

SERUM TUMOR NECROSIS FACTOR α AND INTERLEUKIN-10 ASSAY IN NASSIRYHIAN IRAQI PATIENTS WITH HYPOTHYROIDISM

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Article received 26.8.2018, Revised 2.9.2018, Accepted 8.9.2018

ABSTRACT

Tumor Necrosis Factor α and Interleukin-10 are inflammatory cytokines has a significant role in the pathogenesis of immunological inflammatory processes at multiple levels.

The study was performed on 80 Iraqi patients attended Endocrine and diabetic Medical center in Nassiryhia, with hypothyroidism and 23 healthy adults were enrolled. All subjects were (20-53) years old.

Thyroid hormones triiodothyronine (T3) and thyroxin (T4), concentrations were (1.62 ± 0.399) vs (1.98 ± 1.119) nmol/l, (104.55 ± 48.27) vs (92.03 ± 13.71) nmol/l not significant increase in patients than in control respectively, while thyroid stimulating hormone (TSH) concentrations were (17.63 ± 29.16) vs (2.138 ± 1.09) μ Iu/IP (0.013*) significant increase in patients than in control.

This study supports the fact that some cytokines may play a role in hypothyroidism, so there are a Significant increase of TNF- α and IL-10 concentration in patients when compared with the healthy controls ($p < 0.001$ for both) (Mean \pm standard deviation) (277.5 ± 253.1), and (214 ± 168.3) pg/ml and (7.34 ± 3.3) and (4.75 ± 0.62) respectively.

This finding may indicate that hypothyroidism might influence cytokine production in these patients.

Key words: Hypothyroidism, TNF- α , IL-10

INTRODUCTION

Hypothyroidism is a prevalent condition of thyroid hormone deficiency, which leads to the cause of mortality in severe cases if untreated (Chaker et al., 2017), which is caused by many reasons like autoimmune disease, treatment for hyperthyroidism, radiation therapy, thyroid surgery and certain medications, so it leads to increases in TSH and deficiency of thyroid hormone and developing of hypothyroidism symptoms due to all metabolically active cells need thyroid hormone (Bello and Bakari 2012, Rizzo et al., 2017) and the clinical symptoms can vary with age and sex and presence of other diseases (Aggarwal and Razvi 2013) among different factors but generally well-known symptoms in adults are exhaustion, dormancy, chilly, constipation, weight raise, change in voice and dry skin (Chaker et al., 2017). So, it should be identified and treated early to avoid potentially deficits (Diaz and Lipman Diaz 2014).

Cytokines play important roles in the process of pathogenesis of hypothyroidism disease and seem to show a good correlation with endocrine status, indicating that they could even function as markers of thyroid diseases (Tayde et al., 2017). Several studies indicated an alteration of serum interleukins in hypothyroidism patients like IL-2, IL-6, IL-10, IL-12, TNF- α (Kimura et al., 2005, Marchiori et al., 2015, Tayde et al., 2017) that interact with an inflammatory response.

The aim of this study was to detect serum cytokines interleukin-10(IL-10) levels and TNF- α , to evaluate its utility as a clinical biomarker of thyroid disease (hypothyroidism) and to compare them with normal control subjects. No Iraqi research has been assumed on the link between thyroid hormone changes and cytokines in hypothyroidism patients.

MATERIALS AND METHODS

The study group included 80 Iraqi patients with hypothyroidism, 60 female and 20 male attended Endocrine and diabetic Medical center in Nassiryhia city in Thi-Qar province. They were diagnosed by a physician in the same center, and 23 healthy were enrolled in the study as a control group, 15 females and 8 males. The age of patients and healthy control ranged between (23-50) years.

Five ml of venous blood samples were gained from all subjects enrolled in this study by using an adequate closed system sample then centrifuged at 3000 rpm/ 5 min and stored at -20°C .

Thyroid function tests were assayed by using the Minividis Kit for detection of thyroid hormone (T3, T4, and TSH) provided by biomérieux SA/ France which are enzyme immunoassay for detection of total T₃, T₄ and TSH.

Serum interleukin-10 and tumor necrosis factor α levels were evaluated using a commercially Bio source micro plate ELISA Kits for the quantitative

determination of cytokines in human serum/ Creative Diagnostics/USA.

Statistical analysis: Results were expressed as Mean SD were performed by the Minitab 13 software, The One-way ANOVA was used to compare between patients and control and $p \leq 0.05$ and $p \leq 0.01$ was considered statistically significant.

Table 1: Serum TSH, T4 and T3 Levels in Patient and Control Groups

Groups	Hormones		
	TSH (μ IU/ml) (mean \pm SD)	T4 (nmol/l) (mean \pm SD)	T3 (nmol/l) (mean \pm SD)
Control	2.138 \pm 1.09	92.03 \pm 13.71	1.62 \pm 0.399
Patients	17.63 \pm 29.16	104.55 \pm 48.27	1.98 \pm 1.119
P-Value	0.013*	0.223	0.136

The measured values of T4 and T3 were not significantly increased in patients, while TSH significantly increase in patients were compared with those in healthy controls with $P = 0.013$ table -1, served to confirm the establishment of hypothyroidism in the patients.

Table 2: level of IL-10 & TNF- α in patients and control groups

Cytokines	
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RESULTS AND DISCUSSION

The study was designed to evaluate IL-10 and TNF- α level and to examine their relationship in 80 patients with hyperthyroidism and 23 controls with normal thyroid functions.

Groups	IL-10 (pg/ml) (Mean \pm SD)	TNF- α (pg/ml) (Mean \pm SD)
Control	4.75 \pm 3	7.34 \pm 3.3
Patients	214 \pm 168.3	277.5 \pm 253.1
P-Value	0.000*	0.000*

Significant increased IL-10 and TNF- α concentration in patients when compared with the healthy controls ($p < 0.001$ for both) table- 2 figure (1).

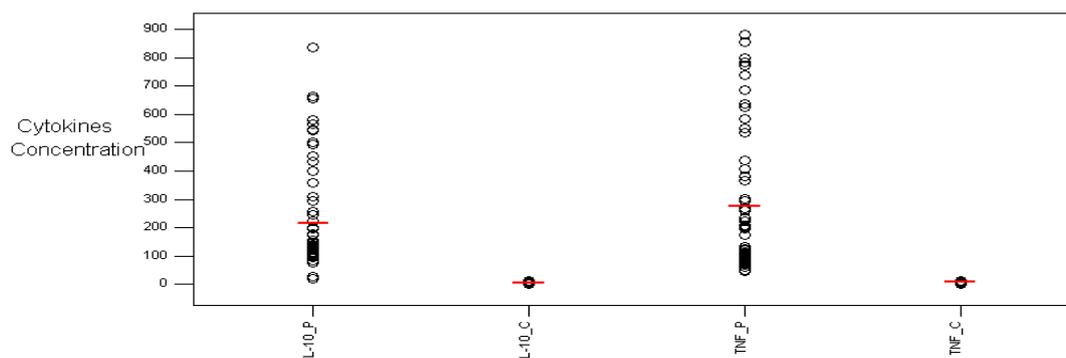


Figure 1: Mean Interleukin (IL)-10 and Tumor necrosis factor (TNF)- α in patients group and control group

The variations in the mean values of TSH, T4, and T3 levels were common, among thyroid disorders patients (Panickera *et al.*, 2008) and they reported that the key test for the diagnosis and management of hypothyroidism and hyperthyroidism is the TSH assay. Current TSH assay has high sensitivity and was recommended as first line strategy and most important measurement for identifying changes in thyroid function (Muller *et al.*, 2008; Gibbons *et al.*, 2010; Aggarwal and Razvi 2013). Plasma T3 and T4 levels were significantly correlated with serum cytokines in the hyperthyroid state.

Tumor necrosis factor alpha (TNF- α) is an example of pro-inflammatory cytokines and IL-10 an example of anti-inflammatory cytokines, which

act to regulate the human immune response (Opal and DePalò 2000).

Many studies were done on attesting the role of different interleukins on thyrotoxicosis, but little old studies were done on hypothyroidism and interleukins spatially IL-10 and TNF- α (Shirin *et al.*, 1999, Bruck *et al.*, 1998, Kızıltunc *et al.*, 1999).

The aim of this study was to examine the association of tumor necrosis factor α (TNF α , a proinflammatory cytokine) and interleukin (IL)-10 (an anti-inflammatory cytokine), that are produced in different tissues in different pathological situations, and hypothyroidism.

Pro-inflammatory or anti-inflammatory cytokines which produced by Th1 (TNF- α) and Th2

(IL-10) cells have a crucial role in protecting against the autoimmune thyroid disease (Mikos et al., 2014).

The elevations in serum TNF- α and IL-10 that occur in hypothyroidism seem to result from the chronic effects of thyroid hormone decrease and the increase of the clinical activity score of disease due to thyroid dysfunction may have been the initiators of developing inflammatory cascade (Diez et al., 2002, Tripathi and Pandey 2014) and the activity of the disease characterized by the extension of inflammation and impairment of function correlated with increasing serum cytokines (De La Vega et al., 1998).

Human IL-10 interferes with synthesis of the inflammatory cytokines, such as TNF- α , IL-1, IL-2, IL-6, IL-8 and others (Brennan et al., 1996).

The results of our study differ from some previous studies that have been found the hypothyroidism could cause reduction in serum TNF- α levels in mice (Shirin et al., 1999), rats (Bruck et al 1998) and in human (Kızıltunc et al 1999), contrarily (Kandir & Keskin 2015) found increased in serum TNF- α levels like our study and Ozcinar and his colleagues (2014) found the TNF- α levels were higher after thyroid surgery inhuman, and this is confirmed by previous studies that have been concluded that serum TNF- α was increased in patients with hypothyroidism (Miyakoshi et al., 1992) and in accordance with prior studies Reikeras and his colleagues (2014), Tripathi and Pandey (2014) they indicate there was a significant increase of TNF- α production mean while slight elevation on the level of the anti-inflammatory cytokine IL-10 might explain as a consequence of the thyroidectomy operation, and demonstrated that inflammatory cytokine profile expressed by a high TNF- α and IL-10 were associated with disease stage and disease activity in hypothyroidism patients and we can say due to interleukins that regulate information transfer among different types of leukocytes during various stages of immune or inflammatory response lead to increase in thyroid stimulating hormone (TSH) and decrease T3, and T4 concentration. This finding may indicate that hypothyroidism might influence cytokine production in these patients.

From the present study, a conclusion can be stated that IL-10 and TNF- α increase concentration in sera of hypothyroidism in Iraqi patients.

Our results point to the fact that thyroid hormones might co-induce raising serum cytokines levels (IL-10 and TNF- α) like other studies (Kimura et al., 2005, Marchiori et al., 2015, Tayde et al., 2017), which activate different pathways of pathogenicity and that reflect the activation and

interplay of mixed T helper cells which may be consistent with long-standing inflammatory and destructive processes of thyroid gland because the significantly increased concentrations of cytokines.

Conclusion

our study suggests that cytokines play a major role in enhancing inflammation in the hypothyroidism patients, and a serologic test for this cytokine could help in choosing more effective treatment protocols in patients with active disease.

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