

Prevalence of hypocalcemia in children examined for serum calcium in Sana'a, Yemen

To the Editor

The article by BinMohanna et al¹ provided a record-based study of neonates, infants, and children with laboratory reporting of isolated hypocalcemia. The authors made suggestion for the mechanism/pathophysiology of such hypocalcemia, yet without laboratory proof or detailed explanatory attribution. Moreover, associated biochemical parameters, which would be of paramount diagnostic importance were unexpectedly missing.

Serum calcium is present in 3 forms: protein-bound, complexed, and free ionized. It is the latter form, which is physiologically active and is maintained by hormonal homeostasis.² Hence, it is the classical practice to always do 'biochemical bone profile', which includes serum total calcium, albumin, inorganic phosphorus, and alkaline phosphatase. By this panel, correction of calcium according to albumin will help in overcoming any protein abnormality, and the values of phosphorus, and alkaline phosphatase will clarify the biochemical look. Unfortunately, the authors did not make use of the profile, which is hoped that it had been carried out for all patients but not included in the study. It is also hoped that it is the local laboratory practice to do them collectively. Measurement of ionized calcium is even preferable to that of total calcium, particularly in the neonatal period, to avoid the effect of hydrogen ions state on calcium ionization. It is the changes in this ionized fraction that produces clinical effects, and so will represent the actual change in diseases, otherwise, assessment of acid-base status may be required.³

In this article, the authors point to a single explanatory cause for the hypocalcemia, which is maternal vitamin D deficiency. Although infants may be easily predisposed to "early" hypocalcemia if there is low maternal vitamin D, however, there are other major causes for neonatal, and infantile hypocalcemia, which are worth to have been considered, and reviewed in BinMohanna et al' series of cases. Conditions known to be associated with such hypocalcemia include:⁴ exaggerated physiological loss (prematurity, and infants of diabetic mothers), low intake (inadequate oral, enteral, parenteral nutrition), parathormone (PTH) related (transient or genetic hypoparathyroidism, maternal hyperparathyroidism, DiGeorge syndrome and hypomagnesemia), vitamin D related (maternal vitamin D deficiency, fat malabsorption, and 1 hydroxylase deficiency), multifactorial (liver or renal diseases, organic acids disorders, and

hypoxic-ischemic encephalopathy), and iatrogenic (increased loss with loop diuretics, and formation of insoluble calcium salts with high phosphate intake, and exchange transfusion). These causes are existing in practice particularly in hospitalized patients, and many of them could had been identified from the case records and hence, presented and added to the aetiology of the hypocalcemia in the reviewed series.

A final comment on neonatal rickets, and its link with calcium metabolism is worth considering.⁵ Protective mechanisms concerning calcium homeostasis, and bone formation are existing to ensure adequate bone formation at incomplete dependence on maternal environment. There is active placental transport of calcium to the fetus throughout the latter part of pregnancy at a rate of 3.2 mmol/kg 24 hour. Calcitriol (1, 25 dihydroxycholecalciferol) does not cross the placenta, and it is synthesized in the placenta itself, and in fetal kidney. Also, PTH, and calcitonin do not cross the placenta, and are synthesized by the fetus. There is massive increase in fetal bone mineralization in the 3rd trimester. From maternal side, during pregnancy a number of calcium influencing hormones are released in excess, which include progesterone, estrogens, prolactin as well as placental hormones. These hormones in turn will stimulate maternal calcitonin secretion as well as 1 hydroxylation leading to maximum intestinal absorption of calcium. These regulating mechanisms offer fetal, and neonatal protection against maternal impairment or deficiency of vitamin D making any consequent hypocalcemia to be mild or moderate that may not warrant hospital admission unless there are other associated diseases.

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Reply from the Author

Our study was a record based on diagnosis, mainly dependent on clinical manifestations, and serum calcium when patients can afford to pay for it. When hypocalcemia was diagnosed by serum calcium level; concentrations below 7 mg/dl establishes the diagnosis; a level below 7.5 mg/dl is suggestive.^{6,7,8} We measured serum calcium (total) in patients who had compliant related to hypocalcemia, namely convulsions, usually generalized short, and without loss of consciousness, carpopedal spasm, Chvostek sign, laryngospasm with cyanosis, and apneic episodes,

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irritability, muscular twitching, jitteriness, and tremors. Vitamin D deficiency was suggested as a main cause of the found high rate of hypocalcemia, this was attributed to the cold weather (Sana'a city is at 2100 meter above sea level), the mothers are completely covered by cultural use of protective clothing, minimal exposure to sunlight, many of them had closely spaced pregnancies, prolonged lactation, and intake of poor diet in vitamin D, and calcium. Children with other diseases, usually come with features of the other diseases for example, infants of diabetic mothers have hypoglycemia, therefore the cases are treated accordingly.

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