Introduction

The terminology of pediatric chronic lung pathologies may include any of the following: bronchiectasis, cystic pulmonary fibrosis, interstitial pulmonary fibrosis, broncho-pulmonary dysplasia, bronchiolitis obliterans, sequasterated lung disease etc. They could be primary or secondary: They could be congenital or acquired ***(Ibrahim et al., 2011).***

Patients with chronic lung diseases may have high prevalence of bacterial colonization of distal airway which is mainly related to the degree of airflow obstruction and disturbed anatomy ***(Zalacain et al., 1999).***

It is postulated that, in chronic lung diseases, lung tissue damage is caused by activation of the immunologically specific inflammatory defense mechanisms of the lung. These mechanisms are initiated by the antibody response and dominated by neutrophil leucocytes and their proteolytic and oxidative products ***(Hoiby, 2000).***

Exacerbation of chronic pulmonary diseases accounts for most of morbidity and mortality of patients with chronic lung diseases ***(Sanata et al., 2003.)***

An acute exacerbation is a sudden worsening of symptoms that typically lasts for several days ***(Rabe et al., 2007).***

Exacerbation represents an increase in the inflammation that is present in the stable state, with increased numbers of inflammatory cells (particularly neutrophils), cytokines, chemokines and proteases in the airways, and increased concentrations of certain cytokines and C-reactive protein in the blood. There are presently no reliable biomarkers to predict exacerbations ***(Celli and Barnes, 2007).***

Chronic lung disease not only affects the patient's quality of life,but also his or her family's.These persons are no longer able to enjoy their hobbies, work,or even go shopping without feeling as if they are suffocating. When patients receive optimal medical care, which includes attending a pulmonary rehabilitation program, they are able to become active participants in their lives again ***(Muir and Diablo, 2005).***

Clinically, exacerbation of chronic pulmonary diseases can be suspected in patients with fever, increased cough, increased sputum production over baseline, increased viscidity of sputum, a foul odor of the sputum and less specific symptoms include dyspnea, pleuritic chest pain, wheezes, and hemoptysis ***(King et al., 2006).***

Some lung diseases, such as cystic fibrosis, are hereditary and show up early in life. Restrictive lung diseases can result from different problems, such as interstitial fibrosis and sarcoidosis. Some cause scarring in the lungs, while others compress the lungs. Some have no known causes while others are due to occupational exposure, chemotherapeutic agents,

radiation, and connective tissue diseases such as lupus or rheumatoid arthritis ***(Rabe et al., 2007).***

Viral Respiratory infections being responsible for approximately half of chronic pulmonary diseases exacerbations. Approximately half of these are due to viral infections and another half appears to be caused by bacterial infections ***(Rabe et al., 2007).***

The initial phase of chronic lung diseases exacerbations could be attributed to viral infections with an incidence ranged from 25-63% ***(Sethi 2000).***

Lower respiratory tract viral infections in patients with COPD may also cause direct damage to the airway epithelium resulting in loss of ciliated epithelium, increased mucus production, sloughing of necrotic cells into the airway lumen, together with increased plasma exudation. In addition to causing airway narrow ***(Hegele et al., 1995).***

The term "atypical pathogen" most commonly refers to Chlamydia pneumoniae, Mycoplasma pneumoniae and Legionella pneumophila. Once believed to be of little clinical significance, a wealth of data accumulated over the past decade suggests that these are important respiratory pathogens in a wide range of respiratory-tract infections (RTIs) and are capable of causing severe, as well as mild-to-moderate, illness ***(File, Plouffe, 1998).***

Aim of the Work

Study of some viruses (influenza A, influenza B, respiratory syncyial virus (RSV), parainfluenza 1, 2 and 3 and adenovirus) and atypical bacreria (legionella pneumophila, mycoplasma pneumonia, coxiella burnetii and chlamydophila as causative agents for acute exacerbations in children with chronic lung diseases.

Chapter (*I*):
Chronic Lung Diseases (CLD)

Chronic lung diseases are the term for a wide variety of persistent lung disorders. Bronchiectasis, cystic fibrosis emphysema, chronic bronchitis, asthma, and restrictive lung diseases are examples of serious lung conditions that can adversely affect the quality of a patient's life ***(Muir and Diablo, 2005).***

Some important causes of chronic lung diseases will be reviewed in the current study.

A- Non cystic Bronchiectasis

Background:

Rene Laennec first described bronchiectasis in 1819, while observing patients with tuberculosis and the sequel of pneumonia in the preantibiotic era. The term bronchiectasis is from the Greek bronchion, meaning windpipe, and ectasis, meaning stretched ***(Spencer, 2005).***

Definition:

Bronchiectasis is defined by pathology and radiology as irreversible, abnormal and permanent dilatation of one or more of the conducting bronchi or airways, associated with frequent bacterial infection and inflammatory destruction of bronchial and peribronchial tissues ***(Currie, 2002).***

Incidence:

The incidence of bronchiectasis in children younger than 15 years is 3.7 per 100.000 population. The incidence is highest among children who live in Pacific regions at 17.8 per 100.000 population ***(Twiss et al., 2005).***

In the USA: Norman Clark estimated an incidence of 1.06:10000 ***(Koh et al., 2006).*** Decline in prevalence is attributable to effective anti tuberculous therapy, immunization, and the effective treatment of bacterial pneumonia and bronchitis. The declining incidence led to suggestions that this problem is now uncommon that it should be considered as an "orphan" disease ***(Spencer, 2005).***

Pathophysiology:

Bronchiectasis generally results from obstruction and inflammation of the airway. The obstruction and inflammation may result from any of the underlying disorders or from infection with acute tuberculosis, adenovirus, measles, Mycobacterium avium, or Aspergillus fumigates ***(Morrissey, 2007).***

The damage may result from chronic infection that leads to recruitment of neutrophils, T lymphocytes, and monocyte derived cytokines. The release of inflammatory mediators, elastases, and collagnases leads to inflammation and destruction of elastic and muscular components of bronchial walls. In addition, the outward elastic recoil forces of surrounding lung parenchyma exert traction, which causes expansion of airway diameter. These

changes may be accompanied by bronchial arterial proliferation, which predisposes to hemoptysis ***(Twiss et al., 2005).***

Bronchiectasis associated with bronchial obstruction may have a focal distribution distal to the site of obstruction. Bronchiectasis associated with underlying disease is likely to be diffuse ***(Morrissey, 2007).***

Pathological features:

- Gross picture:

Bronchiectasis occurs more commonly in the lower lobe of the lung. The bronchi are dilated and usually filled with pus. The intervening lung tissue is destroyed and replaced by dense fibrous tissue. The covering pleura may show pleurisy ***(Karadag et al., 2005).***

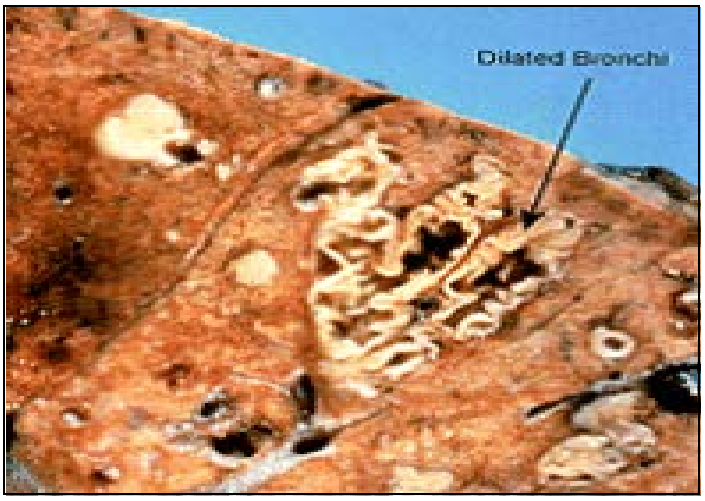

Figure (1): Postmortem pathology slide of end stage bronchiectasis displaying dilated bronchi and mucus impaction. The parenchyma is not severely altered ***(Karadag et al., 2005).***

Microscopic picture:

Bronchial mucosal biopsies reveal infiltration by neutrophils, macrophages and lymphocytes. Areas of fibrosis and ulceration which may erode into a blood vessel resulting in hemoptesis ***(King et al., 2006).***

Bronchial dilatation is associated with loss of cilia, cuboidal and squamous metaplasia, hypertrophy of bronchial glands and lymphoid hyperplasia, along with marked vascular changes ***(Spencer, 2005).***

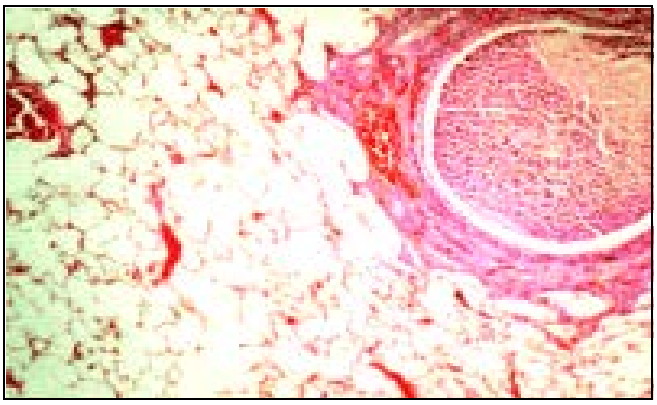

Figure (2): Microscopic picture of airway inflammation in patient with bronchiectasis shows; dilated bronchus with surrounding alveolar tissue. The bronchus and peribronchial region are filled with mucus and inflammatory cells ***(Karadag et al., 2005).***

Pathological forms of bronchiectasis:

Cylindrical or tubular bronchiectasis characterized by diffuse mucosal edema, with minimally dilated bronchi that are straight, regular and end squarely ***(Nicotra et al., 2000).***

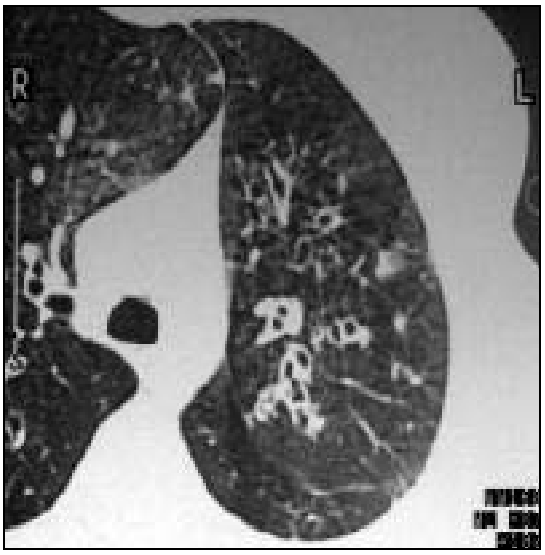

Figure (3): Computerized tomography (CT) scan shows cylindrical bronchiectasis with signet-ring appearance ***(Tsang et al., 2005).***

Cystic or saccular bronchiectasis have ulcerations with bronchial neovascularization lead to progressive dilatation and result in ballooned appearance that may have air-fluid levels (this is the most severe form) ***(Barker, 2002).***

Aetiology:

I-Congenital bronchiectasis:

Congenital bronchiectasis usually affects infants and children ***(Drobnic et al., 2005).***

Congenital diseases leading to bronchiectasis fall into 2 groups:

A-Congenital anatomic defects:

This form of disease is the result of developmental arrest in which the area involved may give rise to cyst that retain fluid

or air and may become infected, resulting in bronchiectasis ***(Emmons, 2004).***

These defects include: bronchopulmonary sequestration, Williams-Campbell syndrome, Mounier-Kuhn syndrome, Swyer-James syndrome, Yellow-nail syndrome and other congenital syndromes associated with cartilage abnormalities such as Ehlers Danlos and Marfan syndrome ***(Pasteur et al., 2002).***

B-Genetic causes:

This can occur in diseases as cystic fibrosis, primary ciliary dyskinesia, Young syndrome and immunodeficiency syndrome ***(Lakser, 2008).***

II - Acquired bronchiectasis:

It usually affects older children and adults, most cases of bronchiectasis are acquired and usually result from chronic pulmonary infection ***(Singleton et al., 2004).***

Acquired bronchiectasis can be the result of the followings:

A-Primary infection:

Bronchiectasis may be the sequela of a variety of necrotizing infections that are poorly treated. These organisms include *Klebsiella species, Staphylococcus aureus, Mycobacterium tuberculosis, Mycoplasma pneumoniae, measles, Bordetella pertussis, Hemophilus influenza, Herpes simplex and Respiratory syncytial* virus ***(Angrill et al., 2002).***

B-Bronchial obstruction:

Bronchiectasis can present in either of two forms; a focal obstructive process of a lobe or segment of a lung or a diffuse process involving much of both lungs. Focal airway obstruction may occur due to:

1. Luminal blockage by a foreign body, broncholith or tumor.
2. Extrinsic narrowing by an abnormally large heart or blood vessel or by enlarged lymph nodes (right middle lobe syndrome).
3. Twisting or displacement of the airways after lobar resection.

(Seijo and Sterman, 2001)

C-Allergic bronchopulmonary aspergillosis (ABPA)

Bronchiectasis in patients with ABPA is due to an immune reaction to *aspergillus* fungus, the action of mycotoxins, elastase, IL-4, IL-5, and direct invasion of the airways by the fungus ***(Stevens et al., 2000).***

D-Traction bronchiectasis:

Traction bronchiectasis is distortion of the airways secondary to distortion of the lung parenchyma from pulmonary fibrosis ***(Eastham et al., 2004).***

E-Asthma:

Very rare, yet reported that protracted and poorly controlled asthma may lead to bronchiectasis ***(Stevens et al., 2000).***

F-Systemic diseases:

Many systemic diseases are associated with bronchiectasis as Marfan's syndrome, tuberous sclerosis, kartagner syndrome, inflammatory bowel disease, xanthomatosis, systemic lupus erthrymatosus, scleroderma, and rheumatoid arthritis ***(Wickremasing et al., 2005).***

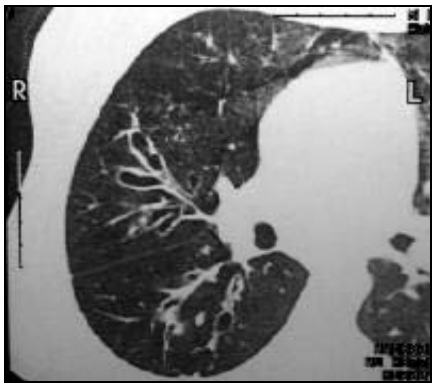

Figure (4): CT scan shows areas of both cystic bronchiectasis and varicose bronchiectasis ***(Tsang et al., 2005).***

Varicose bronchiectasis has a bulbous appearance with a dilated bronchus and interspersed sites of relative constriction and obstructive scarring ***(Wickremasing et al., 2005).***

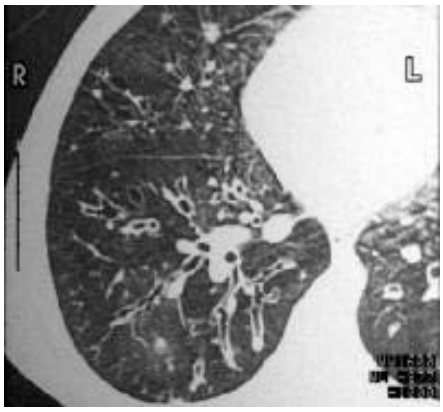

Figure (5): CT scan shows varicose bronchiectasis with alternating areas of bronchial dilatation and constriction ***(Tsang et al., 2005).***

Sites of bronchiectasis:

Bronchiectasis as a result of infection generally involves the lower lobes, right middle lobe, and lingual. Right middle lobe involvement alone suggests right middle lobe syndrome ***(Edwards et al., 2004).***

Bronchiectasis caused by cystic fibrosis, *M. tuberculosis*, milk aspiration or chronic fungal infections tends to affect the upper lobes ***(Ooi et al., 2002).***

Symptoms:

Daily productive cough of longer than 6 weeks duration is a universal finding. It often occurs first thing in the morning, improves throughout the day and increases with change in position ***(Koh et al., 2006).***

Copious purulent sputum is a characteristic feature of bronchiectasis ***(Singleton et al., 2004).***

A rare variant known as dry bronchiectasis manifests by episodic hemoptysis with little to no sputum, it resulting from erosion of bronchi ***(Eastham et al., 2004).***

Box (1): Less specific symptoms for bronchiectasis:

- Dyspnea may occur in extensive bronchiectasis.
- Wheezing is due to airflow obstruction following destruction of the bronchial tree.
- Pleuritic chest pain is an intermittent finding, secondary to chronic cough.

(Emmons, 2004).

Box (2): Symptoms of acute exacerbation in patient with bronchiectasis:

Change of sputum.

- Increased dysnea.
- Increased cough.
- Temperature>38.
- Increased wheezing.
- Malaise, fatigue, lethargy.
- Reduced pulmonary functions.
- Change in chest sounds.
- Radiographic change consistent with new pulmonary infiltration
- increase of C-reactive protein (CRP), and worsening of FEV1%

(EL Seify et al., 2011)

Complications:

- Progressive pulmonary damage may lead to cor-pulmonale, respiratory failure, and death. Empyema, bronchopleural fistula, fatal pneumonia, embolic brain abscess. Amyloidosis, Hemoptysis and chest deformity is minimal in children ***(Koh et al., 2006).***

Investigations:

A] Laboratory studies:

Laboratory evaluation should include the following tests:

- Sweet chloride, Immunoglobulin E (IgE) and serum precipitins for Aspergillus species, A fumigatus-specific IgE, CBC count, Serum IgG, immunoglobulin M (IgM), and IgA, HIV test, Sputum culture or deep oropharyngeal swab in younger children and Antinuclear antibody and rheumatoid factor.

(Emmons, 2009)

B) Radiological studies:

1) Plain chest radiograph: shows increased pulmonary markings, atelectasis or consolidation, parallel markings radiating from the hila (tram tracking or toothpaste) and isolated cyst or multiple cysts (honeycombing) ***(Wickremasing et al., 2005)***.

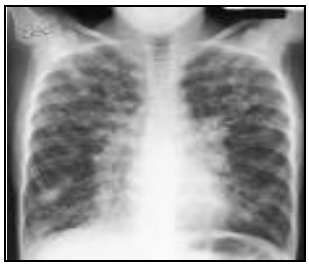

Figure (6): Chest x ray shows cystic and cylindrical bronchiectasis of the right lower lobe ***(Tsang et al., 2005).***

2) Computed tomography:

The diagnosis is usually established using high-resolution CT (HRCT) scanning, which has a sensitivity and specificity of 90%. The key feature on HRCT scanning is an enlarged internal