

# The Relationship between Tumor Necrosis Factors- $\alpha$ (TNF- $\alpha$ ) and Oxidative Stress in Iraqi Patients with Asthma

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## Abstract

Asthma is the most common chronic disease of the airways, involving the imbalance of oxidative and antioxidative agents. There is an increased free radical generation and a decreased antioxidant enzyme activity. This study designed to find out the relation between TNF- $\alpha$  and oxidative stress in Iraqi patients with asthma. Seventy subject were enrolled in this study, twenty patients of them with Asthma and twenty five subjects who are apparently healthy were taken as a control group. Serum TNF- $\alpha$  was determined by using enzyme-linked immunosorbent assay (ELISA). Serum levels of TNF- $\alpha$  was highly significantly increase in asthma group compared with control group ( $p < 0.01$ ) and a significant positive correlation between TNF and malondialdehyde (MDA) by affecting TNF level in patients with Asthma.

**Keywords :** Asthma, TNF- $\alpha$ , oxidative stress

## 1. Introduction

The generation of reactive oxygen species (ROS) through normal cellular metabolism and by means of exogenous insults is a constant problem for which cells have developed multiple protective mechanisms to survive. Elevated levels of ROS may induce a variety of pathological changes that are highly relevant in nasal and airway mucosa (Kim *et al.*, 2012), however Chronic inflammatory disorder associated with reversible airways obstruction (Voynow *et al.*, 2011). All biological membranes are characterized by the large amounts of polyunsaturated fatty acid associated with amphipathic lipid and a variety of membrane proteins. Both isolated polyunsaturated fatty acid and those incorporated into lipid are readily attacked by free radicals, becoming oxidized into lipid peroxidation (Chung *et al.*, 2010), therefore peroxidized membrane lipid occurs as a result of oxidative stress in intact cells. Peroxidation of these labile unsaturated fatty acids can damage both protein and lipids as well as disrupt the structure and function of the membrane in most body cells (Astudillo *et al.*, 2009). MDA is one of the most frequently used indicators of lipid peroxidation (AnaLúcia *et al.*, 2012). TNF are lymphokines that exist in either an  $\alpha$  or  $\beta$  form which capable of causing *in vivo* hemorrhagic necrosis of certain tumor cells, but not affecting normal cells. Cytokines (produced due to activation of T-cells and mast cells) lead to increased production of histamines, leukotrienes and prostaglandin that have multiple activities. They cause the characteristic watery Rhinorrhoea by stimulating gland and goblet cell secretion, vasodilatation and blood vessel leakage (Browning *et al.*, 2013).

Previous study found increased serum levels of TNF and MDA in bronchia asthma and allergic rhinitis (Abdel-Raheim, *et al* 2006).

## 2. Methods and Patients

This study was conducted with seventy patients with Asthma in Babylon Maternity, Pediatric Teaching Hospital and in the laboratory of Biochemistry Department, College of Medicine, University of Babylon. Full history was taken from all patient which include: age, residence, smoking, family history, medical history drug history and surgical history, No drugs were prescribed to those patients that may interfere with the measured parameters. Twenty five apparently healthy subject (who are age and sex-matched with the patients group) were selected as a control group in the study. All control subject have no history of chronic disease such as (diabetes mellitus, hypertension inflammatory disease such as rheumatoid arthritis) and they are non smoking. The statistical analysis was performed by using SPSS version 18 for windows. Data were expressed as Mean  $\pm$  SD. The normality of the distribution of all variables was assessed by the Student's F-test and Pearson correlation analysis that have been used to determine the significant difference between the two groups. P values less than 0.05 is considered significant.

## 3. Results and Discussion

The results (table- 1) reveals a highly significant increase in the sera level of TNF in patients with asthma group cases compared with those of control group ( $P < 0.01$ ). The up regulation of TNF- $\alpha$  production is stimulated by NO, reactive oxygen intermediates, non steroidal anti-inflammatory drugs and hypoxia. The increased production of TNF- $\alpha$  by hypoxia may be due to decreased PGE2. Also TNF- $\alpha$  is inhibited by IL-10, PGE2, dexamethasone (Shimomoto, *et al* 1995).

Elevated levels of ROS such as hydroxyl radicals, superoxides and peroxides may induce a variety of pathological changes that are highly relevant in nasal and airway mucosa (Emin et al., 2012). These include lipid peroxidation, increased airway reactivity, and nasal mucosal sensitivity and secretions, production of chemo attractant molecules and increased vascular permeability. Such association between chronic inflammation and oxidative stress is well documented by many investigators (Halliwell et al., 1994). From the results, we can conclude a high significant positive correlation between TNF alpha and MDA in Asthma group.

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**Table (1): Biochemical parameters of asthma and control Groups.**

Parameter	Asthma group n= 17	Control n=25	P values
TNF- $\alpha$ pg/ml Mean $\pm$ SD Range	4.4 $\pm$ 1.36182 (80.1-84.2)	11.27 $\pm$ 1.42 9.5-14	P <0.01
MDA $\mu$ M Mean $\pm$ SD Range	6.1 $\pm$ 0.40 5.93-6.9 )	5.3 $\pm$ 0.3 5.1-6.1 )	P <0.05

**Table (2): Pearson's correlation between MDA and IgE the levels of in different groups (n= 50)**

parameters	Asthma group		control	
	r	p	r	p
MDA vs TNF	0.855	0.01	0.171	0.05

Significant = P < 0.05      high significant = P < 0.01

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