`Original Article-` MEDICAL SCIENCE

Albumin-Fibrinogen Ratio in rheumatoid arthritis and its relation to disease severity and radiographic progressive changes

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ABSTRACT

Aim of the work: To evaluate the relationship between albumin-fibrinogen ratio (AFR) and radiographic changes in rheumatoid arthritis (RA)

Patients and Methods: 50 rheumatoid patients and 30 control subjects were collected for the study, they were investigated for RF, Anti CCP, ESR, CR, fibrinogen and albumin. Also, they were subjected to x ray andMRI examination

Results: There was significant increase in laboratory parameters and increase in albumin fibrinogen ratio in rheumatoid patients as compared to healthy control subjects. Also, there was positive correlation of the ratio with X ray and MRI score for synovitis and bone destruction

Conclusion: AFR may be easily, rapidly detected and prognostically useful markers of ongoing inflammation and joint affection correspondingly to radiological findings.

Keywords: rheumatoid arthritis, albumin-fibrinogen ratio, MRI

Introduction:

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease of unknown aetiology that affects mainly the joints (1).Several cytokines are released lead to many inflammatory processes with final joint destruction (2).

Plasma fibrinogen expression and production by the liver may be increased during inflammatory process. So, it is considered a positive acute-phase protein similar to erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) (3).Meanwhile, serum albumin is expression may be decreased in during inflammatory process, unlike fibrinogen. So, it is

categorised to a negative acute-phase protein(4). Recently, a new concept of an inflammation-related index using these two variables, fibrinogen to albumin ratio (FAR), has been introduced(5).

There is well-established evidence that albumin to fibrinogen ratio (AFR) is considered a potential biomarker reflecting the inflammatory status in malignant patients (6),in addition, it could be a possible predictor for clinical response to different cancer medications(7).Also, some studies reported the adequate utility of it in expecting recanalization in myocardial infarction (8, 9).

The aim of this work was to investigate the role of albumin fibrinogen ratio in RA patients and to study their correlation with disease activity and joint severity.

Patients and Methods:

The study carried out on 50 RA patients fulfilling the 2010 American College of Rheumatology (ACR)/European League against Rheumatism classification criteria for RA(10), and 30 healthy persons as control group matched in age and sex. Conditions which may change inflammatory markers' levels such as pregnancy, diabetes mellitus, hypertension, renal and/or hepatic dysfunction, malignancy, trauma or haemorrhagic events, and/or other coexisting connective tissue diseases were excluded from the study.

Informed written consents were obtained from the participants in this study. The study conforms to the 1995 Helsinki declaration and approved. The study protocol was treated confidentially corroborated to Helsinki declarations of biomedical ethics and approved by the research ethical committee of Benghazi Medical Centre - Benghazi University.

All the patients were subjected to clinical assessment of disease activity of RA using the disease activity score in 28 joints (DAS 28-ESR)(11).

Laboratory investigations were done to patients and control groups: Erythrocyte sedimentation rate (ESR) in the first hour was estimated by Western method, serum CRP was quantified by immunoturbidimetry (Beckman Coulter) on AU 680 instrument. Serum albumin was measured by bromocresol green (Beckman Coulter) on AU 680. Plasma fibrinogen was quantified by Stago compact analyzer using the Clauss technique. Thus, Albumin to Fibrinogen (AFR) ratios were estimated

Plain x ray in a standard posteroanterior (PA) view of the hands/wrists and anteroposterior (AP) view of the feet were taken and scored according to modified Larsen's score(12)

MRI was done to all patients and all the MRIs were scored for synovitis, bone oedema and bone erosions, as defined in the Outcome Measures in Rheumatology (OMERACT) MRI rheumatoid arthritis recommendations (13). By two radiologists who were blinded to the clinical findings.

Statistical Analysis:

After data collection and check for completeness and logical consistency. Pre-coded data were entered into Microsoft Office Excel 2010. Data were then transferred to Statistical Package for the Social Sciences, version 21. All statistical analyses were performed using two-tailed tests and an alpha error of 0.05. A p-value distributed quantitative data, and frequencies categorical variables. Comparisons between groups were done using the Mann–Whitney test and Chi-square test. Spearman test was used for correlations.

Results:

There was significant increase in laboratory parameters and increase in albumin fibrinogen ratio in rheumatoid patients as compared to healthy control subjects(table 1). table 2 demonstrate radiographic score of rheumatoid patients. Also, there was positive correlation of the AFR with X ray and MRI score for synovitis and bone destruction (table 3)

Table 1 Demographics data and laboratory parameters in rheumatoid arthritis and control groups

	RA patients (n=50)	Controls(n=30)
Age (years)	45.35±6.76	44.9±5.87
Sex (male/female)	2/48	1/29
Disease duration (years)	10.50±43.9	-----------
DAS-28	5.83±1.6	-----------
ESR(mm/1st h)	38.85±18.5*	11.43±0.26
CRP(mg/dl)	25.22±3.6*	1.29±0.17
RF(IU/ml)	67.45±12.4*	5.60± 1.16
Anti-CCP(U/ml)	233.6±67.6*	15.60±6.05
Fibrinogen (g/l) Median	5.23(1.01–4.15)	1.45(1.23–1.10)
Albumin (gm/dl) Median	4(3.9–3.2)	3.8(3.6–4.0)
AFR Median (IQR)	0.90 (0.84–1.04)	3(1.9–3.5)

Table 2: Radiological parameters in rheumatoid arthritis patients (n=50).

Modified larsen score	32.9 ± 11.2
MRI wrist joints scores	
Synovitis	4.4 (1-7)
Bone erosions	3.5(1-13)
Bone defects	2.5 (0-7)
Bone edema	1.6(0-11)
MRI MCP joints scores	
Synovitis	6.9(2-10)
Bone erosions	1.9(0-10)
Bone defects	1.5(0-6)
Bone edema	1.4(0-19)

Values are mean (interquartile ranges) JSN, joint space narrowing; MCP, metacarpophalangeal.

Table 3: Correlation between AFR with clinical, laboratory and radiological data in rheumatoid arthritis patients (n=50).

Parameter	AFR	
	R	P
Age (years)	0.271	NS
Disease duration (years)	0.165	NS
DAS-28	0.819	<0.001*
ESR (mm/1st hr)	0.732	<0.001*
CRP (mg/dl)	0.675	<0.001*
RF (IU/ml)	0.132	NS
Anti-CCP (U/ml)	0.241	NS
Modified Larsen score	0.763	<0.001*
MRIscore for synovitis		
wrist joints	0.522	<0.001*
MCP joints	0.763	<0.001*
MRI score for erosion		
wrist joints	0.861	<0.001*
MCP joints	0.632	<0.001*

* Pearson's correlation coefficient. NS: non-significant, *=significantly different compared to controls. DAS-28, disease activity for 28 joint indices score; ESR, erythrocyte sedimentation

rate; CRP, C reactive protein; RF, Rheumatoid factor; anti-CCP: anti-cyclic citrullinated peptide; mSvH: Modified Sharp/Van der Heijde, MRI: Magnetic resonance imaging, MCP: Metacarpophalangeal. AFR, albumin/fibrinogen

Discussion:

Rheumatoid arthritis is a progressive inflammatory musculoskeletal disease that cause systemic affection in addition to severe joint damage. To avoid its severe manifestations, early diagnosis and detection of disease activity is needed. Increased CRP, fibrinogen, and ferritin as acute phase reactants is a prominent feature of autoimmune diseases such as RA which reflects the inflammatory state (14,15).

Our study revealed significant increase serum level of fibrinogen, ESR and CRP in rheumatoid patients compared with control group and this is usually occur in inflammatory disorders(16).

Some previous studies demonstrated that AFR may be used as convenient laboratory markers, which indirectly reflect the state of inflammation and disease activity in some rheumatic diseases such as RA, AS. (17).

In our study, there was a significant decrease in serum level of AFR in rheumatoid patients as compared to control group and significantly negatively correlated with DAS, ESR,CRP and Larsen score and MRI scores, this is in agreement with previously reported by Yang et al who declared that AFR is correlated with DAS and CRP. Also, they could be simple predictors of disease activity in RA patients (17).

In our study there was no relation between AFR ratio and RF& Anti CCP and this in agreement with another study that revealed no relation between ratio and ACPA, but they are significantly correlated to RF titre (18).

In this study, it was found that AFR ratio are correlated with Larsen score and MRI score for synovitis and erosion These data suggest the strong association of fibrinogen and AFR with RA outcome and joint damage and these results are similar to another study(19).

Fibrinogen (FIB) is a key factor implicated in the process of blood coagulation cascade, and its deposition in the joint was identified to be characteristic of RA and even may be responsible for the formation of pannus tissue(20).

FIB is an important glycoprotein present in human blood plasma and it is involved in many physiological processes such as wound healing, tissue regeneration and regulation of inflammatory responses26. Moreover, FIB has been shown as an important determinant of inflammatory arthritis through its effects on proinflammatory pathways such as NF-κBsignalling (21) A recent study showed that circulating levels of FIB are elevated in RA and correlated with markers of inflammation(22) and this in agreement with our study

Conclusion:

AFR may be easily, rapidly detected and prognostically useful markers of ongoing inflammation and joint affection correspondingly to radiological findings.

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