

*Research Article***Evaluation of YKL-40 Protein Levels in Asthmatic Children****Mostafa A. El-fouly, Mohammed A. Bahaa Eldin and Esraa K. Abdelaleem Fouly**

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Abstract

Introduction: Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. **Aim of the work:** The aim of this study was to evaluate the serum levels of YKL-40 in a group of Egyptian asthmatic children (both stable and acute) and compare them to a matched healthy control group, with emphasis on relation between YKL-40 protein and clinical and laboratory parameters of the patients. **Patients and Methods:** This study was conducted at Minia university hospitals for pediatrics, gynecology and obstetrics in the period from May 2016 to ...April 2017. **Results:** Sixty asthmatic children were enrolled in this study (30 patients of acute asthma and 30 patients of stable asthma), they were age- and sex- matched to 30 healthy control children. Results and data analysis are presented in the following tables and figures: **Discussion:** Asthma is defined as a chronic, complex and heterogenic respiratory disease with inflammation and bronchial hyper responsiveness as major underlying phenomena and characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency. **The study recommends the following:** Conduction of further research on the role of YKL-40 in pediatric asthma with larger sample size with longitudinal design. Construction of future studies on prognostic value of YKL-40 levels in asthmatic children. Study of role of YKL-40 in other pediatric pulmonary diseases characterized by inflammation e.g. pneumonia and cystic fibrosis. Study of YKL-40 as an objective biomarker to the degree of control of asthma.

Keywords: Broncho alveolar lavage, Basic fibroblastic growth factor, Breast regression protein

Introduction

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation (GINA, 2016).

YKL-40 is a member of the mammalian chitinase-like protein class, it is a 40kDA (kilodalton) heparin binding glycoprotein, the name YKL-40 is derived from the protein's molecular weight and three N-terminus amino acids (tyrosine, lysine and leucine) (Johansen et al., 1993). YKL-40 binds chitin which is an abundant, naturally occurring polysaccharide composed of N-acetylglucosamine repeats functioning as a major structural polymer in many lower life forms including cell walls of bacteria and fungi but YKL-40 is deficient in chitinase activity, it is produced at sites of inflammation in many cells and is secreted from vascular smooth muscle cells and macrophages (Rathcke et al., 2006).

YKL-40 is synthesized in neutrophil precursors at the myelocyte–metamyelocyte stage; it is stored in specific granules of neutrophils and released from fully activated cells as well as from macrophages, neutrophils, chondrocytes, vascular smooth muscle and cancer cells (Volck et al., 1998).

It is suggested that YKL-40 has a role in inflammation and tissue remodeling in human diseases, such as joint injury, liver fibrosis, type 2 diabetes (Rathcke., et al., 2006); (Johansen et al., 1993), (Kelleher et. al., 2005). It is established that YKL-40 was increased in the lung and circulation of patients with severe asthma so, they reasoned that YKL-40 could either be a cause or marker for asthma (Kuepper et al., 2008).

Patients and Methods

This study was conducted at Minia university hospitals for pediatrics, gynecology and obstetrics in the period from May 2016 to ...April 2017.

Cases group: Sixty patients were included. They were divided into two sub groups:

1. Sub Group I: included 30 stable asthmatic children diagnosed according to Global Initiative for Asthma (GINA) guidelines and were followed-up in the chest clinic of the hospital.

2. Sub Group II: Included 30 children with acute asthma attacks (mild, moderate, or severe according to GINA guidelines); they were recruited from the emergency department of the hospital.

Inclusion criteria:

1. Age from 2 to 6 years.
2. Family history of atopy
3. With diagnosis of asthma according to GINA guidelines.
4. No associated chest infection or other diseases.
5. Approval to participate in the study.

Exclusion criteria:

Patients who did not fulfill all inclusion criteria or refused to participate were excluded.

Thirty healthy children were included in this study as controls, they were recruited from the follow-up clinics of the hospital after consent

from their caregivers, they were age- and sex-matched to the cases group.

All children were subjected to the following:

1. **Complete history taking:** With emphasis on symptoms of asthma, age of onset, frequency of acute attack and nocturnal symptoms
2. **Complete physical examination:** with emphasis on signs of asthma, degree of respiratory distress and oxygen saturation.
3. **Laboratory investigations:** in the form of (CBC, serum YKL-40 protein)

The aim of this study was to evaluate the serum levels of YKL-40 in a group of Egyptian asthmatic children (both stable and acute) and compare them to a matched healthy control group, with emphasis on relation between YKL-40 protein and clinical and laboratory parameters of the patients.

Results

Sixty asthmatic children were enrolled in this study (30 patients of acute asthma and 30 patients of stable asthma), they were age- and sex- matched to 30 healthy control children. Results and data analysis are presented in the following tables and figures:

Table : Correlation between serum YKL-40 and other variables in cases

Variable		Serum YKL -40 pg/ml
Age(years)	Pearson Correlation	-0.175
	P-value	0.355
Heart rate(/min.)	Pearson Correlation	0.134
	P-value	0.481
Respiratory rate(/min.)	Pearson Correlation	-0.057
	P-value	0.763
Temperature (°C)	Pearson Correlation	0.121
	P-value	0.525
Hemoglobin(g/dl)	Pearson Correlation	-0.186
	P-value	0.326
Total leukocyte count(10^3 /cmm)	Pearson Correlation	-0.099
	P-value	0.604
Eosinophil percentage	Pearson Correlation	0.943
	P-value	<0.001*
Absolute eosinophilic count cell/cmm	Pearson Correlation	0.876
	P-value	<0.001*
Severity	Spearman's rho Correlation	0.748
	P-value	<0.001*

Shows correlation between YKL-40 level and other variables with very highly significant correlation with eosinophilic percentage ($r = 0.943$), absolute eosinophilic count ($r = 0.876$) and severity of asthma ($r = 0.748$) with p value < 0.001

Discussion

Asthma is defined as a chronic, complex and heterogenic respiratory disease with inflammation and bronchial hyper responsiveness as major underlying phenomena and characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency (Diette et al., 2008 & GINA, 2014). Asthma is the most common chronic disease in children and it disproportionately affects minority children those of lower socioeconomic status and those in urban areas (Nelson and Zorc, 2013). The incidence of childhood asthma is increasing, the estimated incidence among at-risk children was 12.5/1000 (Winer et al., 2012). In Egypt 23.2% of wheezy infants were proven to be real asthmatics. In 2003, asthma prevalence among school children aged 5-15 years was found to be 8.2%, half of which are graded as moderate to severe asthmatics (El-Lawindi et al., 2003), without early diagnosis and specific treatment, asthma results in a loss of lung function, impaired quality of life and the risk to die from uncontrolled asthma attacks (Eder et al., 2006).

A group of proteins discovered to be potential biomarkers of asthma are the chitinases and chitinase-like proteins, YKL-40 (chitinase-3-like-1 [CHI3L1]), also synonymed as (human cartilage glycoprotein-39), is a member of the mammalian chitinase like protein class and it is synthesized in neutrophil precursors at the myelocyte-metamyelocyte stage; it is stored in specific granules of neutrophils and released from fully activated cells as well as from macrophages, neutrophils, chondrocytes, vascular smooth muscle and cancer cells (Volck et al., 1998).

YKL-40 is a good biomarker of inflammatory lung diseases and this is because of the correlation of YKL-40 level in serum with that in lining cells of respiratory system (Snell et al., 2008), in asthmatic patients YKL-40 is expressed by macrophages in bronchial-biopsy specimens and cytospin of their bronchial-veolar lavage (Chupp et al., 2007). YKL-40 have been shown to be increased in the serum of asthmatic patients and levels of YKL-40 have also been shown to correlate with markers of disease severity (Bargagli et al., 2010). It has been reported that YKL-40 probably activates interleukin-13 pathway and causes more

inflammation in asthmatic patients (Zhu et al., 2004), it is not known whether YKL-40 is typical for some phenotypes of asthma however, this hypothesis may be confirmed by studies showing its high concentration in allergic inflammation (Gavala et al., 2013 & Lee et al., 2012).

Conclusions and Recommendations

The study reached the following conclusions

YKL-40 protein serum levels are significantly higher in asthmatic children compared to healthy controls.

YKL-40 protein serum levels are significantly higher in acute asthmatics compared to stable asthmatics.

YKL-40 protein levels correlate significantly with severity of acute asthma attack.

The study concludes that YKL-40 protein might have a role in pediatric asthma pathogenesis, however, further research on a larger scale is warranted.

The study recommends the following:

Conduction of further research on the role of YKL-40 in pediatric asthma with larger sample size with longitudinal design.

Construction of future studies on prognostic value of YKL-40 levels in asthmatic children.

Study of role of YKL-40 in other pediatric pulmonary diseases characterized by inflammation e.g. pneumonia and cystic fibrosis.

Study of YKL-40 as an objective biomarker to the degree of control of asthma.

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