symptoms of Carpopedal spasm showing a frequency of 29.5% were as lactating females having 103 out of 400 indicating frequency of 25.75%. The standard age criterion was 32 years ± 2.3 years and parity of 6.2±1.2. The mean calcium levels in serum were 6mg/dl ± 0.4mg/dl in pregnant subjects where as during lactation period females having serum calcium level were 6.4mg/dl± 0.3mg/dl.
Conclusion: The predominance of decreased in serum calcium level were elevated in pregnant women's as compare with those were lactating. Elevated ratio of pregnancies raises the risk factor during pregnancy along with Hypocalcemia here we recommend with the intention of decrease the risk factor to reduce mortality, diet modification along with calcium supplementation must be suggested to women's during antenatal checkups
Keywords: Parathormone, 1, 25-dihydroxyvitamin D, Hypocalcemia, Parity

INTRODUCTION

In female's normal physiological changes occurs during period of pregnancy and in lactation that leads to distorted changes in calcium regulation that causes Hypocalcemia.[2] The developing fetus fulfills its metabolic needs for that reason calcium is obtained from maternal circulation and stores for fetal skeletal growth. For fetal growth the sum necessity of calcium is range between 25gm to 30gm per day and average increase in first trimester which is about 3-4mg/day and in third trimester it reaches up to the level of 200-250mg/[1]. During pregnancy calcium reabsorption thru gastrointestinal tract is increased under the pressure of active form of Vitamin D (1, 25- (OH) D).[7] The full term neonate born had calcium about 29-30gm. During last three months of pregnancy the calcium is transported across the placenta thru active mechanism when bones collagen matrix is going to be ossified. Throughout pregnancy the calcium total amount is low due to decreased albumin related hemodilution.[6] Serum ionized calcium levels and calcium corrected by albumin is considerably normal during pregnancy period.[4] The fetal calcium requirement is meeting by resorption of maternal bone stores which leads to raise the absorption in extracellular compartment and reduced calcium excretion in urine for this reason, it is mirror image of amplified calcium absorption and the other reasons increased serum calcitonin release during pregnancy, the diagnostic test is Immuno-metric assay which is more specified for detection of intact parathyroid hormone which shows that PTH is low during first three months of pregnancy but it will remain normal till nine months otherwise PTH assay is less specific because during pregnancy the mothers parathyroid glands is enlarged and serum levels are usually high (hyperparathyroidism). This decreased PTH is due to oppressive results if increased active vitamin D levels (1, 25 (OH) 2D)[7]. Bone studies are carried out in lactation shows increased levels of bone turn over and resorption indicators elevated alkaline phosphatase (Alpo4) and Parathormone releasing peptide (PTHrP).[5] These indicator markers is normalize in mother when weaning is started after 3-4 months of infant life which leads to maternal bone density is being improved[3]. During lactation this decrease levels of bone mass is due to low levels of estrogen and raised serum prolactin. In previous and current research during lactation period the bone mass density data propose 3-4% decrease in bone mass every month. This shows extremely noteworthy as weigh against to 1–3.5% decrease bone mass in menopause every year. Taken as a whole, this explanation recommend that the necessitate calcium loss during lactation and PTHrP both outcome donate further resorption of bone as compare to hypoestrogenemia[8]. After placental delivery the (tALP) Total alkaline phosphatase level decreased to non pregnant levels but sometimes due to increase in bone turnover it is elevated to some extent. If lactating mother

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breast feed their newborn for at least six months their calcium loss is five times higher as compare in females with pregnancy the rationale is that lactation requires 1.5-3gm calcium. Some researches finding shows that in normal healthy females' serum ionized calcium levels were normal. Even though a few studies propose that ionized / corrected calcium levels in serum is increase to some extent.[9] During lactation breast act as a controller for bone demineralization suckling encourages prolactin (PRL) to be secreted from anterior pituitary gland and this can lead to restrain (GnRH- gonadotropin-releasing hormone) which causing inhibition of (LH - luteinizing hormone) and (FSH - follicle stimulating hormone) this effect can leads to decrease steroidal ovarian sex hormones (E_2 and PROG) estradiol and progesterone respectively both can arouse PTHrP.[5] (PTHrP) generate from breast during lactation together with suckling, prolactin, and calcium receptor. PTHrP penetrates in the circulating blood and united with low levels of serum estradiol to maintain calcium homeostasis as a result calcium (Ca+) and Phosphorus (PO4) is increased in serum due to rise in skeletal resorption. The bone mineral density turns down by 4-9% after 5 month of breastfeed. There is no compensatory rise in bone formation, therefore resorption of bone showed noticeable rise in bone marker levels.

MATERIAL AND METHODS

This is retrospective study, subjects were collected from different obstetrical OPD's from Punjab within one year duration from 2016-2017. The current study comprises of total subjects in which pregnant and lactating mothers have equal numbers (400 x 2) pregnant females are investigated after every trimester total of three times during pregnancy with classical features of Carpopedal spasm (Tetany). Total 221 subjects are on records during both pregnancy and lactation period out of this only 154 cases were responses and their response rate is 69%. Their socio-economic data, demography, presenting complaints, associated diseases and their lab values all are acquired. Patients sign and symptoms, duration of complaints, treatment and retrieval all were recorded. The control serum calcium value is 8.5-9.5mg/L, where as for serum albumin (Alb) 3.5-5.5g/dl. Hemoglobin is used to categorize subject with anemia. Less than 40% measured as anemic. Measured calcium levels in serum along with level of serum Alb added to get corrected form of calcium in serum. Serum calcium below the level of 8.0 is considered. The current data analyzed by means of IBM SPSS Modeler (version 17).

RESULTS

Total 221 patients were presented with sign and symptoms to OPD indicative of hypocalcaemia with prevalence rate of 11.4%, 22.3% patients were literate, only 23.3% females during pregnancy was visited for antenatal checkups, the average mean age of females while attending clinics was 25.5± 5.5 years, with average parity 6.2± 1.2years. Out of all (49%) of participants were multi-parous with the majority of females having age among 21-25years.

At the same time large bulk (47.1%) of females Grand- mutiparous age among 31-32years. Even though only 60 (27.5%) attend during pregnancy all others during lactation. Commonly presenting complain is Carpopedal spam along with leg cramps (38.2%) where as essential hypertension act as co-morbid condition. The typical commencement of sign and symptoms till presenting time was nearly 5-6 days where as delivering presentation gap was 18 days± 8 days along with mostly present in 16-18 days following delivery. The mean calcium level in serum was 6.0±0.4 mg /dl, packed cell volume mean value 0.28± 6.9% the average mean for albumin in serum is 2.74±0.35. There is inverse association among calcium and parity level (n= 0.289, p=0.149). Whereas powerful relationship among multi-parous females (n= 0.410, p=0.239). The time lapse for sign and symptoms were create negative relationship with calcium levels in serum. These values were statistically important while females had deliveries more than five (n=0.689, p=0.027). There is strongly positive relationship among calcium level and delivery time interval with sign and symptoms last longer than eight days but statistically insignificant (n=118, n=8.0, p=0.487). There is positive relationship between females presented during lactation after puerperium with hypocalcemia (n=103, n=7.0, p=0.589) and statistically significant.

Total subjects 800	Hypocalcemia /Carpopedal spasm	Incidence	Mean serum calcium level
Pregnancy (n=400)	118	29.5%	6.0mg/dl±0.4mg/dl
Lactation (n=400)	103	25.75%	6.4mg/dl±0.3mg/dl

DISCUSSION

Multiple hormones play key role in maintaining extracellular calcium constant concentrations in human beings. One of the most important is Parathormone (PTH) and active form of vitamin D (1, 25- OH, D). During third trimester of pregnancy the serum calcium requirement is increased for three to four folds for fetal growth and wellbeing, and this can be accomplished by increased gastrointestinal reabsorption of calcium with the help of vitamin D. while during lactation the normal calcium regulator is PTH with nominal input of (1, 25-OH, D).The average mean age of females with attending OPD clinics were 25.5± 5.5 years with preponderance (49%) of the multi-parous subjects between ages 21-25 years. Despite the fact that (49%) of females were multi-parous and (47.1%) Grand-multi-parous there were statistically significant relationship among female parity and hypocalcemia in after 3-4 deliveries this significance not obvious for deliveries up to five and more. These results show that lower calcium levels and prolonged sign and symptoms rise with increase number of pregnancies. Large number of female patients presented during early period of lactation whereas some subjects presents during pregnancy with hypocalcemia, numerous researches have publicized that um calcium homeostasis achieved by (1, 25- Dihydroxycholecalciferol) by increased the rate of calcium reabsorption into intestine and inhibit done resorption during both pregnancy and lactation and in normal females. During study period it is discovered that active form of vitamin D (1, 25- Dihydroxycholecalciferol)

must be maintained during third trimester of pregnancy.[7] Deprived nutritional condition during pregnancy is assessed by serum albumin levels, low levels of vitamin-D and calcium. This condition is prominent in last trimester during pregnancy. It is therefore mention that appropriate diet and supplements containing vitamin D may progress and improve serum calcium level during pregnancy for betterment of both fetus and mother. During lactation serum calcium level is prejudiced mostly by endocrine hormone Parathormone. The major reason of constant hypocalcemia during postpartum and in lactation period is due to deficient Parathormone. In this research the probable level of PTH is not mention but serum albumin levels were in standard level which can signifying a apparent control of PTH during lactational hypocalcemia. Preponderance of subjects (57.2%) with no extra co-morbidity, merely 20.3% presented with hypertension, 18% having low level of serum potassium (hypokalaemia) and remaining 6.5% had pre-clampsia.[6] Current study discovered that the most common co-morbid condition is encountered during pregnancy is hypertension in association with low level of serum calcium. To avoid hypertension during pregnancy in critical subjects the calcium supplements proved to be beneficial and its outcomes are well predictable. In our study there is weak association found between serum calcium and packed cell volume and were statistically insignificant in patients with routine antenatal checkups and some who taken hemoglobin corrected treatment and persons who are not willing to get treated. All the subjects who taken part in our study were treated with intravenous Calcium Gluconate as standard therapy than following on maintained sea calcium supplements along with vitamin K which help in restoration of bone calcium level[10]. All other problems were treated especially low level of potassium and arterial hypertension. Increased rate of pervasiveness of hypocalcemia during pregnancy and lactation in our society and surroundings might clarify their underprivileged nutritional condition, be deficient in of calcium supplements during pregnancy and increased parity level. Despite the fact that existing National obstetric protocol (NOP) does not take account of schedule vitamin D or calcium supplements during pregnancy, Obstetric principles suggest supplements for females who are at threat of hypocalcaemia during pregnancy and lactation. Higher rate of parity is recognized further hazardous feature acknowledged in this study. Additional studies to determine the PTH and 1, 25-Dihydroxycholecalciferol levels in subsequent deliveries in females having hypocalcemia will facilitate improvement in treatment methods[10].

CONCLUSION

There is difference in maternal adjustment during and pregnancy and in lactation to coup up the fetal skeletal growth requirements. During pregnancy period calcium reabsorption thru intestine in increased and resorption of bones are increased during lactating period which made the major adaptive method for mother to congregate the elevated necessity. After start weaning in child the bone resorption is reversible if it reaches its mild level in pregnancy and lactation and it causes no harm to bones. On the other hand, in our Pakistani society where females belongs to low socio-economic family maternal undernourishment and vitamin D insufficiency is common which leads to rigorous skeletal exhaustion during her reproductive phase and almost certainly have long-term effects on skeletal strength, together with an amplified threat of bone frailty. Additional clarification of the method of skeletal thrashing and re-establishment during reproductive period and lactation may help progress advanced opportunities for treating skeletal ailments. Presently, in our populace, more stress is needed on maternal nourishment, to fulfill sufficient vitamin D and calcium levels, which may overlay long term prevention of osteoporosis like bone conditions in future.

REFERENCES

1. Kovacs CS, Kronenberg HM. Maternal-fetal calcium and bone metabolism during pregnancy, puerperium, and lactation. Endocr Rev 1997;18: 832-72.
2. Kovacs CS, El-Hajj Fuleihan G. Calcium and bone disorders during pregnancy and lactation. Endocrinol Metab Clin N Am 2006;35: 21-51.
3. Kalkwarf HJ, Specker BL. Bone mineral changes during pregnancy and lactation. Endocrine 2002;17:49-53.
4. Juppner H, Gardella TG, Brown EM, Kronenberg H M, Potts J T Jr. Parathyroid hormone and parathyroid hormone-related peptide in the regulation of calcium homeostasis and bone development. In: DeGroot L, Jameson J, editors. Endocrinology. Philadelphia: Saunders; 2005. p. 1377-417.
5. Ardawi MS, Nasrat HA. Calcium-regulating hormones and parathyroid hormone-related peptide in normal human pregnancy and postpartum: A longitudinal study. Eur J Endocrinol 1997; 137: 402-9.
6. Fleischman AR, Rosen JF, Cole J, Smith CM, DeLuca HF. Maternal and fetal serum 1, 25-dihydroxyvitamin D levels at term. J Pediatr 1980;97: 640-2.
7. Turner M, Barre PE, Benjamin A, Goltzman D, Gascon-Barre M Does the maternal kidney contribute to the increased circulating 1,25-dihydroxyvitamin D concentrations during pregnancy? Miner Electrolyte Metabolism 1988;14:246-52.
8. Khovidhunkit W, Epstein S. Osteoporosis in pregnancy. Osteoporosis Int 1996; 6:345-54.
9. Sato K. hyper calcaemia during pregnancy peuerpeium and lactation: review and a case report of hypercalcaemic crises after delivery due to excessive production of Parathormone related peptide (PTHrP) without malignancy (Humoralhypercalcaemia of pregnancy). Endocrine Journal, 2008, 55(6) 959-966.
10. Specker B.L Nutrition in Pregnancy and Lactation, In: Nutrition and Bone Health. Eds.Holick M. F and Dawson-Hughes. B, Humana Press Inc.,Totowa, NJ. Ppg 167-184.