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The association of Toll-like receptor -7 and rheumatoid arthritis in a sample of Iraqi patients

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ABSTRACT

Rheumatoid arthritis (RA) is considered as one of chronic inflammatory autoimmune diseases, which included articular and joints infections. The innate immunity plays a role in the pathogenesis of autoimmune diseases; therefore, the present study attempted to assess the toll-like receptor7 (TLR7) serum level in 47 rheumatoid arthritis patients and 28 individuals as healthy control. The findings revealed a significant difference ($p \leq 0.05$) in the serum level of TLR7 between the studied groups. Therefore, this finding suggested that toll like receptor7 might have a role in pathogenesis of RA.

Keywords: Autoimmune disease, rheumatoid arthritis, toll-like receptor7.

1. INTRODUCTION

When the human body exposed to an immunogenic inducer such as microorganisms, the innate immune and inflammatory response are mediated by Toll-like receptors (TLRs), which result in activating the immune cells such as dendritic cells, macrophages, T and B lymphocytes; this activation produces pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukins (ILs) such as IL-8. These mediators participate in the immune response that enroll the dendritic cells, macrophages, and lymphocytes to engulf and kill the pathogen, then migrate to peripheral lymphoid tissues, where the antigen presenting cells initiate the adaptive immunity response that results in generation of cellular immunity and antibodies [1, 2].

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease with articular, extra-articular and systemic effects, which are influenced by environmental and genetic factors. The combination of genetic factors and environmental exposures result in a cascade of events that involved synovitis with consequent destructive arthritis. Also, it affects a variety of extra-articular organs [3, 4]. Some cases had mild self-limited disease, while other cases suffering from joint destruction and severe physical disability [5]. B and T lymphocytes with the pro-inflammatory cytokines play a pivotal role in the pathogenesis of the disease [6]. Also, interferon-α (INF-α), interleukin-1 (IL-1) and IL-6 considered as mediators in cell migration and inflammation of RA [7]. The molecular mimicry is one of many suggested hypotheses that explain the incidence mechanism of RA [8]. Toll like receptors (TLRs) are family of highly conserved pattern recognition receptors (PRR) that recognize pathogens such as bacteria and viruses [9]. TLR7 is one of the mammalian TLRs that currently known [10], it considered as an endogenous TLR ligands [11], which expressed and released as a result of inflammation in early RA contributing to persistent destruction disease [1]. The initial insult may be the result of immunocomplex containing anti-CCP, this immunocomplex provided danger signal and release endogenous TLRs ligand resulting in self-perpetuating inflammatory process. Releasing a low level of interferon-gama (INF-γ) may sensitize the synovial macrophage to activate endogenous TLR ligand [12]. The present study aimed to evaluate the serum level of TLR7 in clinically diagnosed RA patients.

2. MATERIALS AND METHODS

Forty-Seven Iraqi RA patients (35 females and 12 males) were enrolled in this study with age mean ± standard deviation (SD) (49.9 ± 13.3 years). They referred to the Consultant Clinic at the Department of Rheumatology, Baghdad Teaching Hospital during the period October 2016 – June 2017 for diagnosis and treatment. The diagnosis depended on the clinical symptoms and the clinical laboratory examinations. In addition to patients, 28 apparently healthy individuals (20 females and 8 males) were enrolled in the study as control group, which they matched patients with the age mean ± SD (44.7 ± 11.6 years). The sera of patients were tested to assess the level of TLR7 in the studied groups by using the commercial available kit (SHANGHAI YEHUA Biological Technology Company, China). This test based on biotin double antibody sandwich technology to assay TLR-7 level.

The data of age and TLR7 serum level were expressed as mean ± SD by using the IBM SPSS statistical analysis program version 24

3. RESULTS AND DISCUSSION

The result of present study showed a significant increased level of TLR7 (103.0 ± 73.8 pg/ml) in patients group compared to controls (72.9 ±36.8 pg/m). This finding indicated that the level of TLR 7 was significantly higher in RA group than in the control group, which might be due to the activation of the TLR7 by a specific ligand such as single strand ribonucleic acid (ssRNA), which leads to this increased expression in concurrence with the production of the pro-inflammatory cytokines that causes joint destruction [3, 4]. TLR7 use adaptor protein MyD88, which have a role in the spontaneous release of cytokines and MMPs from human RA synovial tissue [13]. The subsequent chronic production of pro-inflammatory cytokines and matrix metalloproteases (MMPs) leads to destruction the joint architecture, severe disability and a reduced life expectancy due to co-morbid complications such as cardiovascular disease [14].

The finding is in agreement with other results which demonstrated that TLR7 was highly expressed in patients with RA. Elevated levels of TLRs and their associated endogenous ligands have been shown to contribute with the pathogenesis of RA [12, 15]. Roelofs *et al*. (2005) showed that the elevated levels of TLR7 have also been detected in synovium from RA patients compared to healthy controls and patients with osteoarthritis (OA) [16, 17, 18]

4. CONCLUSION

Accordingly, the present finding suggested that TLR7 might has a role in the etiopathogenesis of RA.

Conflict of interest

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

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