Assessment Of Vitamin D Status In Egyptian Children With Acute Bronchiolitis

Thesis

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By

Ahmed Nabih Baklola
M.B., B.CH.,(2001)

Under Supervision of

Prof. Doctor/ Tharwat Ezzat Deraz
Professor of Pediatrics
Faculty of Medicine
Ain Shams University

Doctor/ Asmaa Al Husseiny Ahmed
Lecturer of Pediatrics
Faculty of Medicine
Ain Shams University

Doctor/ Dina El-Sayed El-Shennawy
Lecturer of Clinical Pathology
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
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بسم الله الرحمن الرحيم

"قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَاإِنَّكَ أَنتَ
الْعَلِيمُ الْحَكِيمُ"

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Contents

Introduction

Bronchiolitis is a disorder of the lower respiratory tract that occurs most commonly in young children and is caused by infection with seasonal viruses such as respiratory syncytial virus (RSV) ***(Zorc and Hall, 2010).***

It is the most frequent cause of acute respiratory failure in children admitted to paediatric intensive care units in the UK and North America **(Yanney and Vyas, 2008)**

Almost all clinical cases of bronchiolitis in temperate climate occur between November and March months that are also associated with vitamin D deficiency, also low level of vitamin D have been associated with an increased incidence of pneumonia and lower respiratory tract disease requiring hospitalization ***(Mansbach et al., 2008).***

Vitamin D decreases the inflammatory response to viral infections in airway epithelium. This suggests that adequate vitamin D levels would contribute to reduced inflammation and less severe disease in RSV-infected individuals ***(Hansdottir et al., 2010)***

Aim of the work

The aim of the work is to assess vitamin D status in children with acute bronchiolitis and its relation to clinical severity.

CHAPTER I

BRONCHIOLITIS

Bronchiolitis is the most common viral infection of the lower respiratory tract in infants in their first year of life, with an incidence peak between 3 and 9 months of age **(Carraro et al., 2009)** and it is the most frequent cause of acute respiratory failure in children admitted to paediatric intensive care units in the UK and North America **(Yanney and Vyas, 2008)** also bronchiolitis is a major cause of morbidity and mortality in early childhood worldwide **(Richard et al., 2008).**

Epidemiology:

Predictable seasonal epidemics in many parts of the world are the most notable feature of RSV bronchiolitis **(Williams et al., 2004).**

In temperate climates, the RSV epidemic generally happens during the winter months, but in Hong Kong its peak season is in spring or summer and in other tropical and subtropical areas north of the equator the peak season occurs during the cool rainy season **(Peiris et al.,**

2003) In South America and South Africa, epidemics occur during the cool dry season **(Simoes and Carbonell-Estrany, 2003).**

Hospital admission rates in the USA and Europe for bronchiolitis are reported to be around 30 per 1000 for children younger than 1 year **(Simoes and Carbonell-Estrany, 2003)** But bronchiolitis associated deaths are fortunately very rare. The post-neonatal mortality rate due to bronchiolitis in the UK fell from 21·47 per 100 000 in 1979 to 1·82 per 100 000 in 2000 **(Panickar et al., 2005).**

Risk factors

Bronchiolitis is more common in males, in those who have not been breast-fed, and in those who live in crowded conditions. Older family members are a common source of infection but may experience only minor respiratory symptoms **(Goodman, 2004)** The risk also was elevated for infants born to young mothers (<20 years of age) or mothers who did not initiate breastfeeding in the hospital. Infants with low birth weight (1500-2400 g) or very low birth weight (<1500 g) and those with congenital anomalies also had increased risk. Maternal smoking during pregnancy increased the risk of bronchiolitis hospitalization **(Koehoorn et al., 2008).**

High-risk groups for severe infections are infants younger than 6 weeks; premature infants; and those with chronic lung disease of prematurity, congenital heart disease, neurological disease. Patients with three or more risk factors were at very high risk for having a severe or complicated disease course associated with admission to the PICU, placement on mechanical ventilation and a longer hospital length of stay **(Purcell and Fergie, 2004).**

Air pollution may act as a trigger for the occurrence of acute severe bronchiolitis cases **(Segala et al., 2008)** also there may be a modest increased risk of bronchiolitis attributable to chronic traffic-derived particulate matter exposure particularly for infants born just before or during peak RSV season **(Karr et al., 2009)** also atopic dermatitis aggravates the allergic airways inflammation in acute viral bronchiolitis **(Marchand et al., 2008).**

There is strong evidence that smoking increases the risk of admission with bronchiolitis and this appears to be a postnatal exposure rather than antenatal **(Meates-Dennis, 2005)** so Infants should not be exposed to passive smoking ***(AAP, 2006).***

Etiology:

The respiratory syncytial virus accounts for most cases of bronchiolitis it is responsible for more than 50% of cases **(Carraro et al., 2009)**, however, new virus isolation techniques have led to the discovery of previously unrecognized viruses, including the human metapneumovirus and bocavirus which also play a significant role **(Yanney and Vyas, 2008).**

RSV bronchiolitis in infants is probably exclusively viral disease, although there is increasing evidence that bacterial pneumonia is often triggered by respiratory viral infection **(Mcintosh, 2007)** Also there is no evidence of a bacterial cause for bronchiolitis, although bacterial pneumonia is sometimes confused clinically with bronchiolitis **(Goodman, 2004).**

To describe the frequency of viral pathogens in children with bronchiolitis **Stempel et al., 2009** found that viruses were detected in (93%) of the children with bronchiolitis. A single virus was identified in (71%) of the children and multiple viruses in (23%) of the children . Respiratory syncytial virus (RSV) was the most common virus detected (77%), followed by adenovirus (15%), human metapneumovirus (11%), coronavirus (8%), parainfluenza (6%) and influenza (1%).

The presence of more than one pathogen may influence the natural history of acute bronchiolitis in infants. Dual viral infection is a relevant risk factor for the admission of infants with severe bronchiolitis to the PICU **(Richard et al., 2008).**

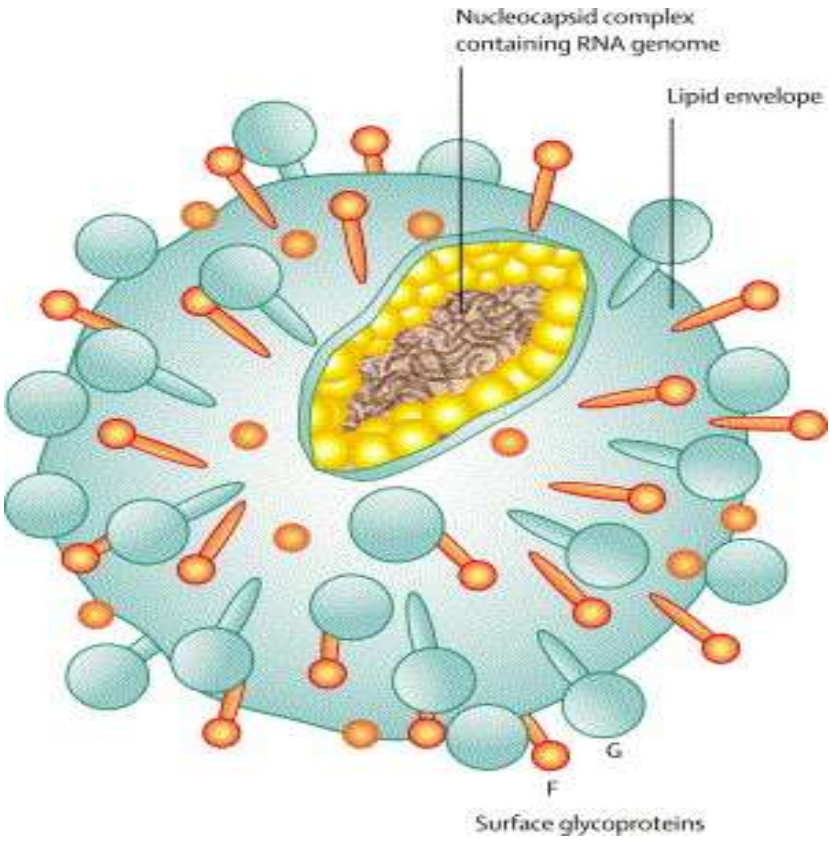

Figure 1. Schematic diagram of RSV, illustrating surface glycoproteins, lipid envelope, and nucleocapsid complex **(Smyth and Openshaw, 2006)**

Severity of acute bronchiolitis with regards to the viral etiology:

To study severity of acute bronchiolitis with regards to the viral etiology **Marguet et al., 2009** conducted prospective study of infants <1 year old, hospitalized for a first episode of bronchiolitis during the winter epidemic season and with no risk factors for severe disease. Viruses were identified in 95% of cases : RSV only (46%), RV only (7%), hMPV only (4%), dual RSV/RV (14%), and other virus only (2%) or coinfections (9%).And they found that infants with RV had a lower risk to present a severe disease compared to RSV. ***(Marguet et al., 2009).***

Pathogenesis

Bronchiolitis is characterized by virus-induced necrosis of the bronchiolar epithelium, hypersecretion of mucus, and round cell infiltration and edema of the surrounding submucosa. These changes result in formation of mucous plugs obstructing bronchioles, with consequent hyperinflation or collapse of the distal lung tissue. Infants are particularly susceptible to experience small airway obstruction because of the small size of the normal bronchioles **(Mcintosh, 2007).**

The sites of inflammation in bronchiolitis are the small bronchi and bronchioles; the alveolar spaces are

spared **(Hanson & Shearer 2006)** the distribution of involvement in bronchiolitis is patchy: Some areas are obstructed, and some are not. Those that are completely obstructed become atelectatic; those that are partially obstructed become overinflated. The unaffected areas remain normal and "hyperventilate" in an attempt to maintain normal arterial Po2 and Pco2. The consequences of these changes are small airway obstruction, air trapping, increased inspiratory , expiratory resistance, increased work of breathing and hypoxemia **(Roberts and Akintemi, 2000).**

During expiration, the additional dynamic narrowing produces disproportionate airflow decrease and air trapping. The effort of breathing is increased due to increased end expiratory lung volume and decreased lung compliance. Recovery of pulmonary epithelial cells occurs after 3–4 days, but cilia do not regenerate for approximately two weeks. The debris is cleared by macrophages ***(Meates-Dennis, 2005).***

Several facts suggest immunologic injury as a major factor in the pathogenesis of bronchiolitis caused by RSV. Extensive studies in small animal models showed an important role for the immune system in the respiratory pathology induced by RSV infection. Recent studies in

infants and in animal models indicate that a large number of soluble factors (e.g., interleukins, leukotrienes, and chemokines) with the potential to stimulate inflammation and tissue damage are liberated during RSV infection. Children who received a highly antigenic, inactivated, parenterally administered RSV vaccine experienced, upon subsequent exposure to wild-type RSV, more severe and more frequent bronchiolitis than did their age-matched controls **(Mcintosh, 2007).**

RSV infection incites a complex immune response. Eosinophils degranulate and release eosinophil cationic protein, which is cytotoxic to airway epithelium. Immunoglobulin E (IgE) antibody release may also be related to wheezing. Other mediators invoked in the pathogenesis of airway inflammation include chemokines such as interleukin 8 (IL-8), macrophage inflammatory protein (MIP) 1α, and RANTES (regulated on activation, normal Tcell expressed and secreted) ***(Watts and Goodman, 2007).***

Airway obstruction from fibrinous debris and mucus plugs, combined with the abnormal mechanics of respiration in bronchiolitis, increases substantially the work of breathing for affected infants and also leads to mismatching of pulmonary ventilation and perfusion. Not

surprising, arterial hypoxemia can be documented frequently during clinical disease. Retention of carbon dioxide is not a common problem, but, when it is present, it can result in acute respiratory acidosis and the need for prompt ventilatory assistance. Blood pH level abnormalities can be documented and may reflect contraction alkalosis related to the dehydration associated with poor oral intake and the contraction of extracellular spaces. ***(Hanson & Shearer 2006)***

Traditionally, inflammatory responses after viral infection are thought to be cell-mediated, with lymphocytic infiltration followed by the recruitment of macrophages to clear debris. In children with RSV-associated bronchiolitis, an evaluation of nasal and bronchial washings shows that the normal immune cytokine response is aberrant, with a shift towards a T helper cell type 2 (Th2) inflammatory response and poor or absent Th1 cytotoxic response. This shift in cytokine response likely is responsible for ineffective viral clearance and the production of proinflammatory cytokines that result in a continued inflammatory response. Therapeutic and/or preventive intervention for bronchiolitis will be defined better as more information on the immune response of bronchiolitis-