

Hypocalcemia and Nutritional Rickets in Children: Common Etiological Factors

H I KHAN* A ABDULLAH M Y KAZI M F AFZAL

Department of Paediatric Medicine, King Edward Medical College, Lahore

Correspondence to Dr. Humayun Iqbal Khan, Assistant Professor E mail: hik70@hotmail.com

Background: Hypocalcemia can be defined as a state when serum calcium level is less than 7 mg/dl in preterm neonates and less than 8 mg/dl in term neonates and less than 8.5 mg/dl in older children. Nutritional rickets is commonly associated with rickets in children. **Objective:** To determine the common etiological factors of hypocalcemia and nutritional rickets in children. **Study design:** Cross sectional analytical study. **Place and duration of study:** This study was conducted in the department of Pediatrics, King Edward Medical University/Mayo hospital Lahore from March 1998 to January 2001. **Patients and methods:** 120 patients (2 months to 60 months) who presented with tetany, clinical and skeletal manifestations of rickets and seizures were included in the study. Biochemical profile (serum calcium, phosphate and alkaline phosphatase) and radiographs of wrist joint were done. Each child was accessed for age, sex, feeding pattern, exposure to sunlight, number of children in family, maternal age, educational status of mothers, presenting features of the disease, total calcium, phosphate and alkaline phosphatase level in the serum and X-ray wrist. **Results:** The study group comprised of 120 children (72 boys & 48 girls) ranging from 2 months to 3.5 years. 65% of the children had weight below 5th centile on National Center for Health Statistics charts. 32% of children got sunlight exposure for less than 30 minutes/week and 16% got it for 30-120 minutes/week. Out of total 120, 110 were below 2 years among these 110, 9% were exclusive breast fed, 35% got diluted fresh milk, 1% got formula milk and 13% got both breast and bottle feeding. In 45% children weaning was not started. 47.5% couples had 2 or more children. 72% mothers were below 30 years of age, at the time of interview. 31% of the mothers were uneducated. 85% children had seizures at the time of presentation. Out of these 24.51% had upper respiratory tract infection and 51.96% had lower respiratory tract infection 79% had clinical signs of florid rickets. 67.5% of patients were had serum calcium between 6 & 7mg/dl, 69% were had serum phosphate level < 4 mg/dl and 76% had alkaline phosphatase level >1000IU/L. **Conclusion:** Hypocalcemia represents a major health problem in Pakistani children. Infants under 2 years of age are liable to have vitamin D deficiency rickets particularly if they are exclusively breastfed or received fresh milk with reduced exposure to sunlight. The higher the level of education of mothers, the less likely is the chance that their children become rachitic. Hypocalcemia can present with a wide variety of symptoms, the most important of which are seizures and recurrent chest infections. Rickets must be looked for as an underlying cause of these complaints.

Key words: Hypocalcemia Rickets Children

Calcium is a biologically important mineral required to maintain stability of membranes, muscle contraction and enzymatic activity in nearly all the cells¹. Calcium and phosphate salts provide mechanical rigidity to bones and teeth. Bony skeleton holds 99% of body calcium. Skeletal calcium has additional role to act as a reserve supply of calcium to meet body's metabolic needs in states of calcium deficiency². Hypocalcemia is seen commonly in children who have nutritional rickets which remains a common condition in developing countries³.

Hypocalcemia can be defined as a state when serum calcium level is less than 7 mg/dl in preterm neonates, less than 8 mg/dl in term neonates^{4, 5} and less than 8.5 mg/dl in older children^{5, 6}. Tetany is a state of hyperexcitability of central and peripheral nervous system and conditions resulting in tetany includes alkalosis and decrease in calcium and magnesium ions⁷. Extra-cellular calcium is a tightly controlled variable⁸. Maintaining normal calcium level is important because hypocalcemia is associated with poor outcome as measured by either survival or length of intensive care stay. Vitamin D, its active metabolites, parathyroid hormone and calcitonin are principal regulators of skeleton. Vitamin D deficiency gives rise to

rickets. During daily activities, casual exposure to sunlight provides most of our vitamin D requirements. In this way, sunlight also plays an important role in maintaining calcium homeostasis.^{9, 10, 11} In growing age, calcium deficiency impairs growth, delays consolidation of skeleton and gives rise to rickets.² Hypocalcemia is also common in babies who are fed with buffalo's/cow's milk or formula containing high amount of phosphate.⁵ We conducted a study to determine the common etiological factors of hypocalcemia and nutritional rickets in children.

Patients and methods:

This study was conducted in the department of Pediatrics, King Edward Medical University/Mayo hospital Lahore from March 1998 to January 2001. This was a cross sectional analytical study. A total of 120 patients were included in the study. We included children of ages ranging from 2 months to 60 months. These patients presented with tetany, clinical and skeletal manifestations of rickets and seizures. Permission of the parents was obtained before including the patients in this study. Patients with serious systemic disorders like meningitis, cerebral palsy and other neurological disorder were

excluded from the study. Detailed history was obtained and physical examination was done. All children were weighed and their weights were plotted on National Center for Health Statistics (NCHS) centile charts for weight.

Three to five cc of venous blood was sent for biochemical profile (calcium, phosphate and alkaline phosphatase level in the serum). Radiographs of wrist joint were taken and if required, other X-ray like chest and long bones were also obtained. The diagnosis of rickets was confirmed on the presence of clinical features and radiological changes on x-ray of wrist joint. Each child was assessed for age, sex, feeding pattern, exposure to sunlight, number of children in family, maternal age, educational status of mothers, presenting features of the disease, total calcium, phosphate and alkaline phosphatase level in the serum and X-ray wrist. The data were analyzed for determining frequencies by calculating percentages.

Results:

After analyzing the data, following results were obtained.

(a) Age and sex distribution

There was a total of 120 children ranging from 2 – 42 months. Out of them 60% (72) were boys and 40 % (48) were girls. (Table I) Out of the total, 55% of the children were below 6months, 19% were between 6 – 12 months, 18% were 1 – 2 year old and 8% were above 2 year of age. Mean age was 13 months.

(b) Anthropometric data

65% of the children were severely malnourished having weight below 5th centile on National Center for Health Statistics (NCHS) charts.

(c) Exposure to sunlight

32% of children got sunlight exposure for less than 30 minutes/week, 16% got it for 31 – 120 minutes/week and rest of them got it for more than 121 minutes.(Table I)

(d) Feeding pattern

Feeding pattern was analyzed in children below 2 years of age (110 out of the total). Among these 110 children, 9% were exclusive breast fed, 35% got diluted fresh milk, 1% got formula milk and 13% got both breast and bottle milk. In 45% children between 6 months and 2 years of age weaning was not started. (Table I)

(e) Parity

48% couples were having 2 or less children, 43% had more than 2 and less than 5 children while 9% had more than 5 children. (Table I).

(f) Maternal age

72% mothers were below 30 years of age, 24% were between 31 - 40 years and 3% were above 40 years of age at the time of interview. (Table I) Mean maternal age was 28.65 years.

(g) Maternal educational status

Regarding educational status of the mothers, our results showed that 31% of the mothers were uneducated, 37% had primary education, and 22% were matriculate while 9% got higher education. (Table I)

(h) Mode of presentation

When mode of presentation was analyzed, it was found that 85% children had seizures at the time of presentation and 15% were discovered on routine examination in children who reported to the emergency or outpatient's clinic. Out of those who had seizures 24.51% had upper respiratory tract infection, 51.95% had lower respiratory tract infection (pneumonia and bronchiolitis), 10.78% had other febrile illness and 12.75% presented with other diseases. 79% children had clinical signs of florid rickets. (Table II)

Table I: Etiological factors of Children having Hypocalcemia and Rickets n=120

Age distribution n=120	
Age	N (%)
<6months	66 (55)
6months-1year	23 (19.17)
1-2years	21 (17.5)
>2years	10 (8.33)
Sex distribution n = 120	
Sex	N (%)
Boys	72 (60)
Girls	48 (40)
Weight of the children n=120	
Weight	N (%)
< 5 th centile	78 (65)
> 5 th centile	42 (35)
Exposure to sunlight n=120	
Minutes/week approximately	N (%)
<30	39 (32.5)
31-120	19 (15.83)
>121	62 (51.67)
Feeding pattern in children <2years of age n=110	
Feeding Pattern	N (%)
Exclusively breast fed	45 (40.91)
Fresh diluted milk	39 (35.45)
Formula feed	13 (11.82)
Breast + bottle fed	13 (11.82)
Number of children in family n=120	
No. of children	N (%)
1-2	57 (47.5)
3-5	52 (43.33)
>5	11 (9.16)
Maternal age n=120	
Maternal age	N (%)
<30 years	87 (72.5)
31-40 years	29 (24.17)
>40 years	4 (3.33)
Educational status of mothers n=120	
Educational status	N (%)
Uneducated	38 (31.67)
Primary school education	44 (36.67)
High school education	27 (22.5)
College/University graduate	11 (9.16)

(i) Biochemical and radiological evidence

Results of biochemical profile showed that 67.5% of patients had serum calcium level equal to or below 7 mg/dl, 14% had less than 6 mg/dl, 18% had 7.1 – 7.5 mg/dl and non had the level equal to or more than 7.6 mg/dl., 69% had serum phosphate < 4 mg/dl and 31% had between 4 – 7 mg/dl and no patient was had serum phosphate above 7 mg/dl. Similarly, 5% of the children had alkaline phosphatase level <500, 19% had 500 – 1000 and 76% had >1000. (Table III).

Table II: Mode of presentations of children n=120

Mode of presentations	n (%)
Seizures	102/120 (85)
Lower respiratory tract infection (pneumonia & bronchiolitis)	53/102 (51.96)
Upper respiratory tract infection	25/102 (24.51)
Other febrile illnesses	11/102 (10.78)
Others	13/102 (12.75)
Discovered on routine examination / investigations	18/120 (15)
Clinical signs of florid rickets	79/120 (65.83)

Table III: Laboratory findings n=120

Laboratory findings	mg/dl	n (%)
Serum Calcium	< 6	17 (14.20)
	6.1 – 7	81 (67.5)
	7.1 – 7.4	22 (18.3)
Serum Phosphate	< 4	83 (69.2)
	4.1 – 7	37 (30.8)
	> 7	0 (0.00)
Serum Alkaline phosphatase (IU/L)	<500	6 (5)
	500–1000	32 (19.2)
	>1000	91 (75.8)

Discussion:

Hypocalcemia and rickets are emerging as a very common problem perhaps due to falling socioeconomic status of majority of the people. Nutritional rickets results from vitamin D deficiency. Extreme restriction of dietary calcium has also been documented as a cause.¹² In our research hypocalcemia presented most commonly (85%) with seizures. Sixty six percent of these children also had rickets. Our investigation was limited to cases of hypocalcemia and rickets among hospitalized patients. This study probably underestimated the magnitude of the problem in the population. Hypocalcemia and rickets are often diagnosed in our inpatients as well as in outpatient clinics.

We found that majority (53%) of the children presented below the age of 6 months. In most of the studies done in developing countries like Ethiopia¹³, Kuwait¹⁴ and Saudi Arabia¹⁰ the age range of hypocalcemic rachitic children was between 6 – 18

months. This is probably because of deficiency of vitamin D content of the maternal milk and fresh milk being fed to most (88%) of our children. We also observed slight male preponderance (male to female ratio 1.5:1). This is similar to results of studies conducted in Ethiopia¹³ and in a study conducted by Pinsloo¹⁵ whereas one to one ratio was reported from Saudi Arabia¹⁰.

We also found that more educated the mother, lesser is the chance of their children suffering from hypocalcemia. In our study, 38% children of uneducated mothers were found to be hypocalcemic and the results were comparable to the study conducted in Saudi Arabia.¹⁰ This appears to be logical as educated mothers are more aware of healthy ways of rearing their children. Similarly offsprings of younger mothers were more likely to have hypocalcemia (72% in mothers < 30 years old) than more experienced older mothers. Parity also plays an important role and in our study, mothers having large family size had more children affected from hypocalcemia. These results are also comparable to the study from Saudi Arabia¹⁰.

Inadequate exposure to sunlight is an important factor associated with the development of vitamin D-deficient rickets which in turn is a common cause of hypocalcemia in children. It has been documented that good exposure to sunlight reduces the incidence of hypocalcemia.⁹ Our study highlighted this fact and the results showed that hypocalcemia is due to lack of sunlight exposure in significant number of children (32.5%) and these results are comparable with other studies.^{3, 10} It is very difficult to define how much sun exposure is needed to prevent rickets because the amount of ultraviolet light that penetrates the skin is affected by many factors. Some of these factors are skin pigmentation, amount of body surface covered by clothing, air pollution, latitude, time of day and amount of cloud cover.¹⁶ 30 – 120 minutes exposure per week of sunlight exposure is needed depending on clothing coverage.¹⁶ No accurate estimate is available for children with darker skin. Sixty seven percent children in our study had exposure to sunlight for 30 – 120 minutes or more. This indicates that there may be an association of skin pigmentation and amount of clothing coverage with rickets and hypocalcemia in these children.

Breast-fed children are less likely to develop hypocalcemia as compared to those who receive fresh milk with high phosphorus content.⁶ However Hatun et al¹¹ observed that 83% infants who had vitamin D deficiency were exclusively breast-fed without supplemental vitamin D. We observed that 41% children were exclusively breast-fed and 35% were receiving fresh diluted milk. The results of our study are comparable with other studies.¹⁶ Mothers in Pakistan are not supplemented with vitamin D during pregnancy. Fresh milk because of its high phosphorus content also leads to hypocalcemia. Only 12% children in our set of patients were on formula milk that may have appropriate amounts of calcium.

Hypocalcemia can present with a wide variety of symptoms, the most important of which are seizures and recurrent chest infections. Rickets must be looked for as an underlying cause of these complaints. Elevated level of serum alkaline phosphatase is consistent finding in hypocalcemic patients. We observed that majority of the patients (85%) were admitted with seizures whereas 15% were diagnosed as cases of hypocalcemia on routine examination. Those children who had seizure because of hypocalcemia also had other problems. 76% of these children had acute respiratory infection. In a study from Karachi, only 15% of the rachitic children who reported to a health facility had acute respiratory infection.¹⁷ A significant number (15%) of patients were identified during routine examination and investigation. This indicates that the magnitude of the problem may be quite high in general population.

Conclusion:

We conclude from our study that hypocalcemia represents a major health problem in Pakistani children. Infants under 2 years of age are liable to have vitamin D deficiency rickets particularly if they are exclusively breast-fed or on fresh milk and having inadequate exposure to sunlight. Unfortunately, sunlight exposure can not be assessed easily and the minimum amount received to prevent rickets in our population is unknown. We also conclude that the higher the level of education of mothers, the less likely is the chance that their children become hypocalcemic and rachitic. Large family size is also an important factor that leads to reduced amount of care given to individual children.

References:

1. Broadus A E. Mineral metabolism. In: Felig P, Editors. Endocrinology and metabolism. New York: McGraw-Hill, 1981; 963-1079.
2. Nordin BE. Calcium and osteoporosis. Nutrition, 1997 Jul-Aug; 13(7-8):664-86.
3. Mivako K, Kinjo S, Kohmo H. Vitamin D deficiency rickets caused by improper lifestyle of Japanese children. *Pediatr Int* 2005; 47(2): 142 – 6.
4. Samiya N. Infant of diabetic mother: good outcome with appropriate care. *Pak Paediatr J* sep.1994; 18(3):125-8.
5. Singhal A, Campbell D. Hypocalcemia. [online]2005[cited 2005 Sep 27]. Available from:URL:<http://www.emedicine.com/ped/topic1111.htm>.
6. Potts J T Jr. Hypocalcemia. In: Braunwald E, Fauci A S, Kasper D, Hauser S L, Jameson J L, editors *Harrison's Principles of Internal Medicine*.15th ed. New York: McGraw-Hill; 2001: 2220 – 6.
7. Greenbaum L A. Hypocalcemia. In: Behrman R E, Kliegman R M, Jensen H B, editors *Nelson textbook of pediatrics*.17th ed. Philadelphia: WB Saunders; 2004: 208 - 14.
8. Gupta MM. Calcium imbalance in hypothyroidism. *J Assoc Physicians. India*, 1991 Aug; 39(8):616-8.
9. Makin HJ. Rickets. Osteomalacia and renal osteodystrophy. Part I & II. *J Bone Joint Surg*. 1974 ;(aA) 56: 101-28 and 352-86.
10. Erfan A, Nafia OA, Aziz A et al. Vitamin D deficiency rickets in maternity and children's hospital, Makkah, Saudi Arabia. *Ann Saudi Med* 1997; 17(3): 371-3.
11. Hatun S, Ozkan B, Orbak Z, Doneray H, Cizmecioglu F, Toprak D, Calikoglu AS. Vitamin D deficiency in early infancy. *J Nut* 2005; 135(2): 279 – 82.
12. Pettifor JM, Ross FF, Travers R, Glorieux FH, Deluca HF. Dietary calcium deficiency: a syndrome associated with one deformities and elevated serum 1, 25-hydroxy vitamin D concentrations. *Etab Bone Dis Related Res*. 1981; 2:301-5
13. Lulseged S. Severe rickets in Children's Hospital in Addis Ababa. *Ethiop Med J* 1990; 28(4): 175 – 81.
14. Lubani MM, Al Shab TS, Al Saleh QA, Sharda DC, Quattawi SA, Ahmed SA, Moussa MA, Reavy PC. Vitamin D deficiency rickets in Kuwait: the prevalence of preventable disease. *Ann Trop Paediatr* 1989; 9(3): 134 – 9.
15. Prinsloo JC. Aspects of juvenile rickets/osteopenia in black children. *S Afric Med J* 1987; 72(3): 201 – 4.
16. Temashek KM, Nesby S, Scanlon KS et al. Nutritional rickets in Georgia. *Pediatrics* 2001; 107(4):45.
17. Azra J, Billoo A G, Rafique M. Rickets in a slums of Karachi. *Specialist Pakistan J, Med Sci* 1996; 12(3):247-50