

RESEARCH ARTICLE

Serum galectin-3 concentrations in patients with ankylosing spondylitis

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Abstract

Objective: The aim of our study was to assess potential correlations between serum galectin-3 concentrations and Ankylosing Spondylitis Disease Activity (ASDAS) index in patients with ankylosing spondylitis (AS).

Methods: A total of 112 patients with AS were included, and 130 healthy subjects were considered as controls. We collected the detailed medical history, and ASDAS index was used to assess the disease severity in patients with AS.

Results: The serum galectin concentrations were higher in AS patients compared to the health groups (14.1 ± 9.6 vs 9.2 ± 3.7 , $P < 0.001$). The correlation analysis showed that serum galectin concentrations were significantly positively correlated with C-reactive protein and erythrocyte sedimentation rate ($r = 0.369$, $P < 0.001$; $r = 0.240$, $P = 0.011$). In addition, the positively correlation of serum galectin-3 with global pain index ($r = 0.238$, $P = 0.011$) was observed in AS patients. A significant positively correlation between serum galectin and ASDAS index in AS patients was found ($r = 0.367$; $P < 0.001$). In multiple linear regression analysis, the results indicated that increased serum galectin still was correlated with ASDAS index ($r = 0.322$, $P < 0.001$) in patients with AS.

Conclusions: Serum galectin concentrations were found to be correlated with ASDAS index in patients with AS.

KEYWORDS

ankylosing spondylitis, ASDAS index, serum galectin-3

1 | INTRODUCTION

Ankylosing spondylitis (AS) is a chronic and multisystem inflammatory rheumatic disease with spinal and extra-spinal features, which mainly affects the joints of the axial skeleton.¹ AS is characterized by tissue inflammation with structural damage and fibrosis,² and the limited activity and persistent pain may lead to a poor quality of life during the active disease.³ It has suggested that intracellular cytokines, inflammatory cells, and inflammatory chemokines were

associated with the pathogenesis of structural damage and fibrosis in patients with AS.⁴⁻⁶

Galectin-3 is a member of soluble β -galactoside-binding lectin, which plays an important role in the development of inflammation and fibrosis.⁷⁻⁹ Previous studies have shown that increased galectin-3 expression was observed in various cancer cells.¹⁰ Recently, the increased expression of galectin-3 has been suggested in autoimmune diseases such as systemic sclerosis, Behcet's disease, and rheumatoid arthritis¹¹⁻¹³; these studies indicated that serum

galectin-3 might be associated with the pathogenesis and progression of rheumatic disease. Therefore, the aim of our study was to assess the potential correlation of serum galectin-3 levels and ASDAS index in patients with AS.

2 | MATERIALS AND METHODS

2.1 | Participants

A total of 112 patients with AS were included, and 130 healthy subjects were considered as controls in this study. The AS patients were diagnosed according to the modified New York criteria.¹⁴ Patients were excluded as follows: coronary heart disease, active infection, diabetes, polycystic ovary syndrome, liver and kidney disease and tumors. We collected the detailed history of all participants, and ASDAS index was used to assess the disease severity in patients with AS, the formula is $(0.121 \times \text{back pain} + 0.058 \times \text{morning stiffness duration} + 0.110 \times \text{overall patient assessment} + 0.073 \times \text{peripheral pain/inflammation} + 0.579 \times \text{Ln}(\text{CRP} + 1))$.¹⁵ Moreover, the global pain index was assessed in the study, and other clinical information such as smoking, body mass index, family history of AS, disease duration, and medication use were collected. The protocol of our study was approved by the ethics committee of Sixth Affiliated Hospital of Xinjiang Medical University.

2.2 | Clinical and biochemical assessment

Laboratory indexes such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were measured by standard laboratory methods. Serum was collected and frozen at -80°C at refrigerator for the galectin-3 measurement. Afterward, serum galectin-3 concentrations were tested with a commercially available enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions.

2.3 | Statistical analysis

SPSS 20.0 (Chicago, IL, USA) was used for all statistical analyses, and the results were taken as statistically significant if two-sided $P < 0.05$. The comparisons between AS patients and control groups were performed by using t tests or Mann-Whitney U tests for continuous variables, and chi-square test for categorical variables. We used the Spearman correlation to identify correlations between serum galectin-3 and laboratory tests. A stepwise multiple linear regression analysis was used to assess the correlation between the serum galectin-3 and ASDAS index in patients with AS.

3 | RESULTS

3.1 | Clinical and laboratory characteristics

The demographic and clinical data are shown in Table 1. The age, sex, and body mass index were matched between the AS patients and healthy controls. The mean values for the ASDAS index were

TABLE 1 The main data characteristics in AS patients and healthy controls

	AS patients n = 112	Healthy controls n = 130	P-values
Gender (F/M)	21/91	23/107	0.832
Age (y)	31.8 ± 9.6	29.8 ± 13.4	0.165
Smoking (n, %)	25 (22.3%)	28 (21.5%)	0.883
Body mass index (kg/m ²)	23.1 ± 2.9	22.7 ± 3.6	0.366
Family history of AS (n, %)	8 (7.1%)	0 (0%)	0.834
Disease duration (y)	4.0 ± 5.1	-	-
NSAID	110 (98.2%)	-	-
Sulfasalazine	43 (38.4%)	-	-
Corticosteroid	5 (4.5%)	-	-
ASDAS index	3.4 ± 1.6	-	-
Global pain index	50.3 ± 24.1	-	-
Erythrocyte sedimentation rate (mm/h)	19.3 ± 13.4	5.7 ± 3.2	<0.001
C-reactive protein (mg/L)	16.3 ± 13.1	1.7 ± 2.0	<0.001
Serum galectin-3 (ng/mL)	14.1 ± 9.6	9.2 ± 3.7	<0.001

3.4 ± 1.6 in patients with AS. Compared to control groups, the levels of the CRP and ESR were higher in patients with AS. Moreover, the serum galectin-3 levels were higher in AS patients compared to the health groups (14.1 ± 9.6 vs 9.2 ± 3.7 , $P < 0.001$).

3.2 | The correlation coefficients in patients with AS

The correlation analysis showed that serum galectin-3 concentrations were significantly positively correlated with CRP and ESR ($r = 0.369$, $P < 0.001$; $r = 0.240$, $P = 0.011$) in patients with AS. A significant positively correlation between serum galectin-3 and ASDAS index in AS patients was found ($r = 0.367$; $P < 0.001$, Figure 1). In addition, the positive correlations of serum galectin-3 with global pain index ($r = 0.238$, $P = 0.011$) were observed in AS patients.

3.3 | The multiple linear regression analysis between serum galectin-3 and ASDAS index in AS patients

In multiple linear regression analysis, the variables in age, sex, smoking, body mass index, family history, disease duration, ESR, CRP, global pain index, and ASDAS index were included as independent variables; the results indicated that increased serum galectin-3 concentrations still were correlated with ASDAS index ($r = 0.322$, $P < 0.001$) in patients with AS, and the additional correlations of serum galectin-3 with CRP and ESR ($r = 0.173$, $P = 0.041$; $r = 0.354$, $P < 0.001$) were observed in AS patients, as shown in Table 2.

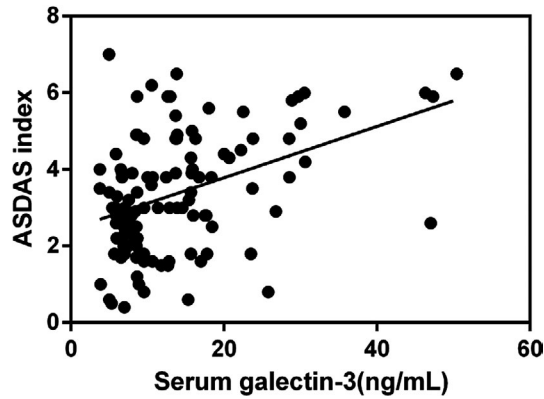


FIGURE 1 The correlation between serum galectin-3 and ASDAS index in ankylosing spondylitis patients

TABLE 2 The correlation between serum galectin-3 and ASDAS index in multivariable linear regression analysis

	Unstandardized coefficients		Standardized coefficients		P-Value
	B	SE	β	t	
Erythrocyte sedimentation rate	0.255	0.058	0.354	4.422	<0.001
C-reactive protein	0.128	0.062	0.173	2.073	0.041
ASDAS index	1.996	0.506	0.322	3.946	<0.001

4 | DISCUSSION

Over the past decade, a series of studies have shown that galectin-3 played an important role in the development of the pathological conditions. Ho JE et al¹⁶ found that higher serum galectin-3 concentrations were associated with increased heart failure risk. Similar studies suggested that serum galectin-3 expression was increased in fibrotic liver disease and pulmonary fibrosis.^{17,18} These studies indicated that serum galectin-3 may be a marker of active fibrosis. In addition, the serum galectin-3 levels were higher in inflammatory disorders patients with systemic sclerosis, Behçet's disease, and systemic lupus erythematosus.^{11,12,19} Serum Gal-3 concentrations were found to be also increased in patients with rheumatoid arthritis.¹³ Our study first found that serum galectin-3 levels were higher in patients with AS than healthy controls. In addition, serum galectin-3 concentrations were independently correlated with ASDAS index in AS patients, and the positive correlations of serum galectin-3 with global pain index were observed in AS patients, suggesting that serum galectin-3 may be a potential marker for the assessment of disease severity in patients with AS.

Although the pathogenesis of AS is still unclear, there are several explanations for the phenomenon. First, the galectin-3 may regulate inflammatory responses in immune cells, and galectin-3 as a pro-inflammatory cytokine accelerates the release of tumor necrosis

factor- α and interleukin-6,²⁰ and galectin-3 gene deficiency can reduce the development of experimental autoimmune encephalomyelitis.²¹ Second, galectin-3 can activate myofibroblasts and promote fibrosis, galectin-3 can promote inflammatory cytokine secretion in tissue fibroblasts, and galectin-3 is a critical mediator of transforming growth factor- β -induced pulmonary fibrosis.^{22,23} Third, the galectin-3 gene expression is increased in inflammatory tissues in patients with juvenile idiopathic arthritis,²⁴ and the gene expressions of galectin-3 are elevated in immune cell in systemic lupus erythematosus patients.²⁵ Therefore, inflammation and immune dysfunction may increase serum galectin-3 levels in patients with AS, and these pathological changes corporately contribute to the progression of disease in AS patients.

Several potential limitations should be considered. First, we did not evaluate the effects of drugs on serum galectin-3 levels such as NSAID, sulfasalazine, and corticosteroid. Second, we did not observe the expression of galectin-3 in pathological tissue sections in patients with AS. Third, our study was a small sample, so the results needed to be further replicated with larger sample. Despite of these limitations, serum Gal-3 concentrations were found to be correlated with ASDAS index in patients with AS, indicating serum galectin may be a useful biomarker to assess the disease activity in AS patients.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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