Egyptian Pediatric Association Gazette (2016) **64**, 86–90

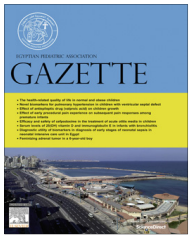
HOSTED BY

ELSEVIER

Contents lists available at ScienceDirect

Egyptian Pediatric Association Gazette

journal homepage: http://www.elsevier.com/locate/epag



Serum levels of 25(OH) vitamin D and immunoglobulin E in infants with bronchiolitis

Bahaa El Din Mohamed Hassanein [a], Doaa Refaey Soliman [a], Sahar Mohamed Abd Elhameed Fayed [b], Mohamed Mosaad Mohamed Suleiman [a,*]

[a] *Pediatric Department, Faculty of Medicine, Benha University, Benha, Egypt*
[b] *Clinical Pathology Department, Faculty of Medicine, Benha University, Benha, Egypt*

Received 11 September 2015; accepted 1 February 2016
Available online 21 March 2016

KEYWORDS

Bronchiolitis;
25(OH) D;
IgE

Abstract Vitamin D status has a great effect on respiratory health throughout the lifespan.
The aim of this study: The aim of this study was to estimate and find the relationship between both 25(OH) vitamin D and immunoglobulin E serum levels and bronchiolitis in infancy.
Methods: We quantified serum 25(OH) D and serum immunoglobulin E using (ELISA) in 50 infants with bronchiolitis and 31 healthy controls of matched age and sex.
Results: The mean serum 25(OH) vitamin D was significantly lower in cases than in controls; it was (12.3 ± 3.9 & 26.2 ± 10.0 ng/ml, respectively with $p = 0.003$). The mean serum IgE was significantly higher in cases than in controls; It was (170 ± 66 & 43.8 ± 14.2 IU/ml, respectively and $p = 0.01$). Serum IgE showed a non-significant negative correlation with serum 25(OH) vitamin D ($r = -0.141$, $p = > 0.05$).
Conclusions: Serum 25(OH) vitamin D was found in decreased quantities in infants with bronchiolitis and it was negatively correlated with serum IgE, suggesting that vitamin D may play a role in the pathogenesis of bronchiolitis.

Introduction

Bronchiolitis is the most common lower respiratory tract disease and the most common reason for hospital admission in infants.[1] In addition to the role of vitamin D in bone metabolism, it has been found that vitamin D status has a great effect on respiratory health throughout the lifespan. And there is emerging evidence of the potential importance of vitamin D deficiency in susceptibility to acute respiratory infection.[2]

Immunoglobulin E (IgE) was first described by Ishizaka in 1967. It has the lowest serum concentration of all circulating immunoglobulin isotypes. And it has found to be involved in the pathogenesis of many diseases.[3] Immunoglobulin E mediates Type 1 allergic reactions that play role in the pathogenesis of bronchiolitis.[4]

Aim of the work

We aimed to estimate and find the relationship between both 25(OH) vitamin D and immunoglobulin E serum levels and bronchiolitis in infancy.

* Corresponding author.
Peer review under responsibility of Egyptian Pediatric Association Gazette.

http://dx.doi.org/10.1016/j.epag.2016.02.002

Subjects and methods

Subjects

This case control study was conducted on 81 infants in Benha University Hospital and Toukh Fever Hospital; 50 infants with first episode of acute bronchiolitis as described by the American Academy of Pediatrics statement, which states that children with bronchiolitis typically have "rhinitis, tachypnea, wheezing, cough, crackles, use of accessory muscles, and/or nasal flaring".[5] Their age ranged from 2 months to 2 years and 31 healthy infants of matched age and sex were selected as controls. Patients were excluded from the study if they had one or more of the following characteristics: history suggestive of chronic cardiopulmonary disease, history of previous attacks of chest wheezing, immunodeficiency, on corticosteroid therapy, malnutrition or rickets, any chromosomal, genetic or endocrinal disorders, renal or hepatic disorders, malignancy and atopy.

Methods

The study protocol received approval of the research ethics committee of the pediatric department at Benha University. All infants included in this study were subjected to the following; Full medical history with special emphasis on chest symptoms and thorough clinical examination including chest examination and diagnosis of cases of bronchiolitis on the basis of history and physical examination according to the American Academy of Pediatrics recommendation. Blood sample was taken from each subject, about 2 ml of venous blood, withdrawn into a plain tube, left to clot then centrifuged and the separated serum stored at −20 °C. Then serum levels of 25(OH) D and immunoglobulin E were measured using Enzyme Linked Immunosorbent Assay technique (ELISA).

Statistical analysis

Data were analyzed using Statistical Package of Social Science program (SPSS) 16 software package under *Windows 8* enterprise edition 2013 operating system & statistics package BS3 on android 4.4 ice cream sandwich operating system. Graphic presentation of data was done by using EXCEL 2007 and SPSS 16 software package software.

Results

Demographic and laboratory data for cases and controls are demonstrated in Tables 1 and 2, respectively. The mean serum 25(OH) vitamin D was significantly lower in cases than in controls; it was (12.3 ± 3.9 & 26.2 ± 10.0 ng/ml, respectively with $p = 0.003$) as shown in Table 3. Table 4 shows that the mean serum IgE was significantly higher in cases than in controls; It was (170 ± 66 & 43.8 ± 14.2 IU/ml, respectively and $p = 0.01$). And there was a non-significant negative correlation between serum 25(OH) vitamin D and serum IgE ($r = -0.141$, $p = > 0.05$) as seen in Fig. 1.

Table 1 Analysis of basic characteristics and laboratory data of cases.

		Cases No = 50	
		No.	%
Gender	Male	31	62
	Female	19	38
Age (mean ± SD)		7.2 ± 3.3 months	
Residence	Rural	32	64
	Urban	18	36
Social class	Low	17	34
	Medium	32	64
	High	1	2
Sun exposure	Adequate	17	34
	Inadequate	33	66
Vitamin D supplementation	Adequate	12	24
	Inadequate	38	76
Serum 25(OH) vitamin D	Minimum	6.67	(ng/ml)
	Mean	12.3	
	Maximum	28.4	
Serum Immunoglobulin E	Minimum	11.8	(IU/ml)
	Mean	170.3	
	Maximum	604.22	

Table 2 Analysis of basic characteristics and laboratory data of controls.

		Controls No = 31	
		No	%
Gender	Male	14	45.2
	Female	17	54.8
Age (mean ± SD)		6.6 ± 1.6 months	
Residence	Rural	18	58.1
	Urban	13	49.9
Social class	Low	4	12.9
	Medium	22	71
	High	5	16.1
Sun exposure	Adequate	27	87
	Inadequate	4	13
Vitamin D supplementation	Adequate	25	80.6
	Inadequate	6	19.4
Serum 25(OH) vitamin D	Minimum	15.3	(ng/ml)
	Mean	26.2	
	Maximum	51.8	
Serum Immunoglobulin E	Minimum	2.35	(IU/ml)
	Mean	43.8	
	Maximum	148.5	

Discussion

In addition to the role of vitamin D in bone metabolism, it has been found that vitamin D status has a great effect on respiratory health throughout the lifespan. And there is emerging evidence of the potential importance of vitamin D deficiency in susceptibility to acute respiratory infection.[2] Immunoglobulin E (IgE) was first described by Ishizaka in 1967. It has the lowest serum concentration of all circulating immunoglobulin isotypes. And it has been found to be involved in the pathogenesis

Table 3 Comparison between cases & controls regarding the mean serum 25(OH) vitamin D.

Serum 25(OH) vitamin D	Cases No = 50	Controls No = 31	*p* value	Significance
Mean ± SD	12.3 ± 3.9	26.2 ± 10.0	0.003	Significant

Table 4 Comparison between cases & controls regarding the mean serum immunoglobulin E (IgE).

Serum IgE	Cases No = 50	Controls No = 31	*p* value (unpaired t test)	Significance
Mean ± SD	170.3 ± 66	43.8 ± 14.2	0.01	Significant

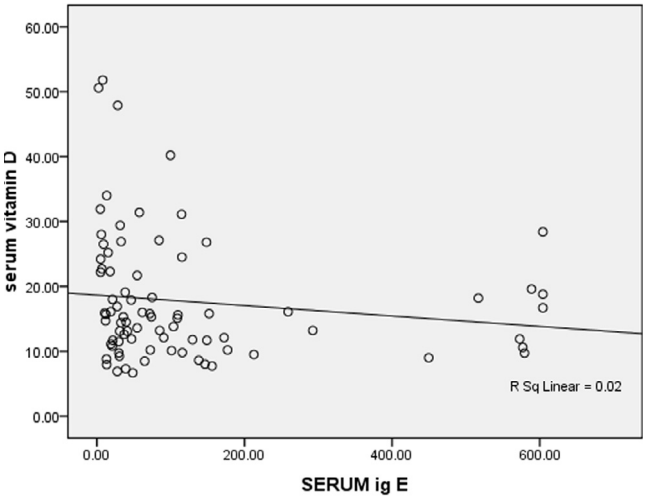


Figure 1 Correlation between serum IgE and serum 25(OH) vitamin D.

of many diseases.[3] Immunoglobulin E mediates Type 1 allergic reactions that play a role in the pathogenesis of bronchiolitis.[4]

In this work we found that males are affected with bronchiolitis more than females; as the male infants with bronchiolitis were (62%) and female ones were (38%) with male to female ratio (1.6:1). This finding is supported by the study done by Balachandra and Puttalingamma[6] to find the prevalence of bronchiolitis in Mysore district in India; they found that it is more common in males. Malla et al.[7] found that bronchiolitis occurs 1.25 times more frequently in males than in females and they reported that the exact reason for this difference is unknown. Malik et al.[8] explained that the high incidence of acute bronchiolitis in males as compared to females may be attributed to the presence of two X chromosomes which provide greater genetic diversity to the female immunologic defences.

Most of cases (64%) were from rural residence and (36%) were from urban. This is in agreement with Sharma et al.[9] who found that rural children are affected by acute respiratory infections, including bronchiolitis more than urban children. Similar finding was reported by Carroll et al.[10] who found that infants in rural areas were more likely to have a bronchiolitis diagnosis than infants in urban areas. Suliaman[11] on his study on bronchiolitis, found that most of the cases were from rural areas (63%) while the urban cases were (37%), and he reported that infants and children at the rural areas, due to lack of mothers' education and health awareness, are more prone to URTI which precedes the onset of bronchiolitis while Hamid et al.[12] found that urban children are more affected with bronchiolitis than children in rural areas, but they were from poor urban families with low socioeconomic status in Bangladesh.

In our study we found that the incidence of bronchiolitis was higher in the lower social class than in high class. Similarly Caballero et al.[13] found that the incidence of bronchiolitis is higher in low socioeconomic communities. Also Vissing et al.[14] found that low socioeconomic status increases the risk for bronchiolitis. Grimwood et al.[15] attributed the high incidence of bronchiolitis in low socioeconomic communities to the household crowding which facilitate infection spread, and to the decreased access to health care facilities.

Our study revealed that most of bronchiolitis cases were not adequately exposed to the sun. This is in agreement with Chen et al.[16] who reported that children who are not adequately exposed to the sun are more liable to have RSV bronchiolitis and also in agreement with Linday et al.[17] who found that acute lower respiratory infections, including bronchiolitis, are more frequent in children lacking sun exposure. And Mansbach and Camargo[18] noted that almost all cases of bronchiolitis occur in winter months where sun exposure is inadequate.

We found that most infants with bronchiolitis had inadequate vitamin D supplementation. This came in concordance with Leis et al.[19] who found that vitamin D intake of children with bronchiolitis was low. Bergman et al.[20] in their meta-analysis study found evidence that supplement with vitamin D reduced significantly the risk of respiratory tract infections including bronchiolitis. And El-Mazary et al.[21] found in their study that bronchiolitis is less common in infants supplemented with vitamin D than those not supplemented, and they attributed that to the immunomodulatory effect of vitamin D which may lead to an increased resistance to infection.

In this study we found that the mean serum 25(OH) vitamin D was significantly lower in cases than in controls; it was (12.3 ± 3.9 & 26.2 ± 10.0 ng/ml, respectively with $p = 0.003$). These data came in concordance with the study done by Moreno-Solís et al.[22] who examined the prevalence of hypovitaminosis D in Spanish infants with acute bronchiolitis compared with control subjects. They found that 25(OH) D levels in infants with acute bronchiolitis were significantly lower than in the control group (median 29.9 ng/ml versus median 38.2 ng/ml). Golan-Tripto et al.[23] found that 25(OH) D was significantly lower in the bronchiolitis cases than in controls; (11.2 ± 5.6 ng/ml vs. 31.2 ± 4 ng/ml, $p < 0.001$). Rodriguez et al.[24] reported that vitamin D deficiency is prevalent in infants with bronchiolitis. Watkins et al.[25] found that mean 25 (OH) D levels were lower in children with bronchiolitis than healthy controls. Roth et al.[26] showed that children admitted for acute lower respiratory tract infections including bronchiolitis had lower 25(OH) D levels than age-matched healthy controls. But McNally et al.[27] found that no difference was observed in vitamin D levels between the acute lower respiratory tract infection (ALRI) group and control groups when they compare serum 25(OH) D levels in a group of young children with ALRI with a diagnosis of bronchiolitis or pneumonia ($n = 55$ or 50, respectively), to an age-matched group

without respiratory symptoms ($n = 92$). The mean vitamin D level for the entire ALRI group was not significantly different from the control group. But we can note here that the study of McNally et al.[27] compared the mean vitamin D levels for the entire ALRI including pneumonia with that of controls and not only bronchiolitis cases as our study did.

In the present study we found that the mean serum level of immunoglobulin E was significantly higher in cases than in controls. It was (170 ± 66 & 43.8 ± 14.2 IU/ml, respectively and $p = 0.01$). That came in concordance with the study done by Jiang et al.[28] who estimated the changes in immunoglobulins in children with bronchiolitis. They found that serum IgE levels were significantly higher in cases than in controls ($p < 0.05$). Also Chary et al.[29] found that total serum IgE was significantly higher ($p < 0.01$) in patients with bronchiolitis when compared to the control group. This was in agreement with the study done by Zhu et al.[30] who found significantly increased total serum IgE level in both atopic (241.2 ± 102.5 IU/mL) and nonatopic children (125.5 ± 63.2 IU/mL) with bronchiolitis compared with that in the control group (27.2 ± 10.5 IU/ml) ($p < 0.01$).

In our study, serum IgE showed a non-significant negative correlation with serum 25(OH) vitamin D ($r = -0.141$, $p = >0.05$). This was in agreement with the study done by Jiang et al.[28] who found a negative correlation between serum IgE and serum vitamin D and also with the study done by Demirel et al.[31], who found that there was a negative relationship between 25(OH) D level and IgE values in both wheezy infants with Vitamin D deficiency and the control group. And Luong[32] found a negative relationship between 25(OH) D and total serum IgE in cases with bronchiolitis.

In conclusion, serum 25(OH) vitamin D was found in decreased quantities in infants with bronchiolitis and it was negatively correlated with serum IgE, suggesting that vitamin D may play a role in the pathogenesis of bronchiolitis.

Recommendations

We recommend adequate vitamin D supplementation and encouragement of adequate exposure to sunlight as a natural source for vitamin D, to achieve sufficient levels of 25(OH) D, which may help to reduce the burden of bronchiolitis during infancy. Further studies are needed to assess the correlation between nutritional status and vitamin D status among healthy infants and to assess vitamin D status among infants and children with recurrent respiratory tract infections and also to determine potentiality of vitamin D for therapy /and or prophylaxis, with outcome measurement and pre-post estimation of vitamin D levels in infants with bronchiolitis.

Conflict of interest

There is no conflict of interest.

References

1. Wainwright C. Acute viral bronchiolitis in children – a very common condition with few therapeutic options. *Pediatr Respir Rev* 2010;**11**:39–45.
2. Martineau AR. Vitamin D and respiratory health. *Curr Respir Med Rev* 2011;**7**:394–5.
3. Nowicka U. Disorders with elevated immunoglobulin E levels. *Pneumonol Alergol Pol* 2009;**77**(6):533–40.
4. DeNicola LK, Maraqa NF, Udeani J, Custodio HT. *Bronchiolitis* 2012. Available at: http://emedicine.medscape.com/article/961963-overview.html; accessed 20.09.13.
5. American Academy of Pediatrics, Subcommittee on diagnosis and management of bronchiolitis. Diagnosis and management of bronchiolitis. *Pediatrics* 2006;**118**(4):1774–93.
6. Balachandra HM, Puttalingamma V. Prevalence of bronchiolitis among children under five years of age in Mysore district, Karnataka. (Southern India). International. *J Adv Res* 2015;**3**(2):938–49.
7. Malla T, Poudyal P, Malla KK. Modifiable demographic factors that differentiate bronchiolitis from pneumonia in Nepalese children less than two years – a hospital based study. *Kathmandu Univ Med J* 2014;**47**(3):175–80.
8. Malik G, Singh A, Singh K, Pannu MS, Singh P, Banga S, Jain R. A comparative study to assess the effects of nebulised 3% hypertonic saline, 0.9% normal saline and salbutamol in management of acute bronchiolitis among Indian children. *JEMDS* 2015;**4**(21):3662–8.
9. Sharma D, Kuppusamy K, Bhoorasamy A. Prevalence of acute respiratory infections (ari) and their determinants in under five children in urban and rural areas of Kancheepuram district, South India. *AHRO* 2013;**6**(5):513–8.
10. Carroll KN, Gebretsadik T, Griffin MR, Wu P, Dupont WD, Mitchel EF, Enriquez R, Hartert TV. The increasing burden and risk factors for bronchiolitis-related medical visits in infants enrolled in a state healthcare insurance plan. *Pediatrics* 2008;**122**(1):58–64.
11. Suliaman JR. The efficacy of single dose methyl prednisolone in the treatment of acute bronchiolitis in children. *Tikrit Medical J* 2010;**16**(2):13–7.
12. Hamid F, Quaium MA, Rahman Azizur, Reza AT, Khan T, Hussain T, Fatematuz Zahra. Audit on the management of bronchiolitis: a single centre real world experience in Bangladesh. Can we do better? *Chattagram Maa-O-Shishu Hosp Med Coll J* 2015;**14**(1):6–10.
13. Caballero MT, Serra ME, Acosta PL, Marzec J, Gibbons L, Salim A, Rodriguez A, Reynaldi A, Garcia A, Bado D, Buchholz UJ, Hijano DR, Coviello S, Newcomb D, Bellabarba M, Ferolla FM, Libster R, Berenstein A, Siniawaski S, Blumetti V, Echavarria M, Pinto L, Lawrence A, Ossorio MF, Grosman A, Mateu CG, Bayle A, Dericco A, Pellegrini M, Igarza I, Repetto HA, Grimaldi LA, Gudapati P, Polack NR, Althabe F, Shi M, Ferrero F, Bergel E, Stein RT, Peebles RS, Boothby M, Kleeberger SR, Polack FP. TLR4 genotype and environmental LPS mediate RSV bronchiolitis through Th2 polarization. *J Clin Invest* 2015;**125**(2):571–82.
14. Vissing NH, Chawes BLK, Bisgaard H. Increased risk of pneumonia and bronchiolitis after bacterial colonization of the airways as neonates. *Am J Respir Crit Care Med* 2013;**188**(10):1246–52.
15. Grimwood K, Cohet C, Rich FJ, Cheng S, Wood C, Redshaw N, Cunningham CW, Pearce N, Kirman JR. Risk factors for respiratory syncytial virus bronchiolitis hospital admission in New Zealand. *Epidemiol Infect* 2008;**136**(10):1333–41.
16. Chen ZR, Ji W, Wang YQ, Yan YD, Shao XJ, Zhang XL, Xu J. Etiology of acute bronchiolitis and the relationship with meteorological conditions in hospitalized infants in China. *JFMA* 2014;**113**(7):463–9.
17. Linday LA, Umhau JC, Shindledecker RD, Dolitsky JN, Holick MF. Cod liver oil, the ratio of vitamins A and D, frequent respiratory tract infections, and vitamin D deficiency in young children in the United States. *Ann Otol Rhinol Laryngol* 2010;**119**(1):64–70.
18. Mansbach JM, Camargo CA. Bronchiolitis: lingering questions about its definition and the potential role of vitamin D. *Pediatrics* 2008;**122**:177.

19. Leis KS, McNally JD, Montgomery MR, Sankaran K, Karunanayake C, Rosenberg AM. Vitamin D intake in young children with acute lower respiratory infection. *Zhongguo Dang Dai Er Ke Za Zhi* 2012;**14**(1):1–6.
20. Bergman P, Lindh AU, Bjorkhem-Bergman L, Lindh JD. Vitamin D and respiratory tract infections: a systematic review and meta-analysis of randomized controlled trials. *PLoS One* 2013;**8**(6):e65835.
21. El-Mazary AAM, Abdel-Maaboud M, Mohamed M, Nasef KA. Vitamin D supplementation and the risk of infections in fullterm infants. Correlations with the maternal serum vitamin D. *Arch Dis Child* 2012;**97**:A257.
22. Moreno-Solís G, Fernández-Gutiérrez F, Torres-Borrego J, Torcello-Gáspar R, Gómez-Chaparro Moreno JL, Pérez-Navero JL. Low serum 25-hydroxyvitamin D levels and bronchiolitis severity in Spanish infants. *Eur J Pediatr* 2015;**174**(3):365–72.
23. Golan-Tripto I, Goldbart AD, Loewenthal N, Tal A. 25(oh) Vitamin D insufficiency in infants with bronchiolitis. *Am J Respir Crit Care Med* 2013;**187**:A5906.
24. Rodriguez R, Banerjee S, Zuniga S, Graciano AL. Vitamin D deficiency in infants with bronchiolitis. *Crit Care Med* 2012;**40**(12):307.
25. Watkins RR, Yamshchikovb AV, Lemonovichc TL, Salata RA. The role of vitamin D deficiency in sepsis and potential therapeutic implications. *J Infect* 2011;**63**(5):321–6.
26. Roth DE, Shah R, Black RE, Baqui AH. Vitamin D status and acute lower respiratory infection in early childhood in Sylhet, Bangladesh. *Acta Paediatr* 2010;**99**(3):389–93.
27. McNally JD, Leis K, Matheson LA, Karuananyake C, Sankaran AM, Rosenberg AM. Vitamin D deficiency in young children with severe acute lower respiratory infection. *Pediatr Pulmonol* 2009;**44**(10):981–8.
28. Jiang ZG, Wu J, Liu L, Lin Y, Yang CY. Serum levels of 25-(OH) D3 and immunoglobulin in children with bronchiolitis. *Zhongguo Dang Dai Er Ke Za Zhi* 2012;**14**(8):578–80.
29. Chary AV, Hemalatha R, Babu Narendra, Sivaramaprasad K, Dineshkumar B. CD23 and Th1/Th2 cytokines in bronchial asthma, bronchiolitis and bronchial pneumonia in children. *Asian J Pharm Clin Res* 2012;**5**(3):111–4.
30. Zhu YF, Zhu JY, Li WW, Lan CF, Fang J, Lin HL. Relationship of levels of CD4(+)CD25(+) regulatory T cells and expression of Foxp3 mRNA in peripheral blood with serum immunoglobulin E level in children with bronchiolitis. *Zhongguo Dang Dai Er Ke Za Zhi* 2009;**11**(5):349–53.
31. Demirel S, Guner SN, Celiksoy MH, Sancak R. Is vitamin D insufficiency to blame for recurrent wheezing? *Int Forum of Allergy Rhinol* 2014;**4**(12):980–5.
32. Luong K. Beneficial role of Vitamin D3 in prevention of certain respiratory diseases. *Ther Adv Respir Dis* 2013;**7**(6):327–50.