

Study of Risk Factors of Rickets in Children

¹Zubaida Abdel Nabi Bakeit and ²Fadia Yousif Abdel Megeid

¹Department of Food Science and Nutrition, Women Students Medical Studies & Sciences Sections,
Food Science and Nutrition Department, King Saud University, KSA

²Child Health and Nutrition, King Saud University, Women Students Medical Studies & Sciences Sections,
Food Science and Nutrition Department, King Saud University, KSA

Abstract: The objective of this work to determine some factors contributing to rickets in infant and children with special reference to socio-economic status, the type of feeding, maternal and infant vitamin D administration, calcium intake, exposure to sun light. The subject studied constituted 60 child representing different socio-economic districts who were attending the outpatient clinics of Abu El Rish Hospital for pediatric. They were randomly chosen. Their ages ranged between 6 month and 2 year (37males and 23 females) in comparison to normal sex and age matched (60) healthy controls. A questionnaire was administered to all mothers of the studied group including personal and socio-economic data, complaint, the type of feeding, history of maternal and infant vitamin D administration and calcium intake, also history of some social factors of rickets including the numbers of gravida, dressing habits, gestational vitamin D and calcium supplementation and history of exposure to sun light for both the mother and the infant. A complete examination of the infants and children was performed with special stress on the rachitic manifestations as enlargement of the head, size of anterior fontanel, eruption of teeth and skeletal deformity. Diagnosis of vitamin D deficiency rickets was based on the usual clinical criteria and biochemical findings including low serum vitamin D, calcium, phosphorus and high serum alkaline phosphatase. Results: A significance difference was found between rachitic cases and control as regards their socio- demographic data. ($P < 0.01$) and 58% of the rachitic cases came from slum areas. The sex ratio was found to be 1.56 male /female. As regards to some social factors of rickets, it was found that 75% of rachitic cases with lack exposure to sun light and 21% of rachitic cases are living in open house. Our result revealed that 29% and 32% of mother's of rachitic cases with history of vitamin D supplementation and calcium intake respectively, with significance difference ($P \geq 0.05$). As regards the type of feeding: 62% of the rachitic infants and children were breast fed, 12% had received vitamin D therapy. The most common signs found was enlargement of the head 40%, delayed closure of anterior fontanelle 18%, the complications found on examination were: 28% gastroenteritis: A highly negative correlation coefficient was found between the level of vitamin D, calcium as well as phosphorus and manifestation of the rickets ($p < 0.05$). Also a positive correlation coefficient was found between the level of alkaline phosphatase and manifestation of the rickets ($p < 0.05$). Regarding association between vitamin D deficiency and different predisposing factor, it was observed from that most predisposing factor for vitamin D deficiency rickets was low vitamin D supplement during infancy, less exposure to sun light, gestational deficiency of vitamin D, negative history of calcium supplement in infancy, gestational deficiency of calcium intake and low socio-economic status represented by increased family size and low family income and mother education.

Key words: Vitamin D deficiency • Calcium supplementation • Rachitic manifestations • Alkaline phosphatase

INTRODUCTION

Nutritional rickets is gaining the attention of public health professionals and individual clinicians worldwide as the disease remains an endemic problem in many

developing countries and has re-emerged in a number of developed countries, where it was thought that the disease had been almost eradicated [1]. In the middle East, vitamin D deficiency and rickets continues to be a public health problem despite abundant all year sunshine in

Corresponding Author: Zubaida Abdel Nabi Bakeit, Food Science and Nutrition Department, Women Students Medical Studies & Sciences Sections, Food Science and Nutrition Department, King Saud University, KSA.

many of the regions. The cause of rickets in Middle East children remains an enigma. Limited sunlight exposure, exclusive or prolonged breastfeeding without vitamin D supplements, gestational vitamin D deficiency and low socioeconomic status have a key role in the pathogenesis of the disease [2]. Infants are particularly at risk especially if they are exclusively breast fed. While breastfeeding is the recommended method of infant feeding and provides infants with necessary nutrients and immune factors, breast milk alone does not provide infants with an adequate intake of vitamin D. Most breastfed infants are able to synthesize additional vitamin D through routine sunlight exposure. Rickets among breastfed infants in the United States caused researchers to take another look at whether all breastfed infants were getting adequate vitamin D [3]. The vitamin D stores of the newborn depend entirely on the vitamin D stores of the mother. If the mother is vitamin D-deficient, the infant will be deficient because of decreased maternal fetal transfer of vitamin D [4]. Inadequate exposure to sunlight and less dietary intake during pregnancy and lactation cause both inadequate body stores in the newborn and in breast-milk [5]. We do encourage breast feeding for the first months of life but also we recommend vitamin D supplementation for maternal and infant from the first month of life in order to prevent the nutritional rickets.

MATERIALS AND METHODS

The subject studied constituted 60 Egyptian child representing different socio-economic districts who were attending the outpatient clinics of Abu El Rish Hospital for pediatric, Egypt. They were randomly chosen. Their ages ranged between 6 month and 2 year (37males and 23 females) in comparison to normal sex and age matched healthy controls (60).

Methods: A questionnaire was administered to all mothers of the studied group including:

Personal and Socio-Economic Data: Including, name, age, sex, address, education and occupation of both the mother and the father and family income, also questions about some social factors related to rickets including the numbers of gravida, dressing habits, gestational vitamin D and calcium supplementation and history of exposure to sun light for both the mother and the infant.

Dietetic History: Including: the type of feeding, breast, artificial or both, solids and history of vitamin D administration for both infant and mother.

Health History: A-Questions related to any manifestation of rickets and history of complication.

A Complete Examination: Of the infants and children was performed with special stress on the rachitic manifestations as enlargement of the head, size of anterior fontanel, eruption of teeth, any skeletal deformity and rosary beads, etc. All infants were healthy with normal weight for their ages.

Investigation: Diagnosis of Vitamin D deficiency rickets was based on the usual clinical criteria and low level of serum calcium, phosphorus and 25-hydroxy vitamin D (25(OH) D) and high serum alkaline phosphatase. : Blood samples were collected and were analyzed by atomic absorption spectrophotometer (AAS) to measure Serum calcium and phosphorus [6]. Serum 25-hydroxy vitamin D (25(OH) D) level was assessed by Jean-Claude Alvarez, Philippe Demazzancourt [7]. Serum alkaline phosphatase was measured [8].

Statistical Analysis: Data were expressed as mean \pm SD and were analyzed statistically using SPSS package; collected data was statistically analyzed using suitable statistical tests (chi square, t-test, correlation coefficient, odd's ratio). The P value was considered significant at ($P \leq 0.05$) [9].

RESULTS

The study was conducted on 60 rachitic cases whose ages ranged from 6 months and 24 months (37males and 23 females) with a mean age of 16.1 ± 2.36 months, As regards to their socio- demographic data (Table 1): 58% of the rachitic cases came from slum areas, while 24% came from rural areas and 18% from urban areas. It was observed from the table that most of the rachitic cases (74%) with families size 2 persons. As regards the educational status, (43%) of children's fathers of rachitic child were preparatory and secondary (49%) of children's mothers of rachitic child were illiterate. On describing the occupation: 38% of fathers of rachitic child were manual and 36% were employees. On describing the occupation of children's mothers about (62%) of mothers of rachitic child were house wives with 60% insufficient family income .A significance difference ($P < 0.01$) was found between rachitic cases and control as regards their socio demographic data. The sex ratio was found to be 1.56 male/female (Table 2). This showed a significant predominance of the male 'sex in comparison to the census done in Egypt 2009 = 1.05 (Central Agency for Mobilization and Statistics).

Table 1: Socio- economics characteristics of the studied group

Variables	Cases		Control		P
	No. (60)	%	No. (60)	%	
Age (months)	6-24				P≤0.01
Mean	16. 1±2.36				
Residence					
Slum areas	35	58	5	9	
Rural areas	14	24	14	23	
Urban areas	11	18	41	68	
Family Size					
≤ 2nd person	16	26	41	69	P ≤ 0.01
> 2nd person	44	74	19	31	
Father education					
Illiterate	15	25	5	8	P ≤ 0.01
Preparatory & Secondary	26	43	13	22	
University & Postgraduate	19	32	42	70	
Mother's education					
Illiterate	29	49	7	11	P ≤ 0.01
Preparatory & Secondary	17	29	20	34	
University & Postgraduate	14	22	33	5	
Father's occupation					
Manual	23	38	2	4	P ≤ 0.01
Employee	22	36	13	21	
Professional	15	26	45	75	
Mather's occupation					
Working	23	38	52	86	P ≤ 0.01
Non Working	37	62	8	14	
Family income					
Sufficient and saving	13	22	41	68	P ≤ 0.01
Sufficient	11	18	14	24	
Insufficient	36	60	5	8	

Table 2: Sex distribution among cases of Rickets

	Sex		Total
	Male	Female	
Rachitic patient			
NO.	37	23	60
%	61	39	100

Sex ratio in our rachitic patients = 1.56

Sex ratio in census done in Egypt 2009 = 1.05

t test = (P < 0.001).

Table 3: Distribution of the studied group according to some maternal characteristic related to rickets

Factors	Mother's of rachitic cases		Mother's of the control		P
	No.(60)	%	No.(60)	%	
Age					
≥ 25 years	29	49	34	56	p ≥ 0.05
≥ 25 years	31	51	26	44	
Numbers of gravida					
1	13	21	27	45	P ≥ 0.05
2-3	11	19	27	45	
≥ 4	36	60	6	10	
Gestational vitamin D supplementation	98	29	41	69	P ≥ 0.05
Gestational calcium intake	19	32	47	79	P ≥ 0.05
Dressing habits					
Completely covered	29	49	23	39	p ≥ 0.05
Un completely covered	31	51	37	61	
Daily exposure time to sun light during pregnancy					
≥ 1 hour / day	42	70	17	29	P ≥ 0.05
≥ 1 hour / day	18	30	43	71	

Table 3 showed distribution of the studied group according to some maternal characteristic related to the rickets : it was observed that 49% of mother's of rachitic cases with aged less than 25 years compared to 56% of mother's of the control while 51% of mother's of rachitic cases with aged more than 25 years compared to 44% of mother's of the control without significance difference was found between the two groups as regards their aged ($P \leq 0.05$), it was observed from the table that 60% of mother's of rachitic cases with history of numbers of gravida ≥ 4 compared to 10% only of mother's of the control with significance difference ($P \geq 0.05$), it was observed from the table that only 29% of mother's of rachitic cases with history of vitamin D supplementation compared to 69% of mother's of the control with significance difference ($P \geq 0.05$), also only 32% of mother's of rachitic cases with history of calcium intake compared to 79% of mother's of the control with significance difference ($P \geq 0.05$), it was observed from the table that 49% of mother's of rachitic cases with history of completely cover the arms and legs compared to 39% of mother's of the control without significance difference was found between rachitic cases and control as regards maternal dressing habits, it was observed from the table that 70% of mother's of rachitic cases exposed to sun light less than one hour compared to 71% of control exposed to sun light more than one hour with significance difference ($P \geq 0.05$).

Table 4 showed distribution of studied group according to some social factors associated with rickets, it was observed from the table that 75% of rachitic cases with history of lack exposure to sun light comparing to 15% of control, while 75% of rachitic cases with history of complete wrapping of child and 21% of rachitic cases are living in open house. As regards the type of feeding (Table 5) 62% of the rachitic infants and children were breast fed, 15% of them were bottles feeding and breast, 11% of them were bottles feeding only while 7% of them were breast, bottles feeding and solid and 5% of them were solids only. It was observed from the table, 12% had received vitamin D therapy. It was observed from the Table 6 the most common signs found were enlargement head 40%, delayed closure of anterior fontanelle 18%, gross motor delay 13%, skeletal deformity 11%, Marfan's sign 8%, delayed eruption of teeth 5%, rachitic rosary beads 3%, umbilical hernia 1% and chest deformity 1%.

Table 7 showed distribution of studied group according to the complications, It was observed from the table that the most common complications found were: 28% gastroenteritis, bronchitis 22%, 20% dwarfism and residual deformities of bones and Joints, 14% convulsion while 16% of the cases of the rickets without complication. Table 8 showed distribution of studied group according to blood analysis, it was observed from the table that there was high percentage (79.5) of rachitic cases with Serum level 25-hydroxy vitamin D (25(OH)D)

Table 4: Distribution of the studied group according to some social factors associated with rickets

Factors	Rachitic cases		Control		P
	No	%	No	%	
≥ 30 minutes exposure to sun light.	15	25%	51	85%	$p \leq 0.01$
Complete wrapping of child	45	75%	20	30%	
Living in open house	13	21%	42	70%	

Table 5: Distribution of the studied group according to type of feeding

Type of feeding	Cases		Cases	
	No	%	No	%
Breastfeeding only	37	62%	18	30%
Bottles and breastfeeding	9	15%	18	30%
Bottles feeding only	7	11%	12	20%
Breastfeeding, bottles feeding and solids	4	7%	11	19%
Solids only	3	5%	1	1%
Vitamin D supplements	7	12%	42	70%

Table 6: Distribution of the studied group according to the manifestation

Manifestation	Rachitic	%
Enlarged head	24	40
Delayed closure of anterior fontanel	11	18
Gross motor delay	8	13
Skeletal deformity	7	11
Mar fans sign	5	8
Delayed eruption of teeth	3	5
Rachitic rosary beads	2	3
Umbilical hernia	1	1
Chest deformity	1	1

Table 7: Distribution of the studied group according to the complication

The complication	No	%
Gastro-enteritis	17	28
Bronchitis	13	22
Dwarfism and residual deformities of bones	12	20
Convulsion	8	14
Without complication	10	16
Total	60	100

Table 8: Distribution of the studied group according to blood analysis

Items	Rachitic cases		Control		Chi square p
	No (60)	%	No (60)	%	
25(OH)D					
≤ 15ng / ml	48	79.5	11	18	P ≤ 0.0
> 15ng / ml	12	20.5	49	82	
Alkaline phosphatase					
≤ 25 K.U	10	16	48	80	P ≤ 0.0
> 25 K.U	50	84	12	20	
Calcium					
≤ 9 mg /dl	36	60	20	30	P ≤ 0.0
>9 mg /dl	24	40	40	70	
Phosphorus					
≤ 3 mg/dl	39	65	10	16	P ≤ 0.0
> 3 mg/dl	21	35	50	84	

Table 9: Correlation coefficient between manifestation of vitamin D deficiency and values of vitamin D, alkaline phosphatase and calcium and phosphorus of the studied groups

Variable	Correlation coefficient	P
Vitamin D	- 0.62	< 0.05
alkaline phosphatase	0.8	< 0.05
Phosphorus	-0.4	< 0.05
Calcium	-0.3	< 0.05

Table 10: Association between vitamin D deficiency rickets and different Predisposing factor

Predisposing factor	Odd's ratio
Low vitamin D supplementation during infancy	5.3
Less exposure to sun light.	- 4.5
Gestational vitamin D supplementation	-3.9
negative history of calcium supplementation in infancy	3.4
Gestational calcium supplement	3.3
Family size	2.8
Family income	-2.2
Mother education	-2.1

less than 15ng/ml, 84% of rachitic cases with serum level alkaline phosphatase more than 25 k.u and there was high percentage (60%) of rachitic cases with Serum level calcium less than 9 mg/dl and high percentage (65%) of rachitic cases with Serum level phosphorus less than 3 mg/dl . A significance difference was found between rachitic cases and control as regards blood analysis ($P<0.01$).

Table 9 showed Correlation coefficient between manifestation of vitamin D deficiency and values of vitamin D, alkaline phosphatase, calcium and phosphorus of the studied groups It was observed from the table: A highly negative correlation coefficient was found between the level of vitamin D, calcium as well as phosphorus and manifestation of the rickets ($p<0.05$). Also a positive correlation coefficient was found between the level of alkaline phosphatase and manifestation of the rickets ($p<0.05$). Table 10 showed Association between vitamin D deficiency rickets and different Predisposing factor: it was observed from the table that most predisposing factor for vitamin D deficiency low vitamin D supplement during infancy (Odd's ratio -5.3), less exposure to sun light (Odd's ratio -4.5), gestational deficiency of vitamin D (Odd's ratio -3.9), negative history of calcium supplement in infancy (Odd's ratio -3.4), gestational deficiency of calcium intake (Odd's ratio -3.3) and low socio-economic status represented by increased family size (Odd's ratio -2.8) and family income (Odd's ratio -2.2) and mother education (Odd's ratio -2.1).

DISCUSSION

During the last 10 to 20 years rickets due to vitamin D deficiency has almost disappeared from the United States and from many countries of Western Europe [3]. However, nutritional rickets still exists in a number of countries like Egypt. Egypt, a country where the sun is shining all the year, has still a high prevalence of nutritional or vitamin D deficiency rickets [10]. This work has demonstrated many epidemiological aspects of rickets in Egypt, one of the important epidemiological aspects of nutritional rickets found in this study, was that most of the rachitic cases with low socioeconomic status and 58% of them came from slum areas, where poverty, ignorance and illiteracy predominate [11]. We have found a high incidence of rickets among male infants, the difference was statistically significant, the sex ratio male/female being 1.56, compared to the normal Egyptian sex ratio of 1.05 (Central agency for mobilization and statistics 2009). The male sex predominance found in our study, is in accordance with previous study of Elkholy [12]. Childs *et al.* [13]

reported that one of the facts of life is the greater susceptibility to disease and to early mortality of the human male. The reasons for these discrepancies are unknown but might be thought in an analysis of differences between the sexes in development and in genetic constitution. The Y chromosome is considerably smaller than the X given the female a 4-5% quantitative superiority in genetic material .So differences between the normal male and female might exit because the female has two such genes while the male has one, expression of this difference might be in susceptibility to vitamin D deficiency rickets. In other word, the presence of a normal allele in the female protects her against the ravages of a mutant which, unopposed by any homologue in the male, does harm. From the present study, it has become clear that some of the factors play a more critical role than others in causing nutritional rickets. These factors have been quantified. Our result revealed that 75% of rachitic cases with history of lack exposure to sun light with history of complete wrapping of child and 21% of rachitic cases are living in open house. This finding was supported by Majeed *et al.* [14], who found lack of exposure to sunlight due to complete wrapping of the child play more important role for contribution of nutritional rickets. Our result revealed that only 29% and 32% of mother's of rachitic cases with history of vitamin D supplementation and calcium intake respectively, also most of mother's of rachitic cases (70%) exposed to sun light less than one hour. This finding is in agreement with those obtained by Pehlivan *et al.* [15], who reported that maternal vitamin D deficiency due to inadequate exposure to sunlight and less dietary intake of vitamin D during pregnancy and lactation cause both inadequate body stores in the newborn and breast milk. Also our study is in accordance with previous study of Thacher *et al.* [16], who found that the breast-milk calcium concentration in mothers of children with rickets was lower than in mothers with unaffected children. This concept is not surprising as low calcium intake increase vitamin D catabolism thus increasing requirements to maintain a normal circulating concentration of 25 (OH)D.

As regards the type of feeding 62% of the rachitic infants and children were breast fed, this result is in agreement with study of Balasubramanian *et al.* [17] who revealed that most of the rachitic children were breast-fed, as breast-feeding rates increase, the incidence of vitamin D deficiency rickets is also expected. This finding was supported by Ponnappakkam [18], who revealed that most of the rickets patients were breast-fed. The increase in the practice of breast-feeding, associated with the belief that

“breast is breast” and that breast milk does not require supplementation because it is a baby’s “perfect food ” may lead to decreased 25-hydroxy vitamin D(25-OHD) intake from other sources and thereby causing rickets[19]. Our result revealed that 12% only of all our rachitic infants had received vitamin D supplementation, this result came in agreement with study from China [20] observed that breast- fed infant with insufficiency intake of vitamin D supplement especially those living in parts of the country where inadequate exposure to sunlight. Hollis [21] noticed that although breast milk is adequate for growth and bone mineralization in the first year of life but vitamin D supplementation must be necessary for breast-fed infants. We do encourage breast feeding for the first months of life but also we recommend vitamin D supplementation from the first month of life in order to prevent the genetic susceptibility especially to male in our country to nutritional rickets. It was observed from our result that the percentage of the rachitic cases were received vitamin D supplementation was low compared to the control, which denotes the low level of health education among the mothers. Health education can be carried out through mass media and health workers must be well established in these respects. Our result revealed that 11% of the rachitic infants and children were bottle feeding only this is obvious due to the expensive formulas sold in comparison to breast milk Gartner [22]. The most common signs found in our rachitic infants were enlargement of the head circumference, delayed closure of anterior fontanelle and skeletal deformity, the investigation support that the most rachitic cases with elevation serum level of alkaline phosphatase, low serum level of 25(OH) D, calcium as well as phosphorus, this is in accordance with previous study of Balasubramanian *et al.* [17] and the present results are in agreement with those reported by Ladhani *et al.* [23] and Biswas *et al.* [24]. Consequently we do recommended complete clinical examination to every infant coming to the outpatient clinics in order to detect early manifestations of vitamin D deficient rickets. So, we advice the routine measurement of skull circumference which must be an essential part of the examination and was found to be an important tool together with the elevated level of serum alkaline phosphatase in the diagnosis of active rickets.

Regarding association between vitamin D deficiency and different predisposing factor, it was observed from our result that the most predisposing factor for vitamin D deficiency rickets was low vitamin D supplement during infancy especially exclusively breast fed, less exposure to sun light, gestational deficiency of vitamin D, negative history of calcium supplement in infancy, gestational

deficiency of calcium intake and low socio-economic status represented by increased family size and low family income and mother education. Similar findings were obtained by Thacher *et al.* [16] and Dawodu *et al.* [25], where their study revealed many risk factors for rickets in infant and children indicating a multi-factorial nature of the disease.

CONCLUSION

Nutritional rickets is a multi-factorial condition. However, several factors seem to make important contributions. Among these, prolonged breast-feeding without vitamin D supplementation, low socio-economic status represented by increased family size and low family income, lack of exposure to sunlight and nutritional status of mother .It was concluded that nutritional rickets is still a problem in our country and much effort should be done in order to combat it. It is suggested that a national campaign to promote awareness of the risks of vitamin D deficiency, particularly among susceptible populations be done to eliminate rickets as a cause of morbidity.

ACKNOWLEDGMENT

This study was supported by a grant from Research Center for Female Scientific and Medical Colleges in King Saud University.

REFERENCES

1. John. M.P., 2008. Vitamin D &/or calcium deficiency rickets in infants & children: a global perspective. *Indian J. Med. Res.*, 127: 245-249.
2. Baroncelli, G., B. Abdullah, M. El Kholy, L. Audi, Y. Cesur, B. Ozkan, M. Rashad, M. Fenández, Y. Weisman, G. Saggese and Z. Hochberg, 2007 . Rickets in the Middle East: Role of Environment and Genetic Predisposition. *The Journal of Clinical Endocrinology & Metabolism*, 93(5): 743-1750.
3. Thacher, T.D., P.R. Fischer, M.A. Strand and J.M. Pettifor, 2006. Nutritional rickets around the world: causes and future directions. *Ann. Trop. Paediatr.*, 26: 1-16.
4. Salle, B.L., E.E. Delvin and A. Lapillonne, 2000. Prenatal metabolism of vitamin D. *Am. J. Clin. Nutr.*, 71(Suppl): 1317S-1324S.
5. Kreiter, S.R., R.P. Schwartz, H.N. Jr. Kirkman, P.A. Charlton, A.S. Calikoglu and M.L. Davenport, 2000, Nutritional rickets in African American breast-fed infants. *J. Pediatr.*, 137(2): 153-7.

6. Elmer, P. and N. Conn, 1975. Analytical Methods for Atomic Absorption Spectro- photometry. London, Oxford Press, pp: 273-290.
7. Jean-Claude Alvarez and Philippe De Mazancourt, 2001. Rapid and sensitive high-performance liquid chromatographic method simultaneous determination of retinol, atocopherol, 25-hydroxy vitamin D3 in human plasma with photo diode-array ultra violet detection, *J. Chromat. B*, 755: 129-135.
8. Miale, J.B., 1972. Lab. Medicine. Haematology. The C.V. Mosby Co. Saint Louis, pp: 1053.
9. Dean, A.G., J.A. Dean and D. Coulombier, 2000. Epi- info (version 6.1): A word Processing Data Base and Statistics Program for Epidemiology and Micro Computer Office. Centers of Disease Control, Atlanta, Georgia, USA.
10. Bereket, A., 2003. Rickets in developing countries. In: Hochberg Z, ed. Vitamin D and rickets. Basel, Switzerland: Karger, pp: 20-232.
11. Manaseki-Holland, S., M. Zulf Mughal, Z. Bhutta and M. Qasem Shams, 2008. Vitamin D status of socio-economically deprived children in Kabul, Afghanistan. *International Journal for Vitamin and Nutrition Research*, 78(1): 16-20.
12. El Kholy, M.S., F.Y. Abdel Megeid and F.A. Farid, 1992. A genetic study of Vitamin D deficiency rickets. Sex differences and ABO typing. *J. Egypt. Public Health Association*, 62: 213-22.
13. Childs, B., 1965. Genetic origin of some sex differences among human beings. *Pediatrics*, 35: 798.
14. Majeed, R., Y. Memon, M. Khowaja, F. Majeed, M. Usman Ali and U. Rajar, 2007. Contributing factors of rickets among children at Hyderabad. *J. Liaquat Uni. Med. Health Sci.*, 6(2): 60-5.
15. Pehlivan, I., S. Hatun, A. Metin, B. Kadir and G. Ayse, 2003. Maternal vitamin D deficiency and vitamin D supplementation in healthy infants. *The Turkish Journal of Pediatrics*, 45: 315-320.
16. Thacher, T.D., P.R. Fisher, J.M. Pettifor, J.O. Lawson, C.O. Lsichei and G.M. Chan, 2000. Case-control study of factors associated with nutritional rickets in Nigerian children. *J. Pediatrics*, 137: 367-373.
17. Balasubramanian, S. and R. Ganesh, 2008. Vitamin D deficiency in exclusively breast-fed infants. *Indian J. Med. Res.*, 127: 250-255.
18. Ponnappakkam, T., A. Ravichandran, E. Bradford, G. Tobin and R. Gensure, 2008. Breast-feeding and Vitamin D Supplementation Rates in the Ochsner Health System. *The Ochsner Journal*, 8: 146-150.
19. Lauer, J.A., A.P. Betran, A.J. Barros and M. Deonis, 2006. Deaths and years of life lost due to suboptimal breast feeding among children in the developing world: a global ecological risk assessment. *Public Health Nutr.*, 9: 673-85.
20. Specker, B.L., M.L. Ho and A. Oestreich, 1992. Prospective study of vitamin D supplementation and rickets in China. *J. Pediatrics*, 120: 733-9.
21. Hollis, B.W. and C. L. Wagner, 2004. Assessment of dietary vitamin D requirements during pregnancy and lactation. *Am. J. Clin. Nutr.*, 79: 717-726.
22. Gartner, L.M. and F.R. Greer, 2003. Prevention of rickets and vitamin D deficiency: new guidelines for vitamin D intake. *Pediatrics*, 111(1): 908-10.
23. Ladhani, S., L. Sirinivasan and C. Buchanan, 2004. Presentation of vitamin D deficiency. *Arch Dis. Child.*, 89: 781-4.
24. Biswas, A.C., M. Molla and K. Al Moslem, 2000. A baby with bulging anterior fontanelle. *Lancet*, 356: 132.
25. Dawodu, A., M. Agarwal, M. Hossain, J. Kochiyil and R. Zayed, 2003. Hypovitaminosis D and vitamin D deficiency in exclusively breast- feeding infants and their mothers in slimmer: a justification for vitamin D supplementation of breastfeeding infants. *J. Pediatrics*, 142: 169-73.