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Association of Interleukin-10 with Severity of Axial Spondyloarthritis in Patients Attending in A Tertiary Care Hospital in Dhaka City

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Abstract

Objective: The aim of the study was to determine the association of interleukin-10 (IL-10) level with severity of axial spondyloarthritis (axSpA).

Materials and methods: According to Assessment of Spondyloarthritis International Society (ASAS) criteria, 38 patients with axSpA (clinically diagnosed by Rheumatologist, attending outpatient department of Rheumatology, Bangabandhu Sheikh Mujib Medical University, BSMMU) and 38 healthy controls (resident doctors, laboratory staffs of BSMMU and general people) were enrolled. Blood samples were collected after taking informed written consent and data in a predesigned data collection sheet. Serum IL-10 levels were measured by Enzyme Linked Immunosorbent Assay (ELISA) at Microbiology and Immunology Department, BSMMU.

Results: Among 38 patients, 63.2% were male. According to Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), 14 patients were in mild to moderate group and 24 in severe group. Serum level of IL-10 were significantly higher in patients compared to controls (3.69 pg/ml vs 0.88 pg/ml, P<0.001). Mean IL-10 levels in inactive disease group were comparatively higher than active disease group (P<0.001).

Conclusion: Serum level of IL-10 is significantly elevated in axSpA patients and is negatively correlated with disease activity.

Keywords: IL-10, ELISA, BASDAI.

Introduction

Spondyloarthritis (SpA) can be divided into peripheral and axial forms. The latter is distinguished by a predominance of spine or sacroiliac joint involvement. The radiographic form of axial SpA, ankylosing spondylitis (AS), and nonradiographic axial SpA (nr-axSpA) are both referred to as axial SpA (axSpA). Both are two distinct stages of the same illness [1]. Adults between 20 to 60 years of age mostly affected, which places a significant socioeconomic burden on their families [2]. In the world's population, AS is thought to affect 0.7% to 3.2% of people [3]. Prevalence is 1.2% (0.7-1.8) in Bangladesh [4]. Only 1%-5% HLAB27 positive people develop AS, despite the fact that HLA-B27 is the dominant gene linked [5]. In addition, there are notable variations in the distribution of HLA-B27 and its subtypes throughout the world [6]. Research has looked into how genetic factors including non-MHC genes are linked. AS has been linked to at least 36 genetic variations in non- major histocompatibility complex (non- MHC) areas [7]. It has Th2 type cytokine secretion pattern [8]. Proinflammatory cytokines are inhibited by IL-10, and Th1 cytokines are typically decreased as a result [9]. Interleukin-10

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production may be noticeably higher in AS patients than in healthy controls, according to earlier investigations. Numerous cytokines and immune regulators' expression levels are also genetically influenced. Therefore, it is quite plausible that genetic variations would affect the pattern of cytokine release in AS5. Monocytes and lymphocytes are the main producers of IL-10, which has been demonstrated to have anti-inflammatory effects and to play a role in inhibiting autoimmune and inflammatory issues. It controls the balance of T helper1 (Th1) vs. T helper2 (Th2) cytokines, which is a key factor in controlling the balance between immunity and autoimmune disease, by down-regulating the expression of Th1 cytokines [10]. The BASDAI score, which incorporates patient self-reported sensations assessed from questionnaire, is frequently used to assess disease activity in AS patients. Joint pain, localized soreness, fatigue, and morning stiffness are included in BASDAI, which measures disease activity. The range of possible BASDAI scores is 0 to 10. Score less than 4 denotes inactive disease, score 4 to 6 denotes the need for a combination of test indicators to identify the disease status. Scores 6 to 10 are indicative of an active illness [11]. According to a Taiwanese study, IL-10 levels were higher in mild to moderate illness and lower in severe. Thus, they demonstrated a link between IL-10 levels and the severity of the axSpA condition [12]. M2 macrophages can help us better understand the role of IL-10 in the etiology, these findings are contentious because IL-10 is an anti-inflammatory cytokine. As the innate immune system's effector cells, macrophages play a crucial role in initiation and resolution of inflammation. Macrophages are divided into two groups: M1 (classically activated) and M2 (alternatively activated), which are primarily involved in tissue remodeling and the production of inflammatory cytokines. The phenotype of macrophages can change with IL-10, going from M1 to M2 [13]. Many studies regarding pro inflammatory cytokines are conducted but studies regarding anti inflammatory cytokines are few. In order to establish its potential as a prognostic marker, this study examined the serum levels of IL-10 in both patients and healthy controls, as well as their relationship to disease activity.

Materials & Methods

This cross sectional study was conducted from September 2021 to August 2022 at the Department of Microbiology and Immunology in Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka.

Study population

Patient group: A total number of 38 axSpA patients attending at out patient department (OPD) of Rheumatology, BSMMU were selected as cases.

Control group: Total 38 healthy controls were selected from resident doctors and laboratory staffs of Department of Microbiology and Immunology, BSMMU and general people were selected as controls.

Selection of study population

Inclusion criteria: Patients were selected according to the Assessment of spondyloarthritis international society (ASAS) criteria for diagnosis of axial spondyloarthritis (axSpA) after taking informed written consent. Persons having no diagnosed autoimmune and/ or rheumatological diseases, related to patient group and belonging to the same ethnic group as the patients were selected as controls.

Exclusion criteria: Pregnancy and breast feeding, alcohol abuse, acute infection and uncontrolled diabetes were the exclusion criterias for cases. Person having family history of axSpA and other rheumatological disorder, pregnancy and acute infection were the exclusion criteria for controls.

Cytokine measurement

Three ml blood from each subjects were centrifuged at 4000 rpm for 5 min and stored at -20°C upto the study period. Properly stored serum were used for determining the level of IL-10 using a sandwich ELISA according to manufacturer's instruction (Elabscience, USA; catalog no: E-EL-H6154).

Statistical analysis

All the data were rechecked, coded, entered in a data base, and analyzed using Statistical Package for the Social Sciences (SPSS) version 22 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). The categorical variables were expressed as numbers (n) and percentages (%), while continuous variables were expressed as Mean ± Standard Deviation. To observe the association of IL-10 level in case and control, Mann–Whitney U test was performed. Statistically significant P value was considered as less than 0.05 for all statistical analysis.

Results

This cross sectional study was conducted on 38 clinically confirmed axial spondyloarthritis patients and 38 healthy controls for determining the association of IL-10 with disease severity in a tertiary care hospital in Dhaka city. Table 1 shows the Clinico-demographic characteristics of patients. The comparison of IL-10 levels between cases and controls are shown in Table 2. The mean serum levels of IL-10 were found significantly higher in ax-SpA patients compared to controls (Mean± SD 4.12± 1.76 pg/ ml vs 0.90± 0.15 pg/ ml, P<0.001). Figure 1 showing, the comparison of IL-10 between cases and controls. Here IL-10 level is significantly higher in the cases than that of controls. The disease activity are categorized in Table 3 into two groups based on BASDAI scoring system. The scoring include inactive disease group (score <4) and active disease group (score >4). Among 38 patients 14 (36.8%) patients were in inactive disease group

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Table 1: Clinico-demographic characteristics of the patients with axial SpA (n=38)

Parameters	Patients with axial SpA
Age (years) Mean±SD	34.66±8.08
Range	(21-49)
Gender Male	24 (63.2%)
Female	14 (36.8%)
Male : Female ratio	1.7:1
Axial spondyloarthritis duration (years)	3.18±1.93
Age at onset (years)	31.5±7.92
Peripheral arthritis	27 (71.05%)
Enthesitis	26 (68.42%)
Dactylitis	25 (65.79%)
Uveitis	6 (15.79%)
Psoriasis	8 (21.05%)
Inflammatory bowel disease	4 (10.53%)
Positive family history	25 (65.8%)
C-Reactive protein (mg/L)	26.9±17.5
HLA-B27 positive	34 (89.5%)
Sacroiliitis on X-ray	38 (100.0%)

Note: SD= Standard deviation
HLA-B27= Human leukocyte antigen B27

Table 2: Comparison of serum IL-10 level in ax-SpA patients and controls (n=76)

Interleukin-10 (pg/ml)	Case (n=38)	Control (n=38)	*P*-value
Mean±SD	4.12±1. 76	0. 90±0.15	**<0. 001***
Median	3.69	0.88	
Range (min-max)	1. 37 -9.40	0. 54 -1.24	

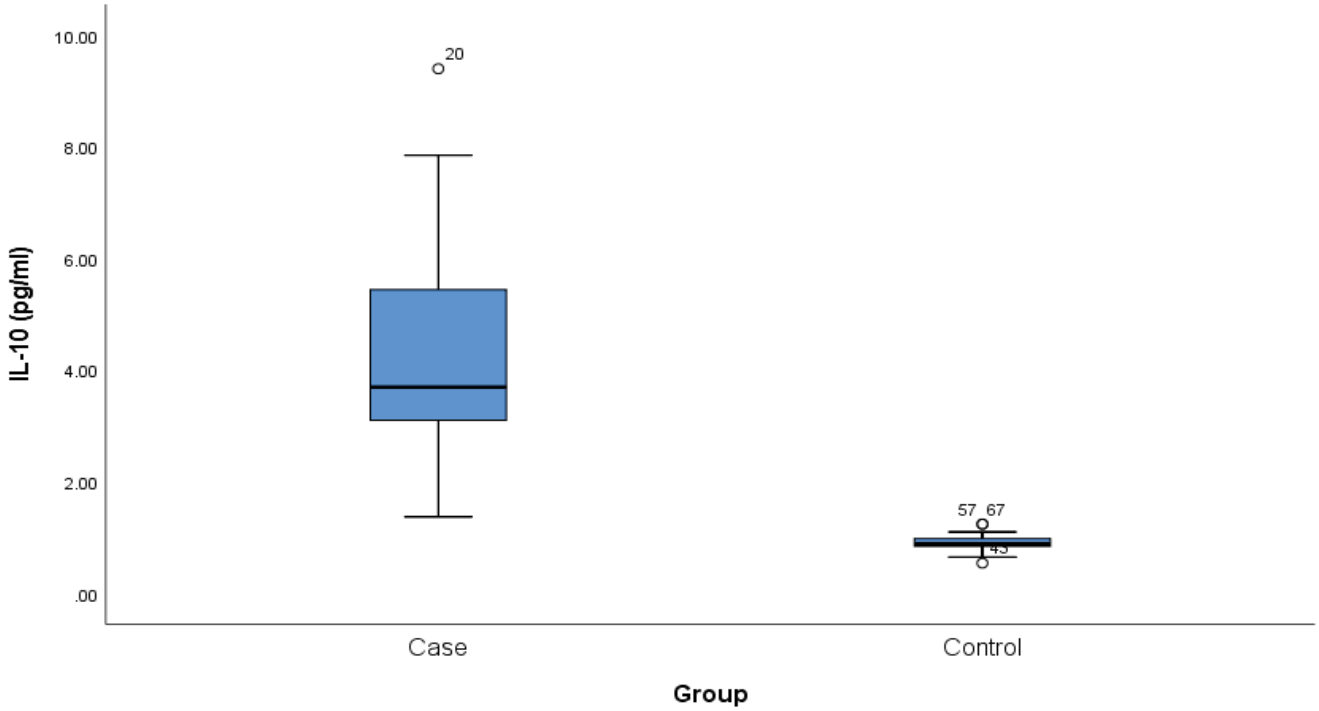
P-value measured by Mann-Whitney U test,
*indicates significant.

Table 3: Association of disease severity with serum IL-10 level according to BASDAI score (n=38)

Cytokine level	Disease severity by BASDAI score		*P*-value
	Inactive (n=14)	Active (n=24)	
Interleukin-10 (pg/ml)			
Mean±SD	5.68±1.66	3. 21±1.05	**<0.001***
Median	5.7	3.31	

P-value reached from Mann-Whitney U test,
*indicate significant.

Figure1: Box plot showing the comparison of Interleukin-10 level between cases and controls. Mean Whitney test was performed. Median is represented by the horizontal line. The box represent the interquartile range and the whiskers represent the overall range.



*indicate significant

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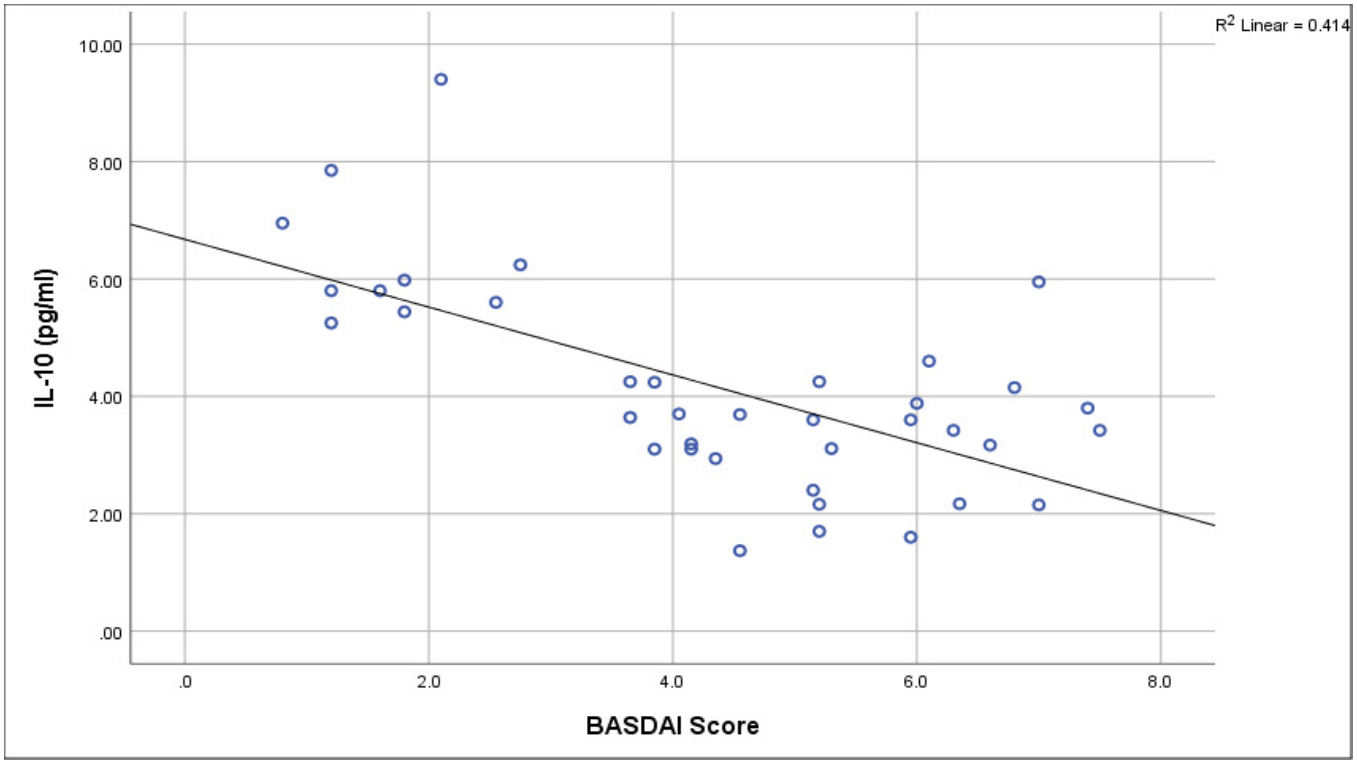
Figure 2: Correlation of BASDAI score with IL-10 levels of the axSpA cases. Spearman's rho correlation were done to see the association.



*indicate significant.

and 24 (63.2%) were in active disease group. Mean IL-10 levels in active group were significantly lower than inactive group (P<0.001) according to BASDAI score. Figure 2 shows that the serum level of IL-10 in patients group were negatively correlated with disease activity according to BASDAI score (P<0.001).

Discussion

Ankylosing spondylitis (AS), a common subtype of SpA, is associated with chronic inflammation of the sacroiliac and peripheral joints and the enthesis and it has been confirmed that genetic and environmental factors play important role in its pathogenesis.. There are increasing evidences to suggest the roles of non-major histocompatibility complex (non-MHC) genes in AS. Cytokine encoding genes associated with Ankylosing spondylitis, can interfere with the production of these cytokines and may be a contributory factor of developing Ankylosing spondylitis [14]. With respect to the Th2 cytokine secretion pattern in AS, there has been some interest in the role of IL-10 in the pathogenesis [5]. The study demonstrated the elevated levels of serum IL-10 in axSpA patients compared to healthy controls similar to a Brazilian study [13]. This finding is also in consistence with Madej et al (2015) [1], Lv et al (2011) [5] and Baeten et al (2001) [8]. Another Brazilian study published in 2018 found that, people with AS have high levels of the anti-inflammatory cytokine IL-10. This increased IL-10 expression may be a suppressive reaction to inflammation. 2011 saw reports of elevated IL-10 serum levels in AS patients from China. The elevated levels of IL-10 most likely indicated a suppressive feedback pathway [15]. Similar to the Chinese study, a recent study of a mixed ethnic group found that AS patients had greater serum levels of IL-10 than controls did [16]. Increased levels of IL-10 and IL-10 positive T cells were detected in synovial fluid of AS patients in other studies [17]. Although these results seem controversial as IL-10 is an anti-inflammatory cytokine, a way to better understand the role of IL-10 in the pathogenesis of disease can be through the expression of M2 macrophages. IL-10 can alter the phenotype of macrophages from M1 to M2 [13]. In this study, among the 38 axSpA patients 14 patients were in inactive group and 24 were in active group according to BASDAI score. A higher concentration of IL-10 was found in inactive disease group (5.68±1.66 pg/ml) compared to active disease group (3.21±1.05 pg/ml), estimated P value is <0.001. According to BASDAI scoring, this study revealed a negative correlation of disease activity with IL-10 levels. Chou et al (2006) also found a negative correlation of IL-10 level with the activity of axSpA based on BASDAI score [12]. Another Chinese study by Wen et al (2017) also showed a negative correlation of IL-10 with the activity of axSpA [18]. So, this study was conducted to demonstrate the serum level of IL-10 and to correlate it with disease severity. From the findings, it is evident that higher level of IL-10 and the association with disease severity might be useful for clinicians

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to predict the prognosis of axSpA. Limitation of the study is, taking drug history from all patients was not possible. That may influence the result. Further studies could be done to find out the association of other anti inflammatory cytokines with severity of Axial spondyloarthritis.

Conclusion

Serum levels of IL-10 is significantly elevated in axSpA patients .Serum IL-10 level is negatively correlated with disease activity assessed by BASDAI score.

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Declarations Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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