



# **Evaluation of Serum Lipoxin A4 in Exercise Induced Asthma**

*Thesis*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك يا معلم لنا  
إلا ما علمتنا إنك أنت  
العليم العظيم

صدق الله العظيم

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## ABSTRACT

**Background:** Lipoxin A4 is a potent anti-inflammatory and several lipoxin forming multicellular interactions occur during strenuous

**Aim of the study:** to evaluate diagnostic value of lipoxin A4 as a biomarker of exercise induced asthma

**Subjects and methods:** This cross sectional study was conducted on forty-five asthmatic children divided in two groups; EIA group: 25 children with history of exercise-induced symptoms of asthma confirmed by spirometry, Non EIA group: 20 patients who did not have history of exercise induced symptoms of asthma. Forty-five apparently healthy children were included as a control group with no history of asthma or atopic conditions. Their age and sex were matched with the patients group. For all patients, pulmonary function tests were done before and after a free running test using portable spirometry. Serum levels of lipoxin A4 were estimated for patients (after exercise) and controls using ELISA

**Results:** A significant difference was detected between the levels of lipoxin A4 in EIA and control groups (p value 0.000). There was significant difference between Non EIA and control groups regarding the level of lipoxin A4 with (P value 0.000). The mean level of lipoxin A4 in EIA patients was lower than that of Non EIA patients; however, the difference was statistically insignificant (P value 0.973).

**Conclusion:** Lipoxin A4 is a promising anti-inflammatory factor in management of asthma.

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**Keywords:** Lipoxin A4, Exercise Induced Asthma, bronchial asthma

# Contents

Subjects	Page
List of abbreviations.....	II
List of Figures.....	V
List of Tables.....	VII
• <b>Introduction and Aim of the work</b> .....	1
• <b>Review of Literature</b>	
♦ <b>Chapter (1):Bronchial Asthma</b> .....	5
♦ <b>Chapter (2):Pulmonary Function Testing</b> .....	43
♦ <b>Chapter (3):Exercise Induced Asthma</b> .....	54
♦ <b>Chapter (4): Lipoxins</b> .....	68
• <b>Subjects and Methods</b> .....	77
• <b>Results</b> .....	92
• <b>Discussion</b> .....	114
• <b>Summary and Conclusion</b> .....	124
• <b>Recommendations</b> .....	128
• <b>References</b> .....	129
• <b>Arabic Summary</b>	

## **List of Abbreviations**

<b>15-Loa</b>	: 15-lipooxygenase a
<b>15-Lob</b>	: 15-Lipooxygenase b
<b>ABG</b>	: Arterial blood gass
<b>APSGN</b>	: Acute poststreptococcal glomerulo- nephritis
<b>ARF</b>	: Acute Renal Failure
<b>ASL</b>	: Airway surface liquid
<b>ASM</b>	: Airway smooth muscle
<b>ATL</b>	: Aspirin-triggered lipoxins
<b>B Blockers</b>	: Beta blockers
<b>BAL</b>	: Bronchoalveolar lavage
<b>BALF</b>	: Bronchoalveolar lavage fluids
<b>BMI</b>	: Body Mass Index
<b>CF</b>	: Cystic Fibrosis
<b>CR3</b>	: Chemokine receptor 3
<b>COPD</b>	: Chronic Obstructive airway disease
<b>EAR</b>	: Early phase Asthmatic Reaction
<b>ECT</b>	: Exercise Challenge Test
<b>EIA</b>	: Exercise Induced Asthma
<b>EIB</b>	: Exercise induced Bronchoconstriction

<b>EIIS</b>	:Exercise induced inspiratory stridor
<b>ELISA</b>	: Enzyme-linked immunosorbent assay
<b>EMTU</b>	: Epithelial Mesenchymal Trophic Unit
<b>FEF25-75</b>	: Forced expiratory flow at 25-75%
<b>FEV1</b>	: Forced Expiratory Volume in 1st Second
<b>FVC</b>	: Forced Vital Capacity
<b>GERD</b>	: Gastro-esophageal reflux disease
<b>GINA</b>	: <u>Global Initiative for Asthma</u>
<b>GWA</b>	:Genom world association
<b>GPCR</b>	:G protein coupled receptor
<b>HRP</b>	:Horseradish peroxidase
<b>ICS</b>	:Inhaled corticosteroids
<b>ICU</b>	: Intensivecare unit
<b>IFN alpha</b>	: Interferon alpha (IFN $\alpha$ )
<b>IFN gamma</b>	: Interferon gamma (IFN $\gamma$ )
<b>IgE</b>	: Immunoglobulin E
<b>IL</b>	: Inter leukin
<b>LABAs</b>	:Long-acting beta <sub>2</sub> -agonists
<b>LTB4</b>	: Leukotriene B4
<b>LTD4</b>	: Leukotriene D4
<b>LT</b>	: Leukotriens
<b>LX</b>	: Lipoxins

<b>MPA</b>	: Major Basic Problem
<b>MDC</b>	: Macrophage derived chemokines
<b>MMEF</b>	: Maximum mid expiratory flow
<b>MVV</b>	: Maximum Voluntary Ventilation
<b>NK</b>	: Neutral killer
<b>NSAIDs</b>	: Non Steriodal Antiinflammatory drugs
<b>PAF</b>	: Plateles activating factor
<b>PEF</b>	: Peak expiratory flow
<b>PEFR</b>	: Peak expiratory flow rate
<b>PFTs</b>	: Pulmonary Function Tests
<b>PFho-lipoxinA4-Me:</b>	Para fluro-phenoxy LipoxinA4 methyl ester
<b>PG</b>	: Prostaglandin
<b>PGE</b>	: Prostaglandin E
<b>PMN</b>	: Polymorph neucleocytes
<b>SABA</b>	: Short acting B2 agonist
<b>SST</b>	: Serum separator tube
<b>TARC</b>	: Thymus activation regulated chemokines
<b>Th</b>	: T- helper cell
<b>TGFB</b>	: Transforming growth factor beta
<b>TNF <math>\alpha</math></b>	: Tumor necrosis factor alpha



## List of Figures

<b><u>No.</u></b>	<b><u>Figure</u></b>	<b><u>Page</u></b>
<b><u>1</u></b>	Diagrammatic presentation of bronchial changes in Asthma	<b>17</b>
<b><u>2</u></b>	Role of Inflammatory cells in Asthma.	<b>19</b>
<b><u>3</u></b>	Management approach based on control (for children $\geq 5$ years)	<b>37</b>
<b><u>4</u></b>	Algorithm management of acute asthma exacerbation	<b>39</b>
<b><u>5</u></b>	Management of acute severe asthma in children.	<b>40</b>
<b><u>6</u></b>	Stepwise approach for managing asthma in children 0-4 years of age	<b>41</b>
<b><u>7</u></b>	Stepwise approach for managing asthma in children 5-11 years of age	<b>42</b>
<b><u>8</u></b>	Volume- time curve	<b>47</b>
<b><u>9</u></b>	Flow-volume loop	<b>47</b>
<b><u>10</u></b>	Child performing spirometry	<b>48</b>
<b><u>11</u></b>	Lung volumes and capacities I	<b>49</b>
<b><u>12</u></b>	Lung volumes and capacities II	<b>50</b>
<b><u>13</u></b>	Pathogenesis of EIA	<b>55</b>
<b><u>14</u></b>	Normal spirometry	<b>63</b>
<b><u>15</u></b>	Normal Spirometry VS Spirometry in Obstructive diseases	<b>64</b>
<b><u>16</u></b>	Structure of Lipoxin A4	<b>68</b>

<b><u>No.</u></b>	<b><u>Figure</u></b>	<b><u>Page</u></b>
<b><u>17</u></b>	Jaeger spirometry	<b>84</b>
<b><u>18</u></b>	Standard curve	<b>90</b>
<b><u>19</u></b>	Frequency of symptoms of Asthma in the two patients groups after exercise	<b>95</b>
<b><u>20</u></b>	BMI centiles in EIA and control	<b>98</b>
<b><u>21</u></b>	BMI in EIA and control	<b>99</b>
<b><u>22</u></b>	Weight centiles in EIA group and control	<b>102</b>
<b><u>23</u></b>	Percentage of reduction in FEV1% of expected in Asthmatic patients and Control	<b>106</b>
<b><u>24</u></b>	FEV1% before and after exercise in Asthmatic patients and Control	<b>107</b>
<b><u>25</u></b>	Serum Lipoxin A4 in both patients groups and Control	<b>109</b>
<b><u>26</u></b>	Receiving Operating Characteristic (Roc) curve to define the best cutoff value of serum Lipoxin A4 in EIA, Non EIA and control	<b>111</b>

## List of Tables

<b><u>No.</u></b>	<b><u>Table</u></b>	<b><u>Page</u></b>
<b><u>1</u></b>	Cytokine stew of asthma. The interplay of inflammatory proteins and cytokines in the onset and maintenance of inflammation and induction of remodeling in asthma	<b>23</b>
<b><u>2</u></b>	Asthma classification according to severity	<b>26</b>
<b><u>3</u></b>	Modified Asthma predictor index	<b>30</b>
<b><u>4</u></b>	Steps to avoid specific allergens in sensitized individuals	<b>33</b>
<b><u>5</u></b>	Criteria of asthma control	<b>35</b>
<b><u>6</u></b>	Assessment of exacerbation severity	<b>38</b>
<b><u>7</u></b>	Demographic clinical and laboratory data of the two patients' groups and control group	<b>93</b>
<b><u>8</u></b>	FEV1 before and after exercise and lipoxin A4 in both patients groups and control group	<b>96</b>
<b><u>9</u></b>	Lipoxin A4 level in Asthmatic patients and control	<b>97</b>
<b><u>10</u></b>	Lipoxin A4 in atopic patients(Mann-Witney test)	<b>97</b>
<b><u>11</u></b>	Comparison between the two patients groups and control regarding socio-demographic Anthropometric measures (Mann-Whitney test)	<b>100</b>
<b><u>12</u></b>	Comparison between EIA patients and control regarding Anthropometric measures and laboratory data (Mann-Whitney test)	<b>101</b>
<b><u>13</u></b>	Comparison between non EIA patients and control regarding Anthropometric measures (Mann-Whitney test)	<b>103</b>

<b><u>No.</u></b>	<b><u>Table</u></b>	<b><u>Page</u></b>
<b><u>14</u></b>	Comparison between the two patients' groups regarding the clinical symptoms of the patients group before exercise and the laboratory data (Chi square test)	<b>104</b>
<b><u>15</u></b>	Comparison between the asthmatic patients and control regarding FEV1 before and after exercise and percentage of reduction and lipoxinA4 (Independent samples t test)	<b>105</b>
<b><u>16</u></b>	Comparison between the two groups of patients and control regarding FEV1 before and after exercise and percentage of reduction and Lipoxin A4(Independent samples t test)	<b>108</b>
<b><u>17</u></b>	Comparison between EIA patients and non EIA regarding FEV1 before and after exercise and percentage of reduction and Lipoxin A4 (Independent samples t test)	<b>110</b>
<b><u>18</u></b>	Comparison between atopic and non atopic patients regarding Lipoxin A4(Independent samples t test)	<b>112</b>
<b><u>19</u></b>	Correlation between serum Lipoxin A4 and clinical parameters in Non-Exercise induced Asthma patients group	<b>113</b>

## Introduction

Bronchial asthma is a chronic disease of respiratory tract constituting a serious public health problem all over the world. Asthma prevalence has increased very considerably in recent decades such that it is now one of the commonest chronic disorders in the world (**Anandan et al., 2010**).

Asthma is characterized by a chronic inflammation of the airways. It leads to a variable airflow obstruction and symptoms such as wheezing, chest tightness, coughing, and dyspnea. Chronic inflammation observed in asthma leads to airway hyper-responsiveness that is defined as abnormal increase in airway flow limitations following exposure to non-allergic stimulus as exercise (**Tahan et al., 2008**).

Asthma affects about 300 million people worldwide. It is the most common chronic disease among children (**GINA, 2009**), affecting nearly 5 million, children younger than age 18 in US. In Egypt 23.2% of wheezy infants were proven real asthmatics. Asthma prevalence among school children aged 5-15 years was found to be 8.2%, half of which are graded as moderate or severe (**Deraz, 2003**).

Exercise induced asthma (EIA) can be demonstrated in up to 70% of patients with asthma, and in other individuals who have (EIA) in the absence of additional features of asthma. The pathogenesis of (EIA) is poorly understood. Although conditioning of the inspired air, leading to drying and cooling of the intra-thoracic airways, may serve as the initial trigger for (EIA), the subsequent events in the airways are unclear (**Belanger et al., 2016**).

The exercise challenge test (ECT) is a common tool to assess exercise-induced asthma in school-aged children. Free running test is used for EIA diagnosis in school-aged children combined with measurements of spirometry (**Vilozni et al., 2007**).

Lipoxin A4 is a biological active lipooxygenase interaction product derived from arachidonic acid. Lipoxins and 15 epilipoxins are lipid mediators that modulate leucocyte trafficking and promote inflammation potential mediators or modulators of inflammation within the lungs (**Bhavsar et al., 2010**). Lipoxin A4 is a potent counter regulator signal for endogenous pro-inflammatory mediators including leukotriens and platelet activating

factor resulting in inhibition of leukocyte dependent inflammation (**Serhan et al., 2006**).

As lipoxins A4 are potent anti-inflammatory and several lipoxin forming multicellular interactions occur during strenuous, an urge is needed to evaluate the lipoxin A4 after exercise.