Evaluation of serum IL-23 in multiple sclerosis in Iraqi patients

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Abstract

Background/aim: A chronic neuroinflammation of disease with unknown cause and variable clinical development is multiple sclerosis (MS). Interleukin-23 (IL-23) is a constituent of the IL-12 cytokine family that has shown through development of T helper type 17 (Th17) cells development could play a chief role in the inflammatory autoimmune responses in multiple sclerosis (MS). Objective: A goal of study is to assess IL-23 level in serum in Iraqi patients with multiple sclerosis (MS) in comparison with healthy control group. Methods: Blood samples were taken from 45 patients with multiple sclerosis and 30 healthy controls. IL-23 level in the serum was assessed by Enzyme-Linked immunosorbent assay (ELISA). Results: IL-23 level in the serum taken from affected persons was found to be significantly higher than its level in the serum of control group (P<0.05). We also observed significantly higher IL-23 serum levels in females than males within patients group (P. Value=0.0349). Conclusions: The results show the increasing level of IL-23 in patients with multiple sclerosis which confirms a role for IL-23 in MS suggested could be a particular biomarker and therapeutic goal in MS therapy through inhibiting.

Keywords: Multiple sclerosis, Interleukin-23, Cytokines


Introduction:

In the industrial world, autoimmune diseases are a major cause of morbidity and death, affect on 3-8% of the people. When breaking the immune system's tolerance against auto-antigens, autoimmunity raises, a process involving numerous distinct molecules yet unwell explained (Kunzl et al., 2009). One of the autoimmune diseases is multiple sclerosis (MS) affecting the central nervous system (CNS) with more than one million patients globally (Sluder et al., 2002). It has been reported that the age of the beginning of MS varies from 20 to 40 years (Kurtzke et al., 1992). Number of studies reported that MS may progress slightly in either offspring or old age (Frohman et al., 2006; Elemadifaret al., 2012)

Multiple sclerosis (MS) is a central nervous system (CNS) chronic neuroinflammatory immune disease with unknown etiology and clinical variable profile (Compston et al., 2006). It has shown that cytokines production through infiltration inflammatory cell and resident cells in the brain is involved in directing and regulating the immune response and also mediating tissue (Brosnan et al., 1996). The most prevalent type is relapsing-remitting MS (PR-MS), which consists of 80% of patients where myelin is destroyed by inflammatory cells result in distortion of transporting of electrical signal (El-behi et al., 2009). The damaged axon is the vital reason of clinical debility and...
development of the disease in spite of the accurate pathogenicity of MS is poorly understood (Bitsch et al., 2000; Zhang et al., 2005). Cytokines play a central role in the immune system disorders pathogenesis (Moudgil et al., 2011).

One of proinflammatory cytokines secreted by stimulated macrophage and dendritic cells is an IL-23 which is considered an element for T-cell dependent inflammatory response growth. In addition, the IL-23 prevents imbalance between regulatory and effectors T-cell response (Brombacher et al., 2003). IL-23 plays an important role in chronic and autoimmune diseases development. Th17 cells initiate IL-23 secretion and stimulate IL-17 production with non T-cells contribution (Izcue et al., 2008). IL-23 promotes production of IL-6, IL-17, IL-2, tumor necrosis factor-α (TNF-α) and granulocyte-monocyte colony stimulating factor (GM-CSF) by TH17 cells (Brennan et al., 2008).

**Materials and Methods**

Our work was achieved on 45 MS patients together with control group that was composed of 30 unaffected persons. The participants’ age was ranging between 19 and 55 years. Patients' samples collected in the multiple sclerosis clinics at Baghdad teaching medical city during the period from December 2014 to February 2015. MS patients were diagnosed according to MC Donald criteria done by a neurologist and confirmed by MRI. All patients were newly diagnosed and these cases had received no treatment with no chronic or systemic diseases. Five ml of blood samples had been derived for each patient in sterile plain tube and left (15-30) minutes to clot at room temperature, then centrifuged for 5 minutes at 3000 rpm. separated Sera were stored in deep-freeze at -20 °C till examination. The level of IL-23 was indicated by employing an available sandwich enzyme-linked immunosorbent assay (ELISA) kit and performed as recommended in leaflet with the kit IL-23 (Biosourse; USA).

**Statistical analyses:** Analysis was done using SPSSv19. The serum IL-23 was expressed as mean ± standard error, the significance of differences in mean was assessed using the t test and fisherman test. Analyses where the P-value was <0.05 were considered to be statistically noticeable.

**RESULTS**

The present study, as demonstrated in (figure-1), IL-23 serum levels in patients were significantly higher than healthy control (105.6±15.5) pg/ml versus (43.7±11.2) pg/ml, (p value<0.05). The measurable t test demonstrated that IL-23 serum level did not pursue an ordinary distribution, so the non-parametric test was utilized for the present examination.
Regarding figure 2 the comparative mean of IL-23 serum level according to gender between affected and unaffected groups, serum level of IL-23 was observed noticeably larger in male, female MS patients than healthy control. Whereas in figure 3 there was significant difference between females and males within patients group (P= 0.0349) higher in females than males.
The results demonstrated in (Table 1) showinga significant difference among IL-23 level in all groups classified according to age of patients and control group (p.0.028, 0.044, 0.049). While, no significant difference was observed within the same group (patients /control).

**Table-1: IL-23 in age subgroups of patient and control**

<table>
<thead>
<tr>
<th>Groups</th>
<th>&lt; 25 years</th>
<th>25-40 years</th>
<th>&gt; 40 years</th>
<th>P. Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>121.3±34.9</td>
<td>82.1±20.4</td>
<td>122.1±28.4</td>
<td>N.S</td>
</tr>
<tr>
<td>Control</td>
<td>18.1±3.6</td>
<td>26±4.8</td>
<td>42.9±10.5</td>
<td>N.S</td>
</tr>
<tr>
<td>P. Value</td>
<td>0.028</td>
<td>0.044</td>
<td>0.049</td>
<td></td>
</tr>
</tbody>
</table>

There was significantly positive correlation between IL-23 and age in both patients and control group (R= 0.333, P.value= 0.0330) and control groups (R= 0.377, P.value= 0.0402) (figure-4).
Discussion:

Interleukin-23 is a significant cytokine in the association of both innate and adaptive immune response (Langrish et al., 2005). This study was directed to investigate the IL-23 in MS as a biomarker in patients with MS. In this research, the results show that circulating higher IL-23 level were the significant elevation in MS patients in comparison with healthy controls (P=0.045). Our study confirmed with Chen et al. (Chen et al., 2012) in Chinese patients who found that IL-23 serum level was significantly larger in subjects with MS than healthy control (P=0.002). In another study by Shajarian et al. (Shajarian et al., 2015) in Iranian patients reports that IL-23 serum levels between affected and unaffected female entities difference significantly (P=0.003) but not about male groups. In addition level of IL-23 does not point any important link within patients and control groups basing on diverse age classification. These results came in agreement with our results. The data revealed that increasing in IL-23 was significant in females than males within patients group. As in other autoimmune disease MS occurs with greater percent in females than males. However, the process of gender disparity is poorly defined (Pelfrey et al., 2000). INF-γ prejudice of gender in MS to T-helper is supposed because of the responding of INF-γ secretion to proteolipid protein peptide. On the other hand, contrastive findings were stated by Nguyen et al (Nguyen et al., 2003). Their work which displayed those male subjects possess larger levels of proinflammatory cytokines than female patients with MS, whereas in other study by Chen et al. (Chen et al., 2012) IL-23 level has no difference between male and female MS patients significantly. Moreover the findings of the current study confirm those of (Li Yet al., 2006; Vaknin-Dembinsky et al., 2006; Krakauer et al., 2008; Mehdizadeh et al., 2018) that that indicating increased plasma and mRNA expression levels of IL-23 in MS patients. It has found that MS patients show increased secreted levels of IL-23 from monocyte-derived Dendritic Cells (DCs) and additionally mRNA overexpression of both IL-23p19 and IL-12/23p40 (21). It was hypothesized that an IL-23 plays an imperative part in the pathogenicity of multiple sclerosis as a Th1 type T-cellmediated inflammatory autoimmune and demyelinating disease of CNS by affecting the
immune system through polarization of the innate immune response toward a Th1 bias might play important role in the pathogenesis of multiple sclerosis as a Th1 type T-cell mediate inflammatory autoimmune and demyelinating disorder of the CNS (Martin et al. 1992; Weiner et al., 2004; Krakauer et al., 2008). Proinflammatory cytokine IL-23 plays a key role in chronic inflammatory autoimmune responses and IL-23 deficient mice have shown a resistance to induction of experimental autoimmune encephalomyelitis (EAE) (Cua et al., 2003). In addition, it has found that MS patients have significantly higher serum level of IL-23 in comparison to healthy subjects (Shajarian et al., 2015). A significant serum and CSF levels of IL-23 and positive correlation of IL-23 with IL-17 and with the reduced effect of MS have been reported in MS subjectsthatrecommend IL-23 as a probably paticular and constant biomarker for development of MS and curing aims for MS (Wen et al., 2012). The ability of IL-23 in enlargement of T helper type 17 (Th17) cells plays a vital role in the advance and the maintenance of autoimmune inflammation (Tang et al., 2012). Stopping of organ-specific autoimmune inflammation by acertainsuppression of the IL-23/IL-17 axis of immune within the mouse recommendsthat an exact obstruction of the IL23 immunological mechanism in humans could also be an efficient and undamaged treatment for inflammatory diseases mediated by immune system dysfunction (Chen et al., 2006).

**Conclusion**

Our results suggest that IL-23 has the role in MS pathogenicity which gives therapeutic guidelines for MS effectively. Additionally the sophisticated process and the connection between cytokines and clinical characteristics of MS are required more explanation.

**References:**


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