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Assessment of Serum Galectin-8 in Iraqi Patients with Rheumatoid arthritis

Tarek.Q.Muss.[1];M.AL-Faham .[2];Faiq I.Gorial.[3]
1,2 Department of microbiology & Immunology, College of medicine, University of Baghdad, 3Rheumatology Unit, Department of Medicine, College of Medicine, University of Baghdad,

Summary: ***Background:****Rheumatoid arthritis (RA) is chronic inflammatory arthritis disease with significant morbidity and mortality .Early diagnosis is important for better treatment and outcome.Galectins are potent immune regulators and modulate a range of pathological processes, such as inflammation, autoimmunity, and cancer, Accumulated evidence shows that several family members of galectins play positive or negative roles in the disease development of RA, through their effects on T and B lymphocytes, myeloid lineage cells, and fibroblast-like synoviocytes. (1).*
Objective: *to assessserumGalectin-8 in Iraqi Patients with RA and its validity in diagnosis of RA*
Patients and Methods: *This case control study included 90 subjects.Fiftyof them were patient diagnosed as established RA according to the 2010 American College of Rheumatology/European League Against Rheumatism (2010 ACR/EULAR) classification criteria for Rheumatoid arthritis and compared with 40 apparently healthy control group.serum Galectin-8 was measured for patients and controls*
Results:*Mean serum level of Galectin-8 was statistically significantly lower in patients group (36.68±25.79) than controls group (182.93±87.83), (P-value < 0.001).At the optimum cut off value of serum gal-8 ≤ 95.7 we found that maximum accuracy was 95.6 , sensitivity98.0%, specificity 92.5% and AUC was 0.971 .*
Conclusion: *serum galectin-8 was significantly lessin RA patients compared to controls, also the biomarker has excellent valid results to differentiate between patients and controls*
Keywords- *Rheumatoid arthritis,Galectin-8,inflammatory arthritis.*

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I. Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disorder of unknown etiology that primarily involves synovial joints. It typically results in warm, swollen, and painful joints. Pain and stiffness often worsen following rest. Most commonly, the wrist and hands are involved, with the same joints typically involved on both sides of the body. The arthritis is typically symmetrical, and usually leads, if uncontrolled, to destruction of joints due to erosion of cartilage and bone, causing joint deformities The disease may also affect other parts of the body. This may result in a low red blood cell count, inflammation around the lungs, and inflammation around the heart. Fever and low energy may also be present.(2)

T cells play a central role in mediating joint damage by driving the activation of other effector cells (3,4). Although CD4+ T cells are the dominant T cell types in the synovium, Th17, a subset of T helper cells secreting IL-17, and regulatory T cells (Treg) also play a critical role in RA pathogenesis (5,6).

Besides the cells mentioned above, numerous proteins have been shown to play a role in RA pathogenesis. Some of them have been successfully adapted in clinical diagnosis and therapies for RA, such as ACPA, TNFα, IL-1, and IL-6 (6).

The family of galectins is involved in a wide range of biological processes. Their immune modulating role has drawn an increasing attention in the field of arthritis research. Galectins are a group of lectins that bind to β- galactoside carbohydrates on the cell surface and in the extracellular matrix. They are expressed in a wide variety of tissues and organs with the highest expression in the immune system. Galectins are potent immune regulators and modulate a range of pathological processes, such as inflammation, autoimmunity, and cancer. Accumulated evidence shows that several family members of galectins play positive or negative roles in the disease development of RA, through their effects on T and B lymphocytes, myeloid lineage cells, and fibroblast-like synoviocytes. (1).

In recent study, function-blocking autoantibodies against galectin-8 were detected in a RA patients (7,8). The blockade of galectin-8 function in RA patients suggests that galectin-8 may play a suppressive role in RA. The potential role of galectin-8 in RA was further supported by a human association study. (9). This study was designed to assess serum galectin-8 in Iraqi patients with RA and its validity in diagnosis.

II. Patients and Methods

Study design: This case control study was done in Baghdad Teaching hospital, Department of Rheumatology outpatient clinic from beginning of November 2016 till end of November 2017,

Patients: Fifty patients (36 females 14 males and), their mean age ± Standard deviation (SD) was (46.5 ± 10.4 years)was diagnosed as RA according to 2010 ACR / EULAR were comparedwith40apparently healthy individualsfrom central blood bank who were randomly selected as control group. Written informed consents for the research were obtained from all the enrolled patients and controls. Ethical approval for study was taken from Baghdad Teaching Hospital and Medical department, College of Medicine

Methods: From each individualtwo (2) ml of venous blood was aspirated and let clot at room temperature, then centrifuged to separate the serum which was collected in aliquots to store in (- 20 ºC) until needed for investigation of Galectin-8. **Kits and reagents:** Human Galectin-8 ELISA kit (SHANGHAI YEHUA, China).

Excluded criteria : patient with overlapping inflammatory disease and connective tissue disease or malignancy

Statistical analysis:statistical analysis in this study was done using SPSS 22.0.0 (Chicago, IL), MedCalc Statistical Software version 14.8.1 (MedCalc Software bvba, Ostend, Belgium; 2014), Prism version 7.00 for Windows (GraphPad Software, La Jolla California USA), software package used to make the statistical analysis, p value considered when appropriate to be significant if less than 0.05

III. Results

This study was included Fifty (50) patients with RA, 36 (72.0.%) female, and 14 (28.0%) male , the disease was more predominance in females than in male with a ratio of 2.6:1.The mean age of patients group did not differ significantly from control group (46.5 ± 10.4 years vs 45.4 ± 4.8years respectively, P > 0.05) as shown in table-1.

Table 1: Baseline characteristics of patients and controls

Variables	Patients	Control	p-value
Number	50	40	-
Age (years), mean ± SD	46.5 ± 10.4	45.4 ± 4.8	0.537
Gender, n (%)			0.476
Female	36 (72.0 %)	26 (65.0 %)	
Male	14 (28.0 %)	14 (35.0 %)	

Serum levels of Galectin-8 by using ELISA technique, the mean serum level of Galectin-8 was lower in patient group (36.68 ± 25.79pg/m) than control group (182.93 ± 87.83pg/m) and this difference was statistically significant ((P <0.001)) as shown in figure 1

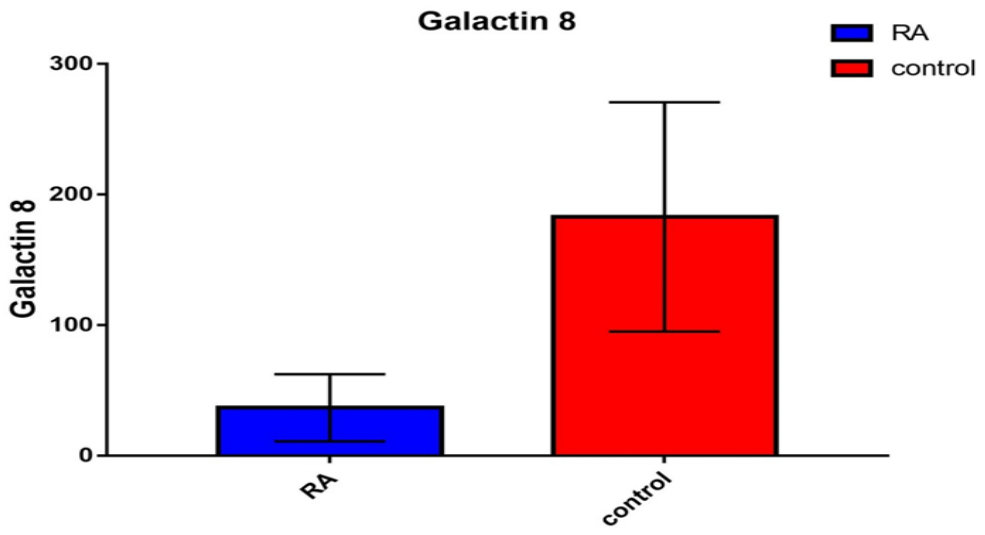

Figure (1): comparison of galectin- 8 in patients and controls

Table-2 and figure 2 showed that Galectin – 8 had an excellent ability as predictor of RA from control

Table-2:ROC analysis of galactin-8 to differentiate between patients and controls

Variable	AUC	p-value
Galactin 8 levels	0.971	<0.001

AUC: area under the curve

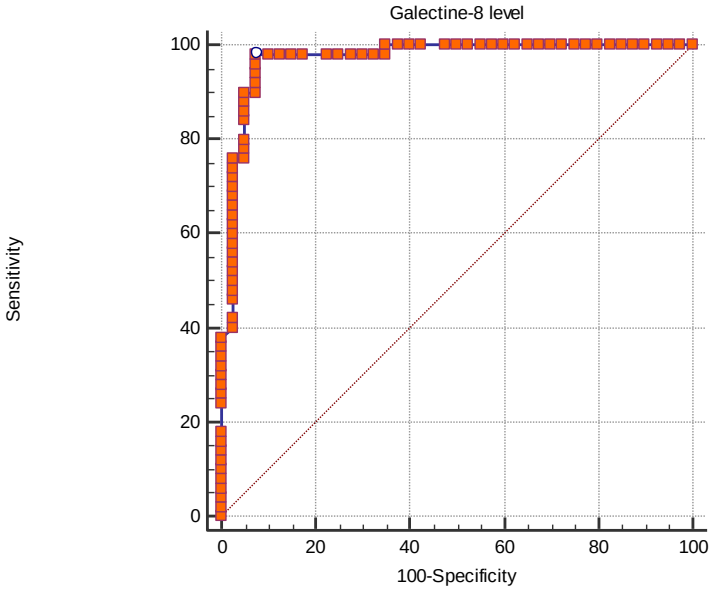

Figure (2): ROC curve of galectin – 8 as predictor of RA from control

Table-3showed that the sensitivity specificity cut off point **of galectin – 8**).Galectin – 8 at optimal cut point of ≤95.7 predict RA, the rest of the validity parameters are illustrated in table (3).

Table(3)Validity parameters of galactin-8 to differentiate between patients and controls

	Cut point	SN	SP	AC	PPV	NPV
Galactin 8 levels	≤95.7	98.0%	92.5%	95.6%	94.2%	97.4%

SN: sensitivity, SP: specificity, AC: accuracy, PPV: positive predictive value, NPV: negative predictive value

IV. Discussion

Rheumatoid arthritis is chronic inflammatory arthritis disease with significant morbidity and mortality .Early diagnosis is important for beter treatment and outcome. The family of galectins is involved in a wide range of biological processes. Their immune modulating role has drawn an increasing attention in the field of arthritis research. Galectins are a group of lectins that bind to β- galactoside carbohydrates on the cell surface and in the extracellular matrix. They are expressed in a wide variety of tissues and organs with the highest expression in the immune system. (1)

This study included Fifty (50) patients with RAwho attended the rheumatology consultation clinic of Baghdad teaching hospital in the period between November 2016 to November 2017,, and forty (40) control healthy person.

The mean age of patients was 46.5±10.4 years, this result was in accordance with previous studies done on Iraqi RA patients by Al-Rawi , Al-Ubaidi and Abdul-Wahid,Al-Karkhi

(10,11,12,15) and other international studies (13,14,) which reported that the RA disease usually starts at middle age and affected commonly people above 40 years of age .

This study showed that females are more predominant for RA than males with a ratio of 2.6:1 which this result nearly in an agreement with local study done by Abdul-Wahid who found the ratio 3.5:1(12).

The current study revealed that serum levels of galectin-8) higher in control group (182.93±87.83) than patient group (36.68±25.79) and this difference is statistically significant (P-value < 0.001).

At the optimum cut off value of serum gal-8 ≤ 95.7 we found that maximum accuracy was 95.6 , sensitivity 98.0%, specifity 92.5% , and AUC was 0.971 this indicate that the biomarker has excellent valid results to defrentiate bet patient and control. Up to our knowledge there is no previous study that report these findings. In conclusion serum galectin-8 was significantly less in RA patients than controls and was valid to differentiate patients with RA from healthy controls.

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