



ISSN NO. 2320-5407

Journal homepage: <http://www.journalijar.com>

INTERNATIONAL JOURNAL
OF ADVANCED RESEARCH

RESEARCH ARTICLE

Interleukin-17 in immunity of thyrotoxicosis

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Manuscript Info

Manuscript History:

Received: 15 June 2015
Final Accepted: 16 July 2015
Published Online: August 2015

Key words:

IL-17, Thyrotoxicosis, Th-17

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Abstract

This study was conducted on the Diabetes and Endocrines Medical Center / Thi-Qar city, during the period between May 2013 till October 2013 comprised ninety five Iraqi Arab with thyrotoxicosis (75 female, 20 male) their ages range (23-50). who were attending Diabetes and Endocrines medical center. All patients were selected for diagnosis on of basis of absolute dependency according to the revised criteria for diagnosis of thyrotoxicosis (goiter, TSH, T4, T3, anti-TPO, anti-TG, anti-TSH). It aims to demonstrate the role of IL-17 in thyrotoxicosis. The results reveal that the level of IL-17 elevated and it had positive correlation with thyroxine (T₄) hormone and anti-TSH (autoantibody)

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INTRODUCTION

Thyroid is a small endocrine gland found in the front of the neck, it produces the hormones thyroxine (T₄) and Triiodothyronine (T₃). Every cell in the body depends upon thyroid hormones for regulation of their metabolism is controlled by a cyclical mechanism relying on both positive and negative feedback. Hyperthyroidism is a set of disorders that involve excess synthesis and secretion of thyroid hormones by the thyroid gland, which leads to the hypermetabolic condition of thyrotoxicosis. The most common forms of hyperthyroidism include diffuse toxic goiter (Graves disease), toxic multinodular goiter, and toxic adenoma. (Davies and Larsen 2003)

Cytokines are chemical signaling molecules that transfer information from cell to cell, and work together to regulate the immune system.

Originally IL-17 was thought to be produced absolutely by T cells (Fossiez, et al., 1996), during the late 1990, studies pointed to IL-17 as a possible effector in rheumatoid arthritis and other diseases, (Gaffen, 2009)

There are six members of the IL-17 family in humans and in mice, some of these molecules newly identified have the ability to modulate immune function. (Aggarwal and Gurney 2002) IL-17A and IL-17F are best understood, these two cytokines share the strongest sequence homology (Wang et al., 2012)

It be secreted by a variety of innate cells including macrophages, dendritic cells, natural killer, lymphoid tissue inducer and T cells (Korn et al., 2009) and play essential role in host defense against many microbes, particularly extracellular bacteria and fungi. (O'Quinn, et al., 2008). A major development in this field with (Park, et al., 2005; Harrington, et al., 2005; Steinman, 2007; Dong 2008;) discuss the involvement of these related Th17 cytokines as they pertain to co-operative target gene regulation.

Material and method:

The study patients consisted of 95 patient and 23 healthy control with age (23-50) year, during the period from May 2013 till October 2013. 5 ml of blood collected from each patient or control, and it left to clot for 1-2 hour at

room temperature and then centrifuged at 3000 rpm for 10 minutes, serum was stored at -20°C until was used. Tested for the determination of thyroid hormone levels: (T_3 , T_4 , TSH) using a miniVidas system. (Biomérieux, France). Thyroid anti-TSH receptor immunoglobulin (anti-TSH), anti-thyropoxidase (anti-TPO) and anti-thyroglobulin (anti-TG) antibodies were measured in all the samples using electrochemiluminescent "ECL" with Modular Analytics cobas e 411 analyzer (Roche Diagnostics, England). ELISA Kits and ELISA system for the quantitative determination of IL-17 was assay employs (Creative Diagnostics/USA)

Statistical analysis:

Values were expressed as mean \pm SD, differences between the mean values were analyzed by chi-square test. While correlation between the data obtained were analyzed by using analysis of variance (ANOVA) to determine the level of significance by using minitab underwindows, The criterion for significance was ($p < 0.01$).

Result:

The serum IL-17 of the patients was highly significantly increased compared with controls(mean \pm SD) (22.9 ± 5.8 vs. 0.098 ± 0.038 pg/L $p = 0.000$).

Table: 1 shows level of IL-17of patients and control

IL-17 (pg/L)	No	Median	Mean \pm SE	P-value
patient	95	1.05	22.9 ± 5.8	0.000*
control	23	0.03	0.098 ± 0.038	

* $p < 0.01$

Parameters were analyzed separately for patients group table (1) and healthy control table .

Table :2 Correlations between parameters in patients group: T_3 , T_4 , TSH, anti-TSH, Anti-TPO, Anti-TG, IL-17

Correlations	T_3	T_4	TSH	anti-TSH	Anti-TPO	Anti-TG
T_4	0.543** 0.000					
TSH	-0.081 0.436	-0.200 0.052				
anti-TSH	0.110 0.291	0.201 0.051	-0.039 0.709			
Anti-TPO	0.006 0.952	-0.124 0.232	-0.056 0.588	0.069 0.508		
Anti-TG	-0.171 0.098	-0.005 0.962	-0.024 0.815	0.106 0.305	0.032 0.759	
IL-17	0.071 0.497	0.269* 0.008	-0.073 0.483	0.483** 0.000	-0.038 0.713	-0.022 0.833

p value less than 0.01were significant

The Correlation between parameters in patients group is shown in Table(2) When the levels of T_3 , and T_4 were compared in the patients positive correlated ($p = 0.000$, $r = 0.543$) and a high significant.

There was also a positive correlation between IL-17 and T_4 and anti-TSH ($p = 0.008$, $r = 0.269$ and $p = 0.000$, $r = 0.483$) and a high significant respectively. However, no significant correlation was found between other parameters in patients group.

Discussion:

Th1 and Th2 immune cells has been postulated to play an important role in the pathogenesis of autoimmune thyroid diseases (AITD). However, recent studies on thyroid diseases suggest a new role for Th17 (T helper 17) cells that have been classified as a new lineage (Firestein,2003; Artur et al.,2013) IL-17 is the founding member of a new subclass of cytokines that have highly proinflammatory properties (Gaffen ,2009) The target cell types of IL-17 are

non-immune origin, particularly epithelial and mesenchymal cells within diseased or inflamed tissues (Yu and Gaffen 2008)and IL-17 differ depending on the target cell (Reiko ,et al., 2010) its signaling target genes in various disease setting and mediates adverse effects in many autoimmune diseases, effects induction of new gene expression with signaling system is operative in disparate tissues such as reticular cartilage, bone, meniscus, brain, hematopoietic tissue, kidney, lung, skin and intestine. Thus, the evolving IL-17 family of ligands and receptors may play an important role in the homeostasis of tissues in health and disease beyond the immune system in add biological actions in cancers (Moseley, 2003; Korn,2009). AnJi et al., (2009) refer to the level of serum IL-17 in hyperthyroid patients is correlated with the increasing level of thyroid hormones. Many studies demonstrated a critical role for IL-17 in the pathogenesis of variety of inflammatory autoimmune diseases, such as rheumatoid arthritis and multiple sclerosis, asthma and systemic lupus erythematosus. (Chang and Dong,2007; Zhu and Qian 2012) other study refer to IL-17 sits at the center of many complex diseases that integrate innate and adaptive immune mechanisms (Jin. and Dong,2013) its receptor expressed universally, and hence most cells can potentially respond to this cytokine. (Yao, et al.,1997;Shen and Gaffen 2008). Gene products induced by IL-17 include cytokines (IL-6, granulocyte-colony-stimulating factor, tumour necrosis factor- α), chemokines (CXCL1, CXCL2, CCL20, among many others), inflammatory effectors (acute-phase, complement) and antimicrobial proteins (defensins, mucins). It also induces prostaglandin E₂ via cyclooxygenase-2, which enhances inflammation by many mechanisms including vasodilatation ,and its harmful properties via specific target gene regulation in the context of disease (Reiko, et al.,2010). A large amount of IL-17A, a cytokine that coordinates tissue inflammation by inducing the expression of proinflammatory cytokines (such as IL-6 and tumor necrosis factor [TNF]), chemokines (such as KC, MCP-1, and MIP-2), and matrix metalloproteases that mediate tissue infiltration and tissue destruction. (Weaver, et al.,2007)

Conclusion:

It conclude that elevated level of IL-17 cytokine and positive correlation with T4 and anti-TSH, suggest their role in initiation and development of immune and inflammatory processes in this disease .

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