

**A Study of The Relationship Between Airway  
Inflammation and Dipalmitoyl Phosphatidycholine  
in Induced Sputum of Asthmatic Children**

*Thesis  
Submitted for Partial Fulfillment of  
Master Degree in Pediatrics*

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## Abbreviations

<b>aa</b>	Amino acid
<b>AHR</b>	Airway hyperresponsiveness
<b>ARDS</b>	Acute respiratory disease syndrome
<b>BALF</b>	Bronchoalveolar lavage fluid
<b>bFGF</b>	Basic Fibroblast growth factor
<b>BMI</b>	Body mass index
<b>CAMP</b>	Children Asthma Management Program
<b>CCR</b>	Chemokine receptor
<b>CD40</b>	Cluster of differentiation 40
<b>CFC</b>	Colony-forming cell
<b>CO-2</b>	Cyclooxygenase-2
<b>COPD</b>	Chronic obstructive pulmonary disease
<b>DC</b>	Dendritic cells
<b>DPPC</b>	Dipalmitoyl phosphatidylcholine
<b>DSPs</b>	Disaturated PLs
<b>ECG</b>	Electrocardiogram
<b>ECP</b>	Eosinophil cationic protein
<b>EGF</b>	Epidermal derived growth factor
<b>EIA</b>	Exercise-induced asthma
<b>EOS</b>	Eosinophils
<b>EPO</b>	Eosinophil peroxidase
<b>EPX</b>	Eosinophil protein X
<b>FEF<sub>25-75%</sub></b>	Forced expiratory flow rate over 25-75% part of FVC
<b>FEV<sub>1</sub></b>	Forced expiratory volume in 1 second
<b>FVC</b>	Forced vital capacity
<b>GER</b>	Gastroesophageal reflux
<b>GINA</b>	Global Initiative for Asthma
<b>GM-CSF</b>	Granulocyte-macrophage colony-stimulating factor

<b>HS</b>	Hypertonic saline
<b>IFN-<math>\gamma</math></b>	Interferon-gamma
<b>IgE</b>	Immunoglobulin E
<b>IGF-1</b>	Insulin-like growth factor
<b>IL</b>	Interleukin
<b>ISAAC</b>	International study of asthma and allergies in children
<b>kDa</b>	Kilodalton
<b>LA</b>	Large aggregates
<b>LT</b>	Leukotrien
<b>MBP</b>	Major basic protein
<b>MC</b>	Mast cells
<b>MCP-1</b>	Macrophage chemoattractant protein-4
<b>MDC</b>	Monocyte-derived chemokine
<b>MMPs</b>	Matrix metalloproteinases
<b>NAEPP</b>	National Asthma Education and Prevention Program
<b>NANC</b>	Non adrenergic non cholinergic
<b>NCICAS</b>	National Cooperative Inner-City Asthma Study
<b>NGF</b>	Nerve growth factor
<b>NO</b>	Nitric oxide
<b>P</b>	Pressure
<b>PaCO<sub>2</sub></b>	Arterial carbon dioxide tension
<b>PAF</b>	Platelet activating factor
<b>PD-ECGF</b>	Platelet-derived endothelial cell growth factor
<b>PDGF</b>	Platelet-derived growth factor
<b>PEF</b>	Peak expiratory flow
<b>PFTs</b>	Pulmonary function tests
<b>PL</b>	Phospholipid
<b>r</b>	Radius
<b>RANTES</b>	Regulated on activation of normal T cell expressed and secreted chemokines

<b>RDS</b>	Respiratory disease syndrome
<b>RSV</b>	Respiratory syncytial virus
<b>SA</b>	Small aggregates
<b>SALP</b>	Surface-active phospholipid
<b>SaO<sub>2</sub></b>	Arterial oxygen saturation
<b>SCF</b>	Stem cell factor
<b>SD</b>	Standard deviation
<b>SP</b>	Surfactant protein
<b>T</b>	Surface tension
<b>TARC</b>	Thymus- and activation-regulated chemokine
<b>TCR</b>	T-cell receptor
<b>TGF-B</b>	Transforming growth factor B
<b>Th-0</b>	Naive T-lymphocyte
<b>Th2</b>	T helper subset 2
<b>TIMPs</b>	Inhibitors of MMPs
<b>TNF-<math>\alpha</math></b>	Tumor necrosis factor-alpha
<b>VCAM-1</b>	Vascular cell adhesion molecule-1
<b>VEGF</b>	Vascular endothelial growth factor
<b>VPF</b>	Vascular permeability factor

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## **Introduction**

Childhood asthma is a growing public health problem in the United States. The number of children affected by asthma grew 75% from 1980 to 1994. This increase was present for all children regardless of race, gender, or age. An increasing burden of asthma is placed on the youngest children: The prevalence of this condition increased 160% for children 0 to 4 years old from 1990 to 1994 (*Steyer et al., 2003*).

Airway inflammation in asthma is extremely complex in origin, regulation, and outcome. The mechanisms involve a cascade of events involving many different kinds of cells, factors, and mediators that interact to create the characteristic inflammatory and tissue remodeling processes of asthma (*GINA, 2003*).

In school children with atopic asthma, the limited data available indicate that the morphological picture with basement membrane thickening and inflammatory cell infiltration in the airway is similar to that encountered in adults, although not all studies have found eosinophilic inflammation. Basement membrane thickening has been demonstrated even in children with mild/moderate asthma (*Barbato et al., 2003*).

Pulmonary surfactant is a unique mixture of lipids and surfactant-specific proteins that covers the entire alveolar, surface of the lungs. Surfactant is not restricted to the alveolar compartments; it also reaches terminal conducting airways and is present in upper airway secretions. While the role of surfactant in the alveolar compartment has been

intensively elucidated both in health and disease states, the possible role of surfactant in the airways requires further research (*Hohlfeld, 2002*).

An intact and well functioning pulmonary surfactant system is critical for normal respiration and protection from lung infection. Alteration of surfactant composition and function occurs with various inflammatory disorders that affect the airways or the lung parenchyma including asthma (*Meyer and Zimmerman, 2002*).

## **Aim of the work**

The present work was carried out to investigate and assess the relationship between sputum and blood markers of inflammation [eosinophils, neutrophils, eosinophilic cationic protein (ECP)] to sputum dipalmitoyl phosphatidyl choline (DPPC) levels, as characteristic and major constituent of pulmonary surfactant in asthmatic children.

## **CHAPTER 1**

# **PEDIATRIC BRONCHIAL ASTHMA**

### **Definition:**

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation causes an associated increase in airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment (*GINA, 2003*).

### **Prevalence of asthma:**

There are approximately 6.3 million children with asthma, admission rates for children young than 4 years of age with asthma are greater than those of other age group, and they account for a significant proportion of high annual rate in asthma mortality (*Mannino et al., 2002*).

The prevalence of asthma symptoms in children varies from 0 to 30 percent in different populations. The international study of asthma and allergies in children (ISAAC) shows the prevalence of wheezing in the last 12 months –documented by written questionnaires – among children 13 to 14 years old in a number of populations.