

## Serum and synovial Interleukin-17A level in Rheumatoid arthritis patients and its relation to disease activity

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### ABSTRACT

#### Objective:

The aim of this study was to measure the level of IL-17A in the serum and synovial fluid of patients with rheumatoid arthritis and correlated its level with disease activity.

#### Patients and methods:

One hundred patients suffering from rheumatoid arthritis, their ages ranged between 20 to 69 years ( $42.7 \pm SD11.3$ ). Their disease duration ranged from 2 to 23 years ( $6.8 \pm SD4.1$ ) and fifty age and sex matched control. All patients and control were subjected to clinical, laboratory investigation and measurement of serum IL-17A. And the patients group only were subjected to synovial fluid IL17A by ELISA technique.

#### Results:

There were statistical significant increase in the serum IL17A level ( $p$  value  $< 0.05$ ) in the RA patients than control and in the patients with high disease activity than those with low disease activity. There were statistical significant increases in the synovial IL17A level in the patients with high disease activity than those with low disease activity.

#### Conclusion:

In our study; the mean serum IL-17A level was found with high titre in patients than control and higher in patients with high disease activity than in those with low disease activity. The mean synovial IL-17A level was found with high titre in patients with high disease activity than in those with low disease activity. The positive correlation between the serum and synovial IL17A in the patients groups.

## INTRODUCTION

Rheumatoid arthritis (RA) is a complex, chronic autoimmune disease characterized by an inflammatory infiltrate of immune cells, in particular T-cells, which represent approximately 40% of the synovial cellular infiltration and participate in a number of inflammatory and destructive events, such as synovial hyperplasia, pannus setting, cartilage and bone erosion, and joint destruction<sup>1,2</sup>.

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Various cells from immune system and from synovium are involved and a panel of cytokines are produced, expressed and become functionally active even in early stages of the disease<sup>2</sup>. Among the cytokines produced by T cells, interleukin (IL)-17A (previously known as IL-17) and IL-17F constitute the signature cytokines of the newly described T helper cell subset (Th17)<sup>3</sup>.

IL-17A enhance their response by stabilizing mRNA of cytokines and enhancing receptor expression, increase the migration, chemokine gene expression and invasiveness of synoviocytes and contribute to disease chronicity by inhibiting synoviocytes apoptosis<sup>3</sup>.

Finally, they enhance metalloproteases secretion leading to cartilage damage. These properties support the combined inhibition of IL-17A and -F to control RA inflammation and joint destruction<sup>3</sup>.

## PATIENTS AND METHODS:

This study was performed at the Rheumatology and Rehabilitation Department, faculty of medicine Menoufiya University Hospital and was approved by its ethical committee.

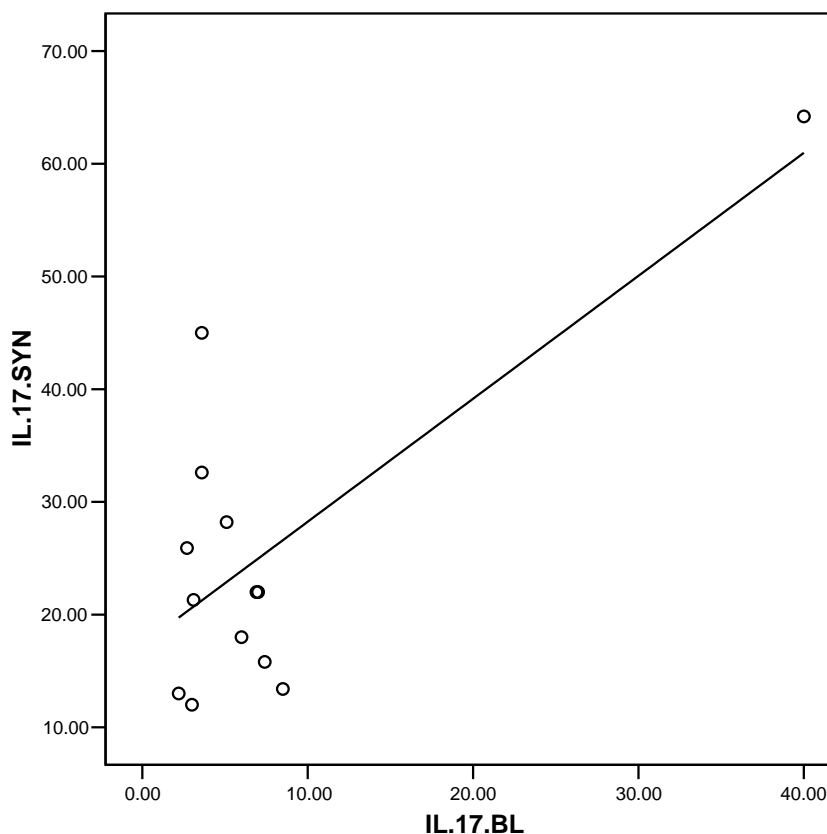
After giving their informed consent, one hundred patients suffering from RA were enrolled in the study

and fifty age and sex matched control. The study included both sex. Seventy eight of the study groups were females (78%) and twenty two were males (22%). The patients group is divided into 3 groups' mild, moderate & severe according to disease activity score DAS28. Their ages ranged between 20 to 69 years (mean age  $42.7 \pm 11.3$ ) of mild group, (mean age  $42.8 \pm 11.6$ ) of moderate group, (mean age  $46.5 \pm 12.2$ ) of severe group. Their disease duration ranged from 2 to 23 years (mean disease duration  $6.8 \pm 4.1$ ) for mild group, (mean disease duration  $6.82 \pm 4.9$ ) of moderate group, (mean disease duration  $9.1 \pm 6.4$ ) of severe group. All patients were subjected to clinical examination in the form of number of tender joints (NTJ), number of swollen joints (NSJ) and visual analogue scale (VAS). Laboratory measures in the form of ESR, CBC, C-RP, RF, AntiCCP, and measurement of IL-17A in the serum of all patients and control and synovial fluid IL17A in the patients group only by ELISA technique.

## RESULTS

The table-1 shows statistically significant increase in the level of serum IL17A with increased disease activity in the patients groups and statistically significant increase in the level of serum IL17A in the patients groups by comparing with the control group.

**Figure-1 Correlation between serum & synovial IL17A (pg/ml) level in the patients groups.**



**Table-1. Comparison between serum IL-17A in the studied groups in relation to disease activity score (DAS28).**

	Patients Groups			Control group	Post hoc test	
	G1 (n=32) X ± SD	G2 (n=34) X ± SD	G3 (n=34) X ± SD		Kruskal-Walis Test	p.value
Serum IL17A	6.15±7.5	6.7±6.06	10.77±10.6	4.7±0.2	7.07 <0.05	P1=0.74 (>0.05) P2=0.006 (<0.01) P3=0.38 (>0.05) P4=0.014 (<0.05) P5=0.2 (>0.05) P6=0.00 (<0.01)

**Table-2. Comparison between synovial IL17A level in the patients groups in relation to disease activity score (DAS28).**

	Patients Groups			Statistical analysis	
	G1 (n=5) X ± SD	G2 (n=5) X ± SD	G3 (n=5) X ± SD	Kruskal-Walis Test	Post hoc test
synovial IL17A	16.5±6.7	26.4±10.2	50.8±27.6	7.6	P1 >0.05 P2 <0.01 P3 <0.05

**Table-3. Comparison between Lab measures in the patients and the control groups.**

Lab Measures	Patients group		Control group		Mann Whitney test (U)	P.value
	Mean±S.D		Mean±S.D			
ESR	37.56±20.36		17.56±3.5		U 927	<0.01**
RF	51.63±82.4		6.16±5.18		U 427	<0.01**
	No	%	No	%	X² Test	
CRP						
Positive	42	42%	0	0%	29.2	<0.01**
Negative	58	58%	50	100%		

The table-2 shows statistically significant increase in the level of synovial IL17A with increased disease activity in the patients groups.

The table-3 shows significant difference between the patients and the control groups as regard to ESR, CRP and RF.

The table-4 show positive correlation between the level of IL17A in the blood & synovial fluid in the patients groups.

**Table-4. Correlation between serum and synovial IL17A level in the patients groups**

Synovial IL17A	Serum IL17A	
	r	P value
	0.73	<0.001

## DISCUSSION

In this study we found significant increase of IL17A level in the blood with increased disease activity in the patients groups of rheumatoid arthritis, this means that in group 3 with high disease activity IL17A level in the blood were higher than that in the group 2 with moderate activity & group 1 with low activity.

Also, we found high statically significant increase of IL17A level in the blood of the patients groups by comparing them with the control group.

And, we reported higher IL17A level in the synovial fluid of group 3 with high disease activity than that in the group 2 with moderate activity & group 1 with low activity.

This comes in agreement with (Anca Rosu et al., 2012) as they reported high level of serum IL17A of RA patients in comparison to normal populations, and in the patient group as they divided according to disease activity score DAS28 in to 3 groups of mild, moderate and sever disease activity, they also, reported high level of serum and synovial IL17A in the group of highest disease activity than that of mild and low disease activity.

Also Metawi et al., (2011); Jimyung Kim et al., (2012); Ucar et al., (2013) and Pavlovic et al.,(2014) studies found Significant positive correlations between both serum and synovial IL-17A levels and DAS-28 score as RA patients with class III functional status showed significantly higher mean serum IL-17A levels than classes I and II . So, the elevated serum and synovial IL-17A levels in RA patients is parallel to the degree of disease activity. And found high statically significant increase of IL17A level in the blood of the patient group when comparing with control group.

This study reported direct relation between the IL17A level in the blood and IL17A in the synovial fluid in the studied groups; this means that high levels of IL17A in the blood were associated with high levels of IL17A in the synovial fluid in RA patients.

This comes in agreement with (Metawi et al., 2011) and (Anca Rosu et al., 2012) as they reported that the Synovial IL-17A levels showed a significant positive correlation with serum IL-17A levels in RA patients.

The present study show significant difference between the patients groups and the control group as regard to ESR, CRP and RF.

This comes in agreement with (Xin Xu et al., 2013 and Radha Krishnan et al, 2015) as they suggest the higher levels of ESR, CRP and RF in the patient group of RA than the control group.

## CONCLUSION

Patients with RA had a significant increase in the serum and synovial IL-17A with increased disease activity in the three groups of RA patients as regard disease activity score DAS 28. Patients with RA had a significant increase in the serum IL -17A than the control group. Direct correlation between the IL17A level in the blood and IL17A in the synovial fluid in the studied groups.

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## Conflict of Interests:

The authors declare that there is no conflict of interests regarding the publication of this paper.

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