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Vitamin D and its binding protein in children with cystic fibrosis: A single center study

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Abstract *Aim:* To measure the level of VDBP (vitamin D binding protein) and serum 25-hydroxy vitamin D (25OHD) in order to assess its role as a nutritional marker in cystic fibrosis (CF). The relationship between vitamin DBP and immunoglobulin G (IgG) levels was assessed as well.

Methods: This is a cross-sectional observational study recruiting 50 patients diagnosed as having CF from the Allergy and Pulmonology Unit, Children's Hospital, Cairo University, from May 2012 until May 2013, twenty age- and sex-matched healthy children were included as a control group. Vitamin DBP and 25OHD were measured using Elisa technique and total IgG was measured using the nephelometer method.

Results: The CF group had significantly lower serum concentrations of DBP ($p < 0.012$) and 25OHD ($p < 0.001$) while IgG levels were within normal values ($p < 0.216$) compared to the control group, patients with failure to thrive (FTT) have significantly lower levels of 25OHD and significantly higher levels of VDBP and nearly the same level of IgG. Patients with pancreatic insufficiency have significantly higher serum levels of VDBP.

Conclusions: The present study has demonstrated that the levels of 25OHD and VDBP are decreased in CF patients while IgG levels are within normal values. In addition, the serum level of 25OHD was significantly lower in patients with FTT, also significant relations of VDBP with failure to thrive and pancreatic insufficiency were noted, emphasizing its role as a marker for the nutritional status in CF patients. As a component of anti-inflammatory and nutritional therapy, vitamin D is a predictor for clinical outcomes.

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Introduction

Cystic fibrosis (CF) is the most common inherited disorder in childhood, involves several organ systems, and results in life-long morbidity and premature mortality. Lung disease in CF is the major cause of death through a complex process involving impairment of mucociliary clearance, infection, inflammation and structural injury.[1] Environmental, nutritional and socio-economic factors as well as modifier genes may affect the clinical manifestations of the disorder.[2] Chronic inflammation has a negative impact on bone metabolism and has been linked to impaired linear growth and bone mineral status.[3]

Vitamin D has long been known to play a critical role in the maintenance of serum calcium levels and bone health. More recently, there has been a growing appreciation of its potential role in respiratory disease. Vitamin D deficiency results in decreased lung volume in animal models, and it has also been shown to have wide-ranging effects on immune functions.[4,5] Recent data suggest that vitamin D deficiency modifies the severity of a variety of lung diseases, including asthma, chronic obstructive pulmonary disease and pneumonia.[6–8]

Hypovitaminosis D is almost universal in CF patients, likely due to a combination of inadequate absorption, impaired metabolism and a lack of sun exposure. Inadequate levels are associated with the high prevalence of bone disease or osteoporosis in CF patients, which is associated with increased morbidity including fractures, kyphosis and worsening of the pulmonary status. For these reasons, screening for and treatment of vitamin D deficiency is a critical component of CF care.[9]

The physiology of vitamin D transport presents a challenge in designing and interpreting studies of the association between vitamin D status and pulmonary outcomes. Both 25 hydroxy vitamin D (25OHD) and 1,25 dihydroxy vitamin D (1,25OH2D) are bound in circulation to vitamin D-binding protein (VDBP) and, to a lesser extent, to albumin. VDBP gene polymorphisms may impact on VDBP levels as well as binding of vitamin D to VDBP.[10]

The effects of low VDBP on vitamin D levels and metabolism are not entirely clear. However, most 25 hydroxy vitamin D (25OHD) is carried by VDBP and very little is free in serum. High concentrations of unbound VDBP in normal patients may function as a reservoir for 25OHD.[11]

The hallmark of CF is chronic lung inflammation. The severity of lung disease is closely correlated with immunoglobulin G (IgG) levels. The Scandinavian CF Nutritional Study found an inverse relationship between vitamin D and serum IgG levels.[12]

Since no studies have assessed whether vitamin D status has an impact on inflammation or clinical outcomes in Egyptian CF, we aimed in this study to evaluate the serum levels of 25OHD, the free VDBP and the level of IgG in Egyptian patients with CF and correlate them with their nutritional status.

Methods

This is a cross-sectional observational case-control study including 50 CF patients. Diagnosis of CF was made based on the clinical presentations of (Chronic lung disease, steatorrhea, failure to gain weight) and confirmed by elevated sweat chloride testing above 60 meq/L. Patients were recruited from the Allergy and Pulmonology Unit, specialized Children's Hospital, Cairo University, over a period of one year from May 2012 until May 2013. Their ages ranged from 18 months to 12 years. Twenty (20) age- and sex-matched healthy children were included as a control group.

The protocol for the research project was approved by the Ethics Committee of the specialized Children's Hospital, Cairo University and it conforms to the provisions of the Declaration of Helsinki (as revised in 2000). Informed consent was obtained from the parents after explanation of the aim of the study.

Blood samples were collected by venipuncture, and serum was separated and frozen at −20 °C. The serum level of DBP and serum level of 25OHDwere measured using the Quantikine Human Vitamin D Binding Protein immunoassay ELISA from R&D Systems, USA.[13] The serum level of immunoglobulin G (IgG) was measured nephelometrically using Antisera to Human Immunoglobulins (NAS IGG) from BN Prospec Siemens Healthcare Diagnostics Inc, Germany.[14] The results were plotted and correlated with each other.

Results

Data management and analysis were performed using Statistical Package for Social Sciences (SPSS) version 17. Numerical data were summarized using medians and ranges. Categorical data were summarized as percentages. Comparisons between the two groups were done using the Mann–Whitney test, a non-parametric test equivalent to the *t*-test used in non-normally distributed variables. To measure the strength of the association between the numeric variables, Spearman's correlation coefficients were calculated.[15] All *p*-values are two-sided. *P*-values $\leqslant 0.05$ were considered significant.

Data were collected for 50 CF children and 20 healthy age- and sex-matched children as controls. Their ages ranged from 1.5 to 12 years and 30% were girls. The rate of consanguinity was 60% and positive family history was 22% as shown in Table 1. Most of the patients (94%) presented with cough, 76% with recurrent pneumonia, 68% with recurrent wheezing, 40% with failure to thrive and 64% with steatorrhea.

Table 1 Demographic and clinical data of the study population.

Characteristic	$N = 50$	%
Age in years		
Median	3	
Range	1.5–13	
Female	15	30
Male	35	70
Positive consanguinity	30	60
Family history of CF	11	22
Cough	47	94
Recurrent pneumonia	38	76
Recurrent wheezing	32	68
Recurrent hospital admission	47	94
Steatorrhea	32	64
Hepatomegaly	15	30
Failure to thrive	20	40
Clubbing	12	24