Assessment of Proinflammatory Th1 Cytokines (IL18-IFN γ) and Th2 Cytokine (IL13) Concentrations in patients with Autoimmune Rheumatic Diseases (Systemic Lupus Erythematous, Rheumatoid Arthritis and Systemic Sclerosis)

Maha M. Sultan*, Fatma M. Abd Al Salam* Doaa A Hassan*, Hodaa S. Abdulla** ,Marwa M. Abd El-Rahim** ,Hyam H. Mansour***, Neama R. Hussein****

* Department of Dermatology and Venereology.
** Department of Physical Medicine, Rheumatology and Rehabilitation Medicine.
*** Department of General Medicine.
**** Department of Clinical Pathology.
Faculty of Medicine for Girls – Al-Azhar University

Abstract

Objective: Several cytokines play a role in the production of autoantibodies and the pathogenesis of rheumatic diseases including systemic lupus erythematous (SLE), rheumatoid arthritis (RA) and systemic sclerosis (SS). This study investigated serum concentration of the proinflammatory Th1 cytokine; IL18 and its inducer IFNγ, the study also investigated serum concentration of proinflammatory Th2 cytokine; IL13, to explain the role of Th1 and Th2 in the pathogenesis of autoimmune rheumatic diseases (SLE, RA and SS)

Patients and methods: IL18, IFNγ and IL13 levels were evaluated by enzyme linked immunosorbent assay (ELISA). Four groups were included in this study. Group I: Comprised (15) patients of SLE. Group II: Comprised (15) patients of RA. Group III: Comprised (15) patients with SS. Group IV: Control group consisted of (15) sex and age matched healthy controls.

Results: Serum levels of IL18 was significantly higher in SLE (3138.200± 1413.096 pg/ml)& RA(3336.667± 921.839 pg/ml) than control group(86.647± 35.370 pg/ml ), while IL18 in SS had no statistically significant difference between patients (103.634± 50.593 pg/ml) and control group (86.647± 35.370 pg/ml). The cut off level was 257.75 pg/ml.

IFNγ was significantly higher in SLE patients (5.439±1.430 IU/ml) and RA patients (2.973±0.598 IU/ml) than control group(0.580± 0.234 IU/ml), while IFNγ in SS had no statistically significant difference (0.592± 0.245IU/ml) than control group (0.580 ± 0.234 IU/ml) .The cut off level was1.2 IU/ml.

As regard IL13 it was significantly higher in SLE patients (55.673±6.892 pg/ml) ,RA patients (59.587±12.183 pg/ml) and SS (61.550± 12.047 pg/ml) than control group (21.427± 7.274 pg/ml) .The cut off level was 44.4 pg/ml. There was significant positive correlation of IL18/ IL13 and IFNγ / IL13 ratio in SLE and RA , while significant negative correlation of IL18/ IL13 and IFNγ / IL13 ratio in SS.

Conclusion: There was a significant increase of both Th1 cytokines (IL18 and IFNγ) and Th2 cytokine (IL13) in SLE and RA with Th1 predominance,while predominance of Th2 cytokine (IL13) in SS than Th1 cytokine (IL18 and IFNγ). This result suggests that IL18, IFNγ and IL13 could be involved in the pathogenesis of autoimmune rheumatic diseases.

Key words: SLE, RA, SS, IL18, IFNγ and IL13
Introduction:

Rheumatic diseases are major cause of morbidity and long-term disability. They include systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis (SS) and Sjögren’s syndrome are those that affect connective tissue (Mosaad et al., 2003). The autoimmune phenomenon of these diseases might be caused by imbalance of T-helper cell cytokines (Wong et al., 2000).

The balance of Th1/Th2 is essential for the normal human immunity and so changes in Th1/Th2 cytokines might be involved in the pathogenesis of autoimmune diseases (Horwitz et al., 1998). Th1 cells produce IL-2, IFNγ, IL-12 and IL-18 while Th2 cells produce IL-4, IL-5, IL-10, IL-13 (Jianxin et al., 2009). IL-18 was initially described as IFNγ-inducing factor (Ewa et al., 2002). It is related to IL-1 family and produced by kupffer cells, activated macrophages, keratinocytes, intestinal epithelial cell, osteoblasts and adrenal cortex cells (Wong, 2000).

IL-18 production can be induced by IL-12, both have synergistic effect on the activation of natural killer (NK) cells and cytotoxic T lymphocytes (CTL). The primary function of IL-18 include the induction of IFNγ production in IL-12 activated T cells and NK cells, up-regulation of Th1 cytokines including IL-2, M-CSF and IFNγ (Dinarello, 1999), stimulation of the proliferation of activated T cells and enhancement of fas ligand expression in NK and CTL (Dao et al., 1997).

Moreover, IL-18 can promote collagen induced inflammatory arthritis when produced by tissue macrophages (Yamamura et al., 2001).

IL-13 is protein secreted by activated Th2. It affects B-cell function and has the capability of inhibiting pro-inflammatory Th1 cytokines such as IL-12 and IFNγ, suggests that IL-13 as well as IL-4 and IL-10 could facilitate a Th2 response and therefore modulate the immune response (Spadaro et al., 2002).

The current study aimed to evaluate serum concentration of IL-18, IFNγ and IL-13 levels as markers of Th1 and Th2 cytokines respectively and to detect the predominance of either Th1 and Th2 in the pathogenesis of autoimmune rheumatic diseases (SLE, RA and SS).

Material and Methods:

The study included 45 patients divided into three groups and fifteen sex and age matched healthy controls. They were selected from the inpatient and outpatient clinics of Internal Medicine, Dermatology and Rheumatology departments of Al-Zahraa University Hospital. Group I: consisted of fifteen patients with SLE; 3 males and 12 females with age range from 25 to 47 years, with disease duration 3-10 years. They were classified according to the updated American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus (Hochberg, 1997).

Group II: consisted of fifteen patients with RA; they were 6 males and 9 females with age range from 35 to 52 years, with disease duration 5-11 years. They were classified according to American Rheumatism Association Criteria (Arnett et al., 1988).

Group III: consisted of fifteen patients with SS; all of them were females with age range from 37 to 53 years, with disease duration 2-9 years. They were classified according to American College of Rheumatology (formerly, the American Rheumatism Association) criteria for the classification of systemic sclerosis (Scleroderma) (LeRoy et al 1988). Control group consisted of 15 healthy subjects. They were 9 males and 6 females; their age ranging from 29-48 years. All studied groups were subjected to complete history taking, general examination, evaluation of the main laboratory parameters including renal function tests, liver function tests, complete blood picture (EDTA blood), ESR (citrated blood), CRP, RF (latex test), anti-double stranded DNA (the standard indirect immunofluorescence technique) and anti–Scl 70.
antibodies. 5 ml of venous blood were withdrawn from each subject. For cytokine estimation the sera obtained were divided into aliquots, and stored at −70 until the time of assay. Measurement of serum level of IL-18, IFN-γ and IL-13 were done for all patients and control groups.

Determination of serum IL-18 has been done using an enzyme linked immunosorbent assay (ELISA) kit. (Biosource International, Inc. 542 Flynn Road Camarillo, California 93012, USA). Determination of serum interferon γ has been done using an immunoenzymometric assay kit. (Biosource IFN-γ EASIA kit). Catalogue number: KAC[231], Bio-source – Europe S.A. Nivelles Belgium.

Serum IL-13 concentration were determined by using commercially obtained immunoassay. Quantitative Sandwich ELISA technique Bender Med systems GmbH compus Veinna. Biocenter 2A-1030 Vienna, Australia, Europe.

**Statistical analysis:**

Statistical analysis was done using statistical software package (SPSS) version 17. Quantitive analysis were presented as means and standard division (Mean ± SD). Standard t-test was used for comparison between means linear regration analysis with determination of correlation coefficient (r) was used for correlation between quantitative variable P-value of ≤ 0.05 was statistically significant.

**Results**

This study included 45 patients, 15 patients with SLE (3 males & 12 females) with mean age 36.00 ± 7.39 and mean disease duration 6.367 ± 2.334 years, 15 patients with RA (6 males & 9 females) with mean age 44.73 ± 6.03 and mean disease duration 8.200 ± 2.111 years, and 15 patients with SS (15 females) with mean age 45.06 ± 5.34 and mean disease duration 5.467 ± 2.264 and 15 sex and age matched healthy control group (9 males & 6 females) with mean age 38.40 ± 6.43 (Table 1).

IL-18 was significantly higher in patients with SLE (3138.200 ± 1413.096 pg/ml) than control group (86.647 ± 35.370 pg/ml), the cut off level was 257.75 pg/ml.

IL-18 was significantly higher in patients with RA (3336.667 ± 921.839 pg/ml) than control group (86.647 ± 35.370 pg/ml), while IL-18 in SS has no statistically significant difference between patients (103.634 ± 50.593 pg/ml) and control group (86.647 ± 35.370 pg/ml) (Table 2 & figure 1).

IFN-γ was significantly higher in SLE patients (5.439 ± 1.430 IU/ml) than control group (0.580 ± 0.234 IU/ml), the cut off level was 1.2 IU/ml. Also IFN-γ was significantly higher in RA patients (2.973 ± 0.598 IU/ml) than control group (0.580 ± 0.234 IU/ml), while IFN-γ in SS had no statistically significant difference between patients (0.592 ± 0.245 IU/ml) and control group (0.580 ± 0.234 IU/ml) (Table 3 & figure 2).

As regard IL-13 it was significantly higher in SLE patients (55.673 ± 1413.096 pg/ml) than control group (0.580 ± 12.183 pg/ml), the cut off level was 1.2 IU/ml. Also IFN-γ was significantly higher in RA patients (2.973 ± 0.598 IU/ml) than control group (0.580 ± 0.234 IU/ml), while IFN-γ in SS had no statistically significant difference between patients (0.592 ± 0.245 IU/ml) and control group (0.580 ± 0.234 IU/ml) (Table 4 & figure 3).

There was significant positive correlation of IL-18/IL-13 ratio and significant positive correlation of IFN-γ/IL-13 ratio in SLE and RA (Figures 4 & 6), while there was significant negative correlation of IL-18/IL-13 and IFN-γ/IL-13 ratio in SS (figure 5 & 7).
Table (1): Demographic data of all studied groups:

<table>
<thead>
<tr>
<th></th>
<th>SLE</th>
<th>RA</th>
<th>SS</th>
<th>control</th>
<th>Statistics value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>12 (80 %)</td>
<td>9 (60 %)</td>
<td>15 (100%)</td>
<td>6 (40 %)</td>
<td>X²=14.28</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>3 (20 %)</td>
<td>6 (40 %)</td>
<td>0</td>
<td>9 (60 %)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>Range</td>
<td>47-25</td>
<td>52-35</td>
<td>53-37</td>
<td>48-29</td>
<td>F=7.739</td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>36.00±7.39</td>
<td>44.73±6.03</td>
<td>45.06±5.34</td>
<td>38.40±6.43</td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>Range</td>
<td>3.0-10.0</td>
<td>5.0-12.0</td>
<td>2.0-9.0</td>
<td></td>
<td>F=5.811</td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>6.367±2.33</td>
<td>8.200±2.111</td>
<td>5.467±2.264</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table (2): The level of IL-18 in all studied groups:

<table>
<thead>
<tr>
<th></th>
<th>IL-18</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ± SD pg/ml</td>
</tr>
<tr>
<td>RA</td>
<td>1966.0 - 4782.0</td>
<td>3336.667 ± 921.839</td>
</tr>
<tr>
<td>SS</td>
<td>40.0 - 223.1</td>
<td>103.634 ± 50.593</td>
</tr>
<tr>
<td>SLE</td>
<td>1401.0 - 5463.0</td>
<td>3138.200 ± 1413.096</td>
</tr>
<tr>
<td>Control</td>
<td>40.8 - 175.3</td>
<td>86.647 ± 35.3701</td>
</tr>
</tbody>
</table>

Tukey's test

<table>
<thead>
<tr>
<th></th>
<th>RA &amp; SS</th>
<th>RA &amp; SLE</th>
<th>RA &amp; C</th>
<th>SS &amp; SLE</th>
<th>SS &amp; C</th>
<th>SLE &amp; C</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-value</td>
<td>0.000</td>
<td>0.917</td>
<td>0.000</td>
<td>0.000</td>
<td>1.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Figure (1): comparison of IL-18 level in all studied groups
Table (3): The level of IFNγ in all studied groups:

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean ± SD IU/ml</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>1.3 - 3.8</td>
<td>2.973 ± 0.598</td>
<td>128.201</td>
</tr>
<tr>
<td>SS</td>
<td>0.3 - 1.2</td>
<td>0.592 ± 0.245</td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>3.2 - 7.6</td>
<td>5.439 ± 1.430</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>0.3 - 1.0</td>
<td>0.580 ± 0.234</td>
<td></td>
</tr>
</tbody>
</table>

Tukey's test

<table>
<thead>
<tr>
<th></th>
<th>RA &amp; SS</th>
<th>RA &amp; SLE</th>
<th>RA &amp; C</th>
<th>SS &amp; SLE</th>
<th>SS &amp; C</th>
<th>SLE &amp; C</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-value</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>1.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Figure (2): comparison of IFNγ in all studied groups
Table (4): The level of IL-13 in all studied groups:

<table>
<thead>
<tr>
<th></th>
<th>IL-13</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ± SD pg/ml</td>
</tr>
<tr>
<td>RA</td>
<td>45.4 - 81.2</td>
<td>59.587 ± 12.183</td>
</tr>
<tr>
<td>SLE</td>
<td>44.7 - 65.3</td>
<td>55.673 ± 6.892</td>
</tr>
<tr>
<td>SS</td>
<td>48.3 - 80.4</td>
<td>61.550 ± 12.047</td>
</tr>
<tr>
<td>Control</td>
<td>9.1 - 33.1</td>
<td>21.427 ± 7.274</td>
</tr>
</tbody>
</table>

Tukey's test

<table>
<thead>
<tr>
<th></th>
<th>RA &amp; SS</th>
<th>RA &amp; SLE</th>
<th>RA &amp; C</th>
<th>SS &amp; SLE</th>
<th>SS &amp; C</th>
<th>SLE &amp; C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.703</td>
<td>0.948</td>
<td>0.000</td>
<td>0.375</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Figure (3): comparison of IL-13 level in all studied groups.
Assessment of Proinflammatory….

Figure (4): Significant positive correlation of IL18/IL13 ratio in SLE and RA.

Figure (5): Significant negative correlation of IL18/IL13 ratio in SS.
Figure (6): Significant positive correlation of INFγ/IL13 ratio in SLE and RA.

Figure (7): Significant negative correlation of INFγ/IL13 ratio in SS.
Discussion

The balance between Th1 and Th2 cytokines plays an important role in the control of immune response (Uhm et al. 2003). Ratios of Th1/Th2 cytokines can reflect the cytokine homeostasis and indicate Th1 or Th2 predominance during the development of rheumatic diseases. Several studies have reported different results for the correlation of Th1/Th2 ratio and rheumatic disease activity (El-Sayed et al. 2008 & Wong et al., 2000). The current study aimed to assess the predominance of Th1 or Th2 in the autoimmune rheumatic diseases (SLE, RA and SS) by investigating the serum level of Th1 cytokines IL-18, INF-γ and Th2 cytokine IL-13.

In the current study IL-18 serum level was increased in SLE than control group. This result agreed with Mosaad et al. (2003) who found that increased serum level of IL-18 and IL-12 in immune rheumatic diseases (SLE, RA, SS, Behcet disease, dermatomyositis, mixed connective tissue diseases and Sjogren syndrome). Also this result agreed with Robak et al. (2002) who found that increased serum levels of IL-18 and IL-12 in SLE and also agreed with Wong et al. (2000) who found that increased serum level of IL-18, IL-17, IL-12 in SLE.

As regard the serum level of IL-18 in RA the result of the current study showed significant higher serum IL-18 level than control this result agreed with Mosaad et al. (2003) who found that increased IL-18, IL-12 and ANA in RA patients than the control group. Also agreed with Bresnihan et al. (2002) who found significant higher serum IL-18 level in RA than psoriatic arthritis they suggesting that IL-18 has a role in pathophysiology of RA but it did not significantly correlate with clinical measures of disease activity or the response to treatment. In a study done by Scala et al. (2002) in juvenile RA they reported that increased expression of mRNA of IL-12, P35 and IL-18.

The result of the serum level of IL-18 in SS had no statistically significant difference between patients and control group this was in contrast with Scala et al. (2004) who observed high levels of IL-18 in patients with SS compared to healthy subjects.

Significantly, elevated IL-18 in SLE may be because IL-18 enhance the Fas ligand expression in NK and CTL, causing Fas-mediated apoptosis in epithelial cells and tissue damage in SLE (Dinarello, 1997). IL-18 in combination with other proinflammatory cytokines, including IL-1 and TNF-α must be an important cytokine for initiating and progressing the catabolic and inflammatory responses in SLE. Also, IL-18 induce production of nitric oxide from macrophages that involved in tissue damage in SLE (Wong et al., 2000). In a study done by Falvia et al. (2009) they found that increased level of IL-18 in both serum and plasma of SLE patients and correlate it with disease severity, they suggesting that the circulating IL-18 levels are predictive for renal damage and could be used as a prognostic marker of renal involvement and useful to identify patients at risk of renal failure. Increased IL-18 in RA may be explained by Gracie et al. (1999) study who found that increased IL-18 in RA induced Th1 response and TNF-α production in short-term cultured cells from RA tissues and synovial fluid mono-nuclear cells. Furthermore, IL-18 facilitated the erosive course in RA animal model of collagen induced arthritis. Moreover, Olee et al. (1999) reported that IL-18 is involved in joint disease by its effect on cartilage destruction.

As regard IFN-γ, the current study showed significant increase of IFN-γ in SLE than control group. This result agreed with EL- Sayed et al., (2008) who found significant increase of IFN-γ levels in SLE patients than controls. The main function of IFN-γ in SLE is the activation of macrophages which stimulate proinflammatory cytokines production (Uhm et al., 2003).

The current study showed significant increase of IFN-γ in RA than
control group this agreed with Canete et al. 1999 who found that significant higher level of IFN γ in RA than psoriatic arthritis. In study done by Bucht et al., (2007) they found that higher expression of IFN γ, IL18 and IL12 mRNA in RA synovial fluid mononuclear cells (SFMC) than peripheral blood mononuclear cells compared to healthy control group using a quantitative reverse transcriptase polymerase chain reaction (RT- PCR) assay.

In the current study IFN γ was decreased in SS patients with no statistically significant difference with healthy control group. This result agreed with Scala et al study (2004) who found reduced amounts of γ- IFN and macrophage derived chemokine (MDC) in SS patients. SS pathogenesis characterized by increase collagen production which may be due to decreased IFN γ level as IFN γ inhibit collagen synthesis by fibroblast (Serpier, 1997).

In the current study IL13 serum level was increased in SLE, RA and SS this result agreed with Spadaro et al. (2002) study who found increased IL13 levels in SLE, RA and SS. Increased IL13 serum level could be explained by predominance of Th2 response that stimulate B-cell and antibody production. IL13 affect B-cell through surface molecule modulation, the enhancement of proliferation, immunoglobulin production and isotopic switching (IgG and IgE) (Spadaro et al. 2002).

The result of current study showed higher levels of both the Th1 cytokines (IL18 and IFN γ) and Th2 cytokine (IL13) in both SLE and RA. This result agreed with El-Sayed et al study (2008) who found that significant increase of both Th1 cytokines (IFN γ and TNFα) and Th2 cytokines (IL4 and IL10) in SLE and Wong et al (2000) who also found an elevation of both Th1 cytokines (IL18 , IL47 , IL12) and Th2 cytokine (IL4) in patients with SLE. Elevation of both Th1 and Th2 cytokines in SLE and RA suggests an imbalance of cytokine profile supported by different cytokine patterns in different time-points to mediate the inflammatory response (Wong et al 2000).

The current study showed significant elevation of Th1/Th2 ratio (IL18/ IL13 and IFN γ/IL13) in both SLE and RA suggesting Th1 predominance . This result agreed with wong et al (2000), who found an elevation of IL18 / IL4 ratio in patients with SLE, and El-Sayed et al study (2008) who found that significant elevation of IFN/IL10 ,IFN/IL4, TNF/IL10 and TNF/IL4 ratios in patients with SLE. Clear -cut distinction between Th1 and Th2 patterns is not without complexity (El-Sayed et al., 2008), this complexity may be due to many factors such as disease activity, treatment and organ involvement (Nagy et al., 2000). So to determine the predominance of Th1 or Th2 in autoimmune rheumatic diseases , it must not only dependant on evaluation of their serum levels but also supported by other sutdies such as gene polymorphism.

Conclusion: There was a significant increase of both Th1 cytokines (IL18 and IFNγ) and Th2 cytokine (IL13) in SLE and RA with Th1 predominance, while predominance of Th2 cytokine (IL13) in SS than Th1 cytokine (IL18 and IFNγ). This result suggests that IL18, IFNγ and IL13 could be involved in the pathogenesis of autoimmune rheumatic diseases.

References:

Assessment of Proinflammatory…. 


تقييم تركيز مفرزات الخلايا الناتج من الخلايا الليمفاوية المساعدة (Th1) (انترلوكين–18، انترفيرون جاما) و مفرزات الخلايا الناتج من الخلايا الليمفاوية المساعدة (Th2) (انترلوكين–13) في الامراض الروماتيزمية (الذئبة الحمراء-الروماتويد، التصلب الجلدي).

مها مكرم سلطان*، فاطمة محمد عبد السلام*، دعاء عبد المليك حسن*، هدى سعد عبد الله**، هيام حمزة منصور***، نعمة رمضان حسين****، مروة محمد*****، هدي سعد عبد الله****.

*قسم الامراض الجلدية والتناسلية، **قسم الطب الطبيعي، ***قسم الباطنة العامة، ****قسم الباثولوجيا العامة، كلية طب بنات جامعة الازهر.

يلعب العديد من مفرزات الخلايا (السيتوكينز) دوراً هاماً في إنتاج الأجسام المضادة كذلك كمسببات للمرض في الامراض الروماتيزمية مثل مرض الروماتويد ومرض الذئبة الحمراء ومرض التصلب الالكلي. تقوم هذه الدراسة برئاسة نسب تركيز مفرزات الخلايا الليمفاوية المساعدة (Th1) (انترلوكين–18، انترفيرون جاما) وكذلك نسبة مفرزات الخلايا الليمفاوية المساعدة (Th2) (انترلوكين–13) وتوضح دور كل من الخلايا الليمفاوية المساعدة 1 والخلايا الليمفاوية المساعدة 2 كسبب لحدوث الامراض الروماتيزمية (الذئبة الحمراء، التصلب الالكلي، انترفيرون جاما، انترلوكين–18).

المريض والطريقة:

تشتمل هذه الدراسة على أربع مجموعات:

المجموعة الأولى: 15 مريضاً بالذئبة الحمراء.
المجموعة الثانية: 15 مريضاً بالروماتويد.
المجموعة الثالثة: 15 مريضاً بالتصلب الالكلي.
المجموعة الرابعة: 15 من الاصحاء كمجموعة ضابطة.

وقد تم قياس نسبة انترلوكين–18، انترفيرون جاما، انترلوكين–13 بواسطة جهاز انزيم ليكُنُدين امبونوسور باستاء.

وتثبت النتائج كالتالي:

كانت هناك زيادة ملحوظة في كل من مفرزات الخلية الليمفاوية-Th1 (انترلوكين–18، انترفيرون جاما) عن مفرزات الخلية الليمفاوية-Th2 (انترلوكين–13) في مرضى الذئبة الحمراء (3138.20 ± 1413.596 ppm عن المجموعة الضابطة 86.647 ppm) والروماتويدي (3336.667 ± 921.839 ppm عن المجموعة الضابطة 35.370 ppm) بينما لم يكن هناك فرق إحصائي في مرضى التصلب الالكلي (50.593 ± 103.634 ppm عن المجموعة الضابطة 35.370 ppm).


وتبين من النسبة بين مفرزات الخلايا الليمفاوية-Th1 ومفرزات الخلايا الليمفاوية-Th2 أن النسبة مرتفعة مما يدل على سيطرة الخلايا الليمفاوية-Th1 في حدوث الامراض الروماتيزمية.

الخلاصة:

هناك زيادة ملحوظة في الدور الذي تلعبه مفرزات الخلايا الليمفاوية-Th1 (انترلوكين–18، انترفيرون جاما) عن مفرزات الخلايا الليمفاوية-Th2 (انترلوكين–13) بالمرضى. حيث في مرضى الذئبة الحمراء ومرض الروماتويد، تلعب مفرزات الخلايا الليمفاوية-Th1 دوراً هاماً عن مفرزات الخلايا الليمفاوية-Th2، مما يرجح أن مفرزات الخلايا الليمفاوية-Th1 مؤثرة كسبب في حدوث الامراض الروماتيزمية.