

Interleukin-17, IL-18, and IL-22 Levels in Autoimmune Thyroid Disease and Polycystic Ovary Syndrome

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ABSTRACT— Polycystic ovarian syndrome (PCOS) is the most frequent endocrine disorder affecting Iraqi women of reproductive age. PCOS has been linked to autoimmune diseases, therefore the study's goal is to comparative the levels of interleukins (IL-17, IL-18, IL-22) among Iraqi women with autoimmune thyroid disease and PCOS. Collected about 90 serum samples from groups study (group of PCOS) (30 samples); group of thyroid disease (30 samples, as well as group of healthy women fertile (30samples) as control during the period (April – November) 2021 from many hospitals in Baghdad- Iraq. And determination levels of interleukins (IL-17, IL-18, IL-22) by quantitative sandwich enzyme immunoassay technique (Cusabio- China). Results of current study showed highest (Mean \pm Std.) of IL-17 (101.17 \pm 19.80) of (\leq 30 -39) age group and (106.63 \pm 15.72) of (40- \geq 50) age group, so higher levels of IL-18 (137.06 \pm 25.53) and IL-22(36.44 \pm 10.05) were among Thyroiditis group. level of IL-17was highly statistically significant (P=0.002) difference between Control and Thyroiditis groups, as well as the levels of Interleukins (IL -17, IL -18 and IL -122) were higher among Hypothyroid cases of Thyroiditis group [(99.1 \pm 14.22), (149.45 \pm 13.31) and (37.80 \pm 11.89) respectively]. The Comparison of Interleukins(IL -17, and IL -18) level of Hypothyroid and Hyperthyroid among Thyroiditis group were highly statistically significant different (P=0.000) but level of IL -22 was no statistically significant(P=0.338), current study showed represented the receiver operating characteristic (ROC) curve Interleukin (IL-17, IL-18 and IL-22) in Thyroiditis group with Control group to diagnosis Thyroiditis disorder show that the cutoff value of IL-17 was >91.17 with 83.3%sensitivity, Specificity46.7%. Also IL-17 had highly significant (P=0.000) and area under the curve (AUC) =0.807. IL-18with cutoff value>144.216 and 16.7%sensitivity, 50.0% specificity, had highly significant (P=0.000). The cutoff value of IL-22was >33.409 had significant (P=0.026) and 23.3% sensitivity, 50.0%specificity. Highest levels of IL-17; IL-18 and IL-22 among Thyroiditis group. as well as the levels of Interleukins (IL -17, IL -18 and IL -122) were higher among Hypothyroid cases of Thyroiditis groups, so IL-17 had highly significant (P=0.000) and area under the curve (AUC) =0.807. IL-18 with cutoff value>144.216 and 16.7%sensitivity, 50.0% specificity, had highly significant (P=0.000). The cutoff value of IL-22was >33.409 had significant (P=0.026) and 23.3% sensitivity,500%specificity.

KEYWORDS: Interleukin-17, IL-18, and IL-22; Autoimmune Thyroid Disease; Polycystic Ovary Syndrome

1. INTRODUCTION

Two of the most frequent endocrine disorders among Iraqi women are thyroid problems and polycystic ovary syndrome (PCOS). Despite the fact that hypothyroidism and PCOS have fundamentally different causes, they share a lot of similarities. Primary hypothyroidism has been linked to an increase in ovarian volume and cystic abnormalities in the ovaries. On the other hand, it's becoming obvious that thyroid problems are more likely among PCOS women [3], [10].

IL-17 has been implicated with tissue inflammation in a number of recent investigations. The release of pro-inflammatory cytokines and other cytokines is induced by IL-17, which activates neutrophils [6]. Th17 cells' main cytokine, IL-17, stimulates T cell activity and induces the endothelium to produce a variety of IL-1, IL-6, tumor necrosis factor (TNF-), NOS-2, metalloproteinase, and chemokines are all pro-inflammatory mediators that increasing endothelial inflammation [6], [7], IL-18 is another one of the pro-inflammatory cytokines that is thought to be elevated in women with PCOS. Our findings support the aforementioned principle, and they agree with [12], [1], who found an increase in levels of IL-18 in PCOS [5].

IL-22 is also known to play a role in host defense within barrier tissues, such as the gut and mucosa, where it protects epithelial barriers from extracellular pathogens (Colonna, 2009). IL-22, on the other hand, has been associated to inflammatory tissue pathology and has been implicated in the etiology of autoimmune disorders (Colonna, 2009).

2. Patients and methods

Collected about 90 serum samples from groups study (group of Polycystic ovary disease (PCOS) (30 samples); group of thyroid disease (30 samples, as well as group of healthy women fertile (30samples) as control during the period (April – November) 2021 from Kamal AL-Samaria, Baghdad teaching hospitals and Teaching laboratories in medical city – Iraq.

2.1 Determination levels of interleukins IL-(17, 18 and 22)

The quantitative sandwich enzyme immunoassay technique (Cusabio-China) is used in this assay. Antibodies specific for each interleukin(IL-17, IL-18, IL-22) are used. on a micro plate that has been pre-coated Interleukins (IL-17, IL-18, IL-22) are bound by the immobilized antibody when standards and samples are pipetted into the wells. After eliminating any unbound compounds, the wells are incubated with a biotin-conjugated antibody specific for interleukin (IL-17, IL-18, IL-22). Horseradish Peroxidase (HRP) is introduced to the wells after they have been hingavidin conjugated After a wash to remove any unattached avidin-enzyme reagent, a substrate solution is added to the wells, and color develops in proportion to the amount of IL bound in the initial phase. The color development is stopped, and the intensity of the color is measured.

3. Results

Results of table (1) showed the highest (Mean \pm Std.) of IL-17 (101.17 \pm 19.80) of (\leq 30 -39) age group and (106.63 \pm 15.72) of (40- \geq 50) age group during Control group . The higher (Mean \pm Std.) of IL-18 and IL-22 were among (\leq 30 -39), (40- \geq 50) age groups [(126.86 \pm 30.93), (141.43 \pm 22.26), (38.36 \pm 7.03) and (35.62 \pm 11.14) respectively]. That comparison between there were no statistically significant difference between the Levels of Interleukins (IL-17, IL-18 and IL-22) in serum between Study groups and age groups. The P- Value of Thyroiditis group were (P=0.645, P=0.155, and P=0.502 respectively), of Polycystic group (P=0.364, P=0.434, and P=0.219 respectively) and of Control group (P=0.411,P=0.347, and P=0.749 respectively).

Table (1): Comparison between Levels of Interleukins (IL-17, IL-18 and IL-22) in Serum between Study groups and age groups

Study Groups	Age Groups (years)	Mean \pm Std.		
		IL-17(pg/ml)	IL-18(pg/ml)	IL-22 (ng/L)
Thyroiditis	(\leq 30 -39)	84.52 \pm 33.92	126.86 \pm 30.93	38.36 \pm 7.03

	(40- ≥50)	88.59 ±14.56	141.43±22.26	35.62±11.14
	P-Value	.645 (NS)	.155 (NS)	.502 (NS)
Polycystic	(≤30 -39)	54.34±11.95	125.73±5.56	31.72±3.06
	(40- ≥50)	60.20±22.74	116.94±35.22	30.42±2.29
	P-Value	.364 (NS)	.434 (NS)	.219 (NS)
Control	(≤30 -39)	101.17±19.80	99.865±32.269	30.570±3.183
	(40- ≥50)	106.63±15.72	111.451±31.783	31.016±3.873
	P-Value	.411 (NS)	.347 (NS)	.749 (NS)

Table (2) show the Comparison between the Levels of Interleukins (IL-17, IL-18 and IL-22) in Serum of Control group with Thyroiditis and Polycystic groups. level of IL-17 was higher in Control group(104.63±17.20). The higher levels of IL-18 (137.06±25.53) and IL-22(36.44±10.05) were among Thyroiditis group. level of IL-17was highly statistically significant (P=0.002) difference between Control and Thyroiditis groups, also was highly significant (P=0.000) difference between Control and Polycystic groups. The IL-18 level was highly significant(P=0.002) difference between Control and Thyroiditis groups, was highly significant (P=0.000), while the difference between Control and Polycystic groups was significant(P=0.050).The difference of IL-22 level was highly significant(P=0.010) between Control and Thyroiditis groups, but the difference between Control and Polycystic groups was no statistically significant(P=0.691).

Table (2): Comparison between between the Levels of Interleukins (IL-17, IL-18 and IL-22) in Serum of Control group with Thyroiditis and Polycystic groups

	Mean ±Std.		
	Thyroiditis	Control	Polycystic
IL-17(pg/ml)	87.37±21.61	104.63±17.20	56.69±16.99
	P=.002 (HS)		P=.000 (HS)
IL-18(pg/ml)	137.06±25.53	107.20±31.91	122.22±29.54
	P=.002 (HS)		P=.050 (S)
IL-22(ng/L)	36.44±10.05	30.85±3.59	31.20±2.81
	P=.010 (HS)		P=.691 (NS)

Table (3) represented the Comparison between Interleukins (L -17, IL -18 and IL -22) of Hypothyroid and Hyperthyroid among Polycystic group and Thyroiditis group. The levels of Interleukins (IL -17, IL -18 and IL -122) were higher among Hypothyroid cases of Thyroiditis group [(99.1±14.22), (149.45±13.31) and (37.80±11.89) respectively]. The Comparison of Interleukins (IL -17, and IL -18) level of Hypothyroid and Hyperthyroid among thyroiditis group were highly statistically significant different (P=0.000) but level of IL -22 was no statistically significant (P=0.338).

The higher levels of Interleukins IL -17 was (56.32±18.62) in Hypothyroid cases of Polycystic, but the levels of IL -18 and IL -122(135.24±22.09 and 31.60±1.87) were higher among Hyperthyroid cases of Polycystic, that comparison of IL -17, IL -18 and IL -122 levels were no statistically significant different between Hypothyroid and Hyperthyroid among Polycystic group(P=0.820, P=0.234 and P=0.701 respectively).

Table (3): Comparison between the Levels of serum Interleukins between Hypothyroid and Hyperthyroid in Polycystic group and Thyroiditis group

	Polycystic			Thyroiditis		
	Means ± Sd.			Means ± Sd.		
	IL -17 (pg/ml)	IL -18 (pg/ml)	IL -22 (ng/L)	IL -17 (pg/ml)	IL -18 (pg/ml)	IL -22 (ng/L)
Hyperthyroid	58.14±8.64	135.24±22.09	31.60±1.87	67.11±16.68	115.65±27.85	34.09±5.33
Hypothyroid	56.32±18.62	118.96±30.65	31.1±3.03	99.1±14.22	149.45±13.31	37.80±11.89
P-value	.820 (NS)	.234 (NS)	.701 (NS)	.000 (HS)	.000 (HS)	.338 (NS)

Table(4) and Fig.(1) represented the receiver operating characteristic (ROC) curve Interleukin (IL-17, IL-18 and IL-22) in Thyroiditis group with Control group to diagnosis Thyroiditis disorder show that the cutoff value of IL-17 was >91.17 with 83.3%sensitivity, Specificity46.7%. Also IL-17 had highly significant (P=0.000) and area under the curve (AUC) =0.807. IL-18with cutoff value>144.216 and 16.7%sensitivity, 50.0%specificity, had highly significant (P=0.000). The cutoff value of IL-22was >33.409 had significant (P=0.026) and 23.3% sensitivity, 50.0%specificity.

Table (4): Receiver Operating Characteristic Curve analysis (ROC) of Thyroiditis group according to Interleukin (IL-17, IL-18 and IL-22)

Variable(s)	Area	Sig.(P-Value)	Cut off	Sensitivity	Specificity
IL-17(pg/ml)	0.807	.000	>91.171	83.3%	46.7%
IL-18(pg/ml)	0.233	.000	>144.216	16.7%	50.0%
IL-22(ng/L)	0.332	.026	>33.409	23.3%	50.0%

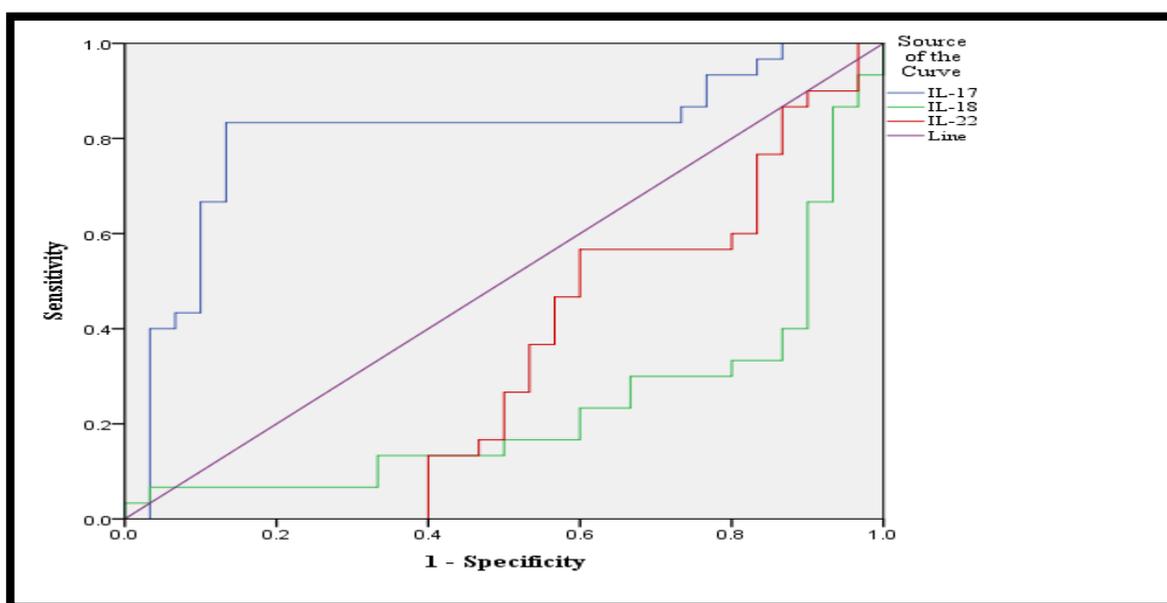


Figure (1): Receiver Operating Characteristic Curve analysis (ROC) of Thyroiditis group according to Interleukin (IL-17, IL-18 and IL-22)

4. Discussion

When the levels of interleukins (IL-17, IL-18, and IL-22) in the serum of the Control group, Thyroiditis, and Polycystic groups were compared. The Control group had a higher level of IL-17 (104.6317.20).

Because T-helper cells that produce interleukin (IL)-17 are involved in this common autoimmune thyroid illness, IL-22 is a pro-inflammatory cytokine that works largely on non-immune epithelial and stromal cells that express receptors for it. IL-22, like IL-17, has the ability to induce pro-inflammatory cytokines and is linked to inflammatory diseases [8]. As a result, it could play a role in the development of thyroid disorders in HT patients. According to [9], increased IL-23 expression was accompanied by a rise IL-17 in HT thyroid tissues.

The levels of Interleukins (IL-17 and IL-18) in Hypothyroid and Hyperthyroid Thyroiditis patients were extremely statistically significant ($P=0.000$), whereas the levels of IL-22 were not statistically significant ($P=0.338$).

The levels of Interleukins IL -17 were higher in Hypothyroid cases of Polycystic (56.3218.62), but the levels of IL -18 and IL -122 were higher in Hyperthyroid cases of Polycystic (135.52422.09 and 31.601.87), indicating that there was no statistically significant difference between Hypothyroid and Hyperthyroid cases of Polycystic ($P=0.820$, $P=0.234$, and $P=0.701$) The role of IL-17 in tissue inflammation. IL-17 stimulates neutrophils by inducing the release of pro-inflammatory cytokines and other cytokines [6].

Th17 cells' main cytokine, IL-17, stimulates T cell activity and induces the endothelium to produce a variety of pro-inflammatory mediators, including tumor necrosis factor (TNF-);IL-1; IL-6; NOS-2; metalloproteinase;and chemokines increasing endothelial inflammation [7].

Clinical studies looking into the relationship between PCOS and IL-18 have shown mixed results. Some of these research found that PCOS is connected to higher levels of IL-18 in the absence of obesity [4].

The levels of IL-18 in PCOS patients and healthy controls were found to be different in our study.

To diagnose Thyroiditis disorder, the receiver operating characteristic (ROC) curve Interleukin (IL-17, IL-18, and IL-22) in Thyroiditis group against Control group showed that the threshold value of IL-17 was >91.17 with 83.3 percent sensitivity and 46.7 percent specificity. IL-17 was also very significant ($P=0.000$) with an area under the curve (AUC) of 0.807. IL-18 had a highly significant ($P=0.000$) cutoff value of >144.216 , with 16.7% sensitivity and 50.0 percent specificity. The cutoff value for IL-22 was >33.409 , which demonstrated a significant ($P=0.026$) sensitivity of 23.3 percent and a specificity of 50.0 percent. Interleukin-18 (IL-18) is a member of the IL-1 cytokine family. IL-18 is made up of inactive precursors that must be digested by the Caspase-1 enzyme to become an active interleukin.

Autoimmunity; intestinal inflammation;myocardial function; metabolic syndromes; emphysema; sepsis; psoriasis and acute kidney injury, among other things, have all been associated to IL-18. Pro-inflammatory properties of IL-18 include enhanced cell adhesion molecules, nitric oxide creation, T-cell and natural killer cell maturation, and chemokine production [2].

Given the numerous biological activities of this cytokine in disease progression, IL-22 appears to be a promising treatment target. SO, [11] findings imply that IL-22 may play a role in the progression of HT. Serum IL-22 levels are higher in newly diagnosed, untreated HT patients than in thyroid autoimmune disease-free individuals [11].

5. Conclusion

Highest levels of IL-17; IL-18 and IL-22 among Thyroiditis group. as well as the levels of Interleukins(IL -

17, IL -18 and IL -122) were higher among Hypothyroid cases of Thyroiditis groups, so IL-17 had highly significant ($P=0.000$) and area under the curve (AUC) =0.807. IL-18with cutoff value>144.216 and 16.7%sensitivity, 50.0%specificity,had highly significant ($P=0.000$). The cutoff value of IL-22was >33.409 had significant ($P=0.026$) and 23.3% sensitivity,. 500%specificity.

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