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Vitamin D deficiency and low hemoglobin level as risk factors for severity of acute lower respiratory tract infections in Egyptian children: A case-control study

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KEYWORDS

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Abstract *Objective:* Acute lower respiratory tract infection (ALRTI) is an important cause of morbidity in the developed world, and both morbidity and mortality in the developing world. Vitamin D has a major role in both acquired and innate immunity. Anemic children have less oxygen carrying capacity of blood. This study was done to determine the relation between vitamin D deficiency, anemia and the severity of ALRTIs in hospitalized children.

Methods: This study included 96 hospitalized infants with ALRTI, 48 diagnosed with pneumonia and 48 with bronchiolitis. Mean age was 10.67 ± 3.143 months. Matched age and sex infants with no respiratory illness were included. Serum 25 hydroxy vitamin D was measured in all cases and controls by Radio-immune assay. Hemoglobin level was measured by Coulter.

Results: Vitamin D deficiency and low hemoglobin level were positively correlated with the severity of ALRTIs ($r = 0.798$ and $P = 0.001$) and ($r = 0.708$, $P = 0.028$), respectively. Low vitamin D level was significantly correlated with low hemoglobin level ($r = 0.708$, $P = 0.028$).

Conclusion: Vitamin D deficiency was associated with severity of ALRTIs. Low hemoglobin level was more prevalent in those children. Improving the nutritional status in children by preventing vitamin D deficiency and low hemoglobin might influence the outcome of children with ALRTI.

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Introduction

Lower respiratory tract infection (LRTI) is frequently used interchangeably to include bronchitis, bronchiolitis, and pneumonia, or any combination of the three.[1] ALRTIs in children less than five years old are the leading cause of childhood morbidity and mortality in the world and represent almost 60% of infant infectious disease hospitalizations.[2]

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WHO estimated that the annual number of Acute Lower Respiratory Tract Infections (ALRTIs) related deaths in children less than five years old was 2.1 million accounting for about 20% of all childhood deaths. In the developing world, the annual incidence of pneumonia is estimated to be 33 per 10,000 in children younger than five years.[3]

Vitamin D from diet or dermal synthesis is biologically inactive and requires enzymatic conversion to active metabolites. Vitamin D is converted to 25-hydroxyvitamin D [25(OH) D], the major circulating form of vitamin D, and then to 1,25-dihydroxyvitamin D, the active form of vitamin D, by enzymes in the liver and kidney. 1,25-hydroxyvitamin D binds to the intracellular vitamin D receptor to activate vitamin D response elements within target genes. The half-life of 1,25-dihydroxyvitamin D is four to six hours, compared with two to three weeks for 25-hydroxyvitamin D and 24 hours for parent vitamin D.[4] Vitamin D has major effects on nearly all cells of the immune system. Antigen presenting cells, such as dendritic cells, macrophages, and T and B cells, express the vitamin D receptor (VDR).[5]

Iron deficiency anemia in children occurs most frequently between the age of 6 months and 3 years, the same period of age when repeated respiratory infections occur.[6] Whatever the etiology of anemia, the relation between low hemoglobin level and ALRTIs has not been fully evaluated, and only few reports are available evaluating this subject.[7]

This study was done to determine the relation between vitamin D deficiency, hemoglobin, and the severity of ALRTIs.

Subjects and Methods

This study was a case control study. Cases were infants less than two years old admitted to the Children's Hospital with the diagnoses of either pneumonia or bronchiolitis. All infants included in the study were subjected to full medical history and clinical examination. Occupational social class of the father was used as the measure of socioeconomic status such as: Level I (professionals, e.g., physicians, engineers), level II (managerial, e.g., teachers, sales managers), Level III (manual and semi-skilled manuals).[8] Weights and lengths of the infants were measured. None of the mothers of cases reported vitamin D supplementation to her infant. Body mass index was calculated. Then we plotted the BMI on the charts of the BMI by WHO.[9] The infants were examined for signs of rickets as delayed closure of fontanelles, parietal and frontal bossing, craniotabes (soft skull bones), enlargement of the costochondral junctions (rachitic rosary), widening of the wrist and bowing of the distal radius and ulna, and *lateral bowing of the femur and tibia*.

Bronchiolitis was defined as a clinical syndrome that occurs in children <2 years of age. It is characterized by upper respiratory symptoms (e.g., rhinorrhea) followed by lower respiratory infection with inflammation, which resulted in wheezing and/or crackles (rales).[10] Severe bronchiolitis was indicated by persistently increased respiratory effort (tachypnea; nasal flaring, intercostal, subcostal, or suprasternal retractions; accessory muscle use; grunting), hypoxemia, apnea, or acute respiratory failure.[11] To score the clinical status of the patients, we used a clinical scoring system for bronchiolitis. This scoring system depends on the physical signs as nasal flaring, respiratory rate, retractions of accessory muscles of respiration, wheezing and general status. Each point is given a score from 0 to 3.[12] Pneumonia was defined as a condition typically associated with fever, respiratory symptoms, and evidence of parenchymal involvement, either by physical examination or the presence of infiltrates on chest radiograph. The scoring of severity of pneumonia depends on the symptoms and signs as patient's temperature less or more than 38 °C, respiratory rate less or more than 50/min, retractions, refusal of oral intake, granting, cyanosis and intermittent apnea.[3]

We recruited matched age and sex infants with no respiratory symptoms or signs from the Health office. They were coming for immunization. Their contact phone numbers were taken to provide them with the results of the tests and treatment as indicated.

Serum vitamin D [25(OH) D] was measured by Radio immune assay. Venous blood samples were collected aseptically from all children who participated in the study by venipuncture using a 5 mL evacuated glass tubes. Blood was allowed to clot at room temperature (20 °C). Then centrifugation was done for 15 min. It was stored at −20 °C till assessment was done.

Vitamin D status in relation to [25(OH) D] level was done as follows: Severe deficiency: 0–5 ng/mL (0–12.5 nmol/L). Deficiency: 5–15 ng/mL ($\leqslant$37.5 nmol/L). Insufficiency: 15–20 ng/mL (37.5–50 nmol/L). Sufficiency: 20–100 ng/mL (50–250 nmol/L).[13]

Another sample was taken on EDTA tubes to measure the Hemoglobin level using a Coulter 1660. According to the World Health Organization (WHO), anemia was diagnosed if Hb% was less than 11 gm/dl.[14]

Statistical methods

Analysis of data was done by IBM computer using SPSS (statistical program for social science version 12). For description of quantitative variables we used mean and SD. While for description of qualitative variables we used numbers and percentages. Chi-square test was used to compare qualitative variables between groups. Unpaired *t*-test was used to compare quantitative variables, in parametric data. Correlation coefficient test was used to rank different variables against each other's positively or inversely. While odds ratio and 95% CI were used to describe the risk factors.

$P < 0.05$ was considered significant.

Results

The present study included 192 infants. Among ninety-six cases, 48 of them presented with clinical picture of bronchiolitis, and 48 presented with clinical picture of pneumonia. Ninety-six infants with no symptoms or signs of respiratory infection were recruited from the Health Office as the control group. They were selected to be age and sex matched for cases. The mean age of infants included in the study was 10.67 ± 3.143 months. Among the total number of studied infants 114 (59.38%) were males and 78 (40.63%) were females.

There was no significant difference in vitamin D levels between cases and controls ($P = 0.136$) (Table 1). The following were risk factors for ALRTI: Low Hb (odds ratio [OR] = 1.187, $P = 0.043$) (Figure 1), low body mass index (OR = 0.976, $P = 0.028$), history of previous attack of ALRTI

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