

FIBRINOGEN LEVEL AND ERYTHROCYTE SEDIMENTATION RATE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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ABSTRACT

Aim of the Study: To assess Plasma fibrinogen level in patients with active rheumatoid arthritis (ARA). **Subjects and Materials:** Sixty patients with ARA attending rheumatology department in Ibn-Sina teaching hospital in Mosul, were included in this study during a period of eight months. Their mean age was (45.15) years ranging between (19-70) years, (50) females and (10) males, those patients were diagnosed to have rheumatoid arthritis according to the criteria of the American College of Rheumatology and patients were considered to have an active disease according to parameters of assessing disease activity. In addition to those patients, thirty healthy persons were included as a control group for measurement of plasma fibrinogen. The study includes clinical evaluation of disease activity depending on the number of inflamed joints and pain intensity (score), plasma fibrinogen, and erythrocyte sedimentation rate (ESR). **Results:** A significant positive correlation was found between plasma fibrinogen level and ESR ($p < 0.05$). **Conclusions:** 76.6% of patients were in fourth - sixth decades of life with a female predominance. Erythrocyte sedimentation rate was elevated in (98.3%). Plasma fibrinogen level had a significant positive correlation with ESR level ($p < 0.05$).

KEYWORDS: Fibrinogen, Rheumatoid arthritis, ESR.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disorder characterized by deforming symmetrical polyarthritis of varying extent and severity, associated with synovitis of joint and tendon sheaths, articular cartilage loss and erosion of juxta-articular bone.^[1] The disease may also affect other parts of the body, including skin, eyes, lungs, heart, nerves and blood.^[2] RA affects between 0.5 and 1% of adults in the developed world with between 5 and 50 per 100,000 people newly developing the condition each year.^[3] Women are affected three to five times as often as men.^[4] The age at which the disease most commonly starts is in women between 40 and 50 years of age, and for men somewhat later.^[5] The diagnosis of RA is primarily dependent on clinical observation of the patient and fulfillment of sufficient number of criteria as outlined by the American College of Rheumatology.^[6]

Fibrinogen is a soluble protein synthesized in the liver and circulates in the blood. At the time of an injury

fibrinogen is converted to fibrin, which is an insoluble material that forms blood clots.^[7] Elevated fibrinogen levels have been observed in a number of inflammatory diseases, including RA.^[8-13] In a small number of prior studies in RA, plasma fibrinogen levels have been shown to parallel disease activity and acute-phase markers (ESR),^[14] meaning that fibrinogen concentration may rise sharply in any condition, which causes inflammation or tissue damage. Elevated concentration of fibrinogen is not specific because it does not tell the cause or location of disturbance. Usually, this elevation is temporary, returning to normal after the underlying condition has been resolved.^[15]

The ESR is usually elevated in patients with RA and it is a helpful measure in some patients specially in following the activity of the disease,^[16] but some patients with active RA show normal level.^[17] The ESR is an index of the acute phase response, reflecting the concentration of plasma proteins, mainly fibrinogen and gamma-globulins which are elevated. This together with various other

factors that affect ESR (including diurnal variation, anaemia, chronic hypoalbuminaemia due to nephrotic syndrome, elevated immunoglobulins) makes it an imprecise guide to disease activity in most cases.^[18-20]

METHOD AND SUBJECTS

During a period of eight months, 60 cases were studied with active rheumatoid arthritis according to the criteria of the American College of Rheumatology. Patients were considered to have an active disease according to the parameters of assessing disease activity.^[21-23]

The patients examined were those attending Ibn-Sina Teaching Hospital, (50) females, (10) males, their ages range between (19-70) years, with mean (45.15) years, and the duration of disease was (1-27) years with mean (6.38) years, and they were under treatment. Thirty healthy persons were taken as a control for measurement of plasma fibrinogen, which was measured by Clauss technique.^[24]

Blood Sampling & Processing

A five ml of venous blood sample were obtained, three ml. of them was added to EDTA tube and kept at room temperature to be used within one hour to perform ESR. While the remaining (1.8) ml. was added to a plain capped disposable plastic tube containing (0.2) ml. of (3.8%) tri-sodium citrate to obtain plasma which was used for performing the plasma fibrinogen level test.^[24] These tests were done as early as possible on freshly prepared plasma strictly within the time allowed by the manufacturer instructions of each kit.

The mean, standard deviation, range, percentage (%), unpaired t-test, Duncan test and correlation analysis were made by using statistical computer programs: Statistical Package for the Social Sciences (SPSS), *P*-value of 0.05 or less was considered significant.

RESULTS

The results of this study listed down show full clinical and haematological data of the patients as demonstrated in the Table (1) and for control in the Table (2) with their relevant statistical analysis Fig. 1 and Fig. 2.

Table 1: Mean, standard deviation and range of parameters.

Parameters	Mean	SD	Range
Age (year)	45.15	11.88	19.00-70.00
Duration (year)	6.38	5.74	1.00-27.00
ESR (mm/hr)	56.10	22.73	18.00-128.00
Fibrinogen (g/l)	2.95	0.79	2.00-6.20

Table 2: Mean, standard deviation and range of controls.

Parameters	Mean	SD	Range
Fibrinogen (g/l)	2.75	0.69	2.0-4.0

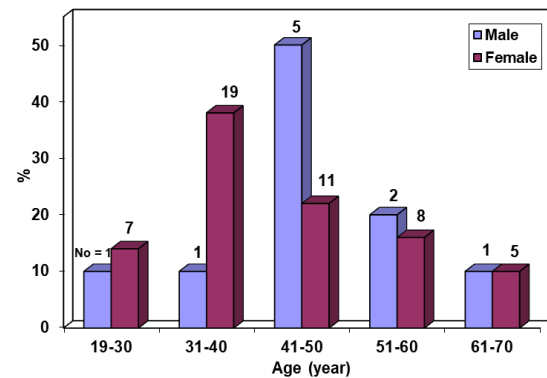


Figure 1: Age and Sex distribution of patients.

There was a significant positive correlation between ESR and plasma fibrinogen level Fig. 2

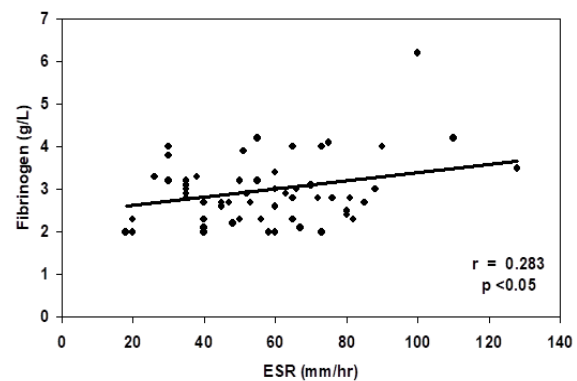


Figure 2: Scatter diagram between ESR and plasma fibrinogen level of patients.

DISCUSSION

The age of patients ranged between (19-70) years, with mean of (45.15) years, and the majority of patients (76.6%) were in Fourth to sixth decades of life. This is quite expected as RA is more common in the fourth to sixth decades of life.^[25,26]

RA, which is 3-4 times more frequent in females than males. The incidence of RA increases with age, and seems to reach a plateau from the age of 60 years. However, the female/male ratio is decreasing with increasing age. The female/male ratio was higher than 4 in the premenopausal age, and lower than 2 after the age of 60.^[27]

Erythrocyte sedimentation rate was elevated in (98.3%) of cases which agrees with other studies. Its assessment is helpful in some patients specially in following the activity of the disease, this elevation may be due to an increase in the level of acute phase proteins like fibrinogen under the effect of proinflammatory cytokines, and also may be due to elevation of non-acute phase reactants immunoglobulins.^[14,16,28,29]

Some studies stated that fibrinogen was regarded as an acute phase reactants meaning that fibrinogen concentration may rise sharply in any condition causing inflammation or tissue damage. In this study plasma fibrinogen has a statistically significant positive correlation with ESR. This significant increase in the level of plasma fibrinogen is also associated with the increase in the Ritchie index, and this may reflect the disease activity and its role in the increase of fibrinogen level.^[7]

CONCLUSION

1. 76.6% of patients were in fourth to sixth decades of life, with male to female ratio of 1:5.
2. Erythrocyte sedimentation rate was elevated in (98.3%) of the cases and it is associated with disease activity as this is reflected in its positive correlation with pain intensity scores.
3. Plasma fibrinogen level had a significant positive correlation with ESR level.

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REFERENCE

1. Owino BO, Oyoo GO, Otieno CF. Socio-demographic and clinical aspects of rheumatoid arthritis. *East Afr Med J*, 2009; 86(5): 204-211.
2. Turesson C, O'Fallon WM, Crowson CS, Gabriel SE, Matteson EL. Extra-articular disease manifestations in rheumatoid arthritis: incidence trends and risk factors over 46 years. *Ann Rheum Dis*, 2003; 62(8): 722-727.
3. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet*, 2016; 388(10055): 2023-2038.
4. Gelber RH. Harrison's principles of internal medicine 18th ed. United States; McGraw Hill, 2012; 2738.
5. Alamanos Y, Voulgari PV, Drosos AA. Incidence and prevalence of rheumatoid arthritis, based on the 1987 American College of Rheumatology criteria: a systematic review. *Semin Arthritis Rheum*, 2006; 36(3): 182-188.
6. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham III CO, Birnbaum NS, Burmester GR, Bykerk VP, Cohen MD, Combe B. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum*, 2010; 62(9): 2569-2581.
7. Tan EM, Feltkamp TE, Smolen JS, Range of antinuclear antibodies in "healthy" individuals. *Arthritis Rheum*, 1997; 40(9): 1601-1611.
8. McEntegart A, Capell HA, Creran D, Rumley A, Woodward M, Lowe GD. Cardiovascular risk factors, including thrombotic variables, in a population with rheumatoid arthritis. *Rheumatology (Oxford)*, 2001; 40(6): 640-644.
9. Yildirim K, Karatay S, Melikoglu MA, Gureser G, Ugur M, Senel K. Associations between acute phase reactant levels and disease activity score (DAS28) in patients with rheumatoid arthritis. *Ann Clin Lab Sci*, 2004; 34(4): 423-426.
10. Loos BG. Systemic markers of inflammation in periodontitis. *J Periodontol*, 2005; 76(11): 2106-2115.
11. Adams RA, Schachtrup C, Davalos D, Tsigelny I, Akassoglou K. Fibrinogen signal transduction as a mediator and therapeutic target in inflammation: lessons from multiple sclerosis. *Curr Med Chem*, 2007; 14(27): 2925-2936.
12. Solomon DH, Curhan GC, Rimm EB, Cannuscio CC, Karlson EW. Cardiovascular risk factors in women with and without rheumatoid arthritis. *Arthritis Rheum*, 2004; 50(11): 3444-3449.
13. Abou-Raya S, Abou-Raya A, Naim A, Abuelkheir H. Rheumatoid arthritis, periodontal disease and coronary artery disease. *Clin Rheumatol*, 2008; 27(4): 421-427.
14. Arvidson NG, Larsson A, Larsen A. Disease activity in rheumatoid arthritis: fibrinogen is superior to the erythrocyte sedimentation rate. *Scand J Clin Lab Invest*, 2002; 62(4): 315-319.
15. Rooney T, Scherzer R, Shigenaga JK, Graf J, Imboden JB, Grunfeld C. Levels of plasma fibrinogen are elevated in well-controlled rheumatoid arthritis. *Rheumatology (Oxford)*, 2011; 50(8): 1458-1465.
16. Scott DL. A simple index to assess disease activity in rheumatoid arthritis. *J Rheumatol*, 1993; 20(3): 582-584.
17. Ahern M, Smith M. Rheumatoid Arthritis. *Med J of Aust*, 1995; 163(3): 156-161.
18. Wolfe F, Michaud K. The clinical and research significance of the erythrocyte sedimentation rate. *J Rheumatol*, 1994; 21(7): 1227-1237.
19. Hertzman A, Evans TI, Sanders KM, Mullinax F. Effects of blood storage on the erythrocyte sedimentation rate. *J Rheumatol*, 1993; 20(12): 2178-2179.
20. Son KM, Kim SY, Lee SH, Yang CM, Seo YI, Kim HA. Comparison of the disease activity score using the erythrocyte sedimentation rate and C-reactive protein levels in Koreans with rheumatoid arthritis. *Int J Rheum Dis*, 2016; 19(12):1278-1283.
21. Haslett C, Chilvers ER, Boon NA. Davidson's Principles & Practice of Medicine. 19thed. Churchill Livingstone: Edinburgh: 2002; 1002-1007.
22. Nielsen O. Anaemia of rheumatoid arthritis: Serum erythropoietin concentration and red cell distribution width in relation to iron status. *Ann Rheum Dis*, 1990; 49: 349-53.
23. Butler R. Monitoring drug therapy in rheumatoid arthritis: In *Collected Reports on the Rheumatic Diseases*. Arthritis and Rheumatism Council for Research, 1996; 172.
24. Lewis SM, Bain BJ, Bates I. Practical haematology. Churchill Livingstone, 2001; 9.

25. Dennis L. Kasper; Anthony S. Fauci; Stephen L. Hauser; Dan L. Longo; J. Larry Jameson; Joseph Loscalzo Harrison's Principles of Internal Medicine. McGraw Hill Education: New York, 2018; 20: 2527-2540.
26. Adam Feather, David Randall, Mona Waterhouse. Kumar and Clark's Clinical Medicine. 10th ed. Elsevier: London, 2021; 437-447.
27. Kvien TK, Uhlig T, Ødegård S, Heiberg MS. Epidemiological aspects of rheumatoid arthritis: the sex ratio. *Ann N Y Acad Sci*, 2006; 1069: 212-222.
28. Gungor Olcum G, Celik Yagan F, Cekin R, Ataman Tasan D, Erdogan M, Aliustaoglu M. Relationship Between Disease Activation, Serum Erythrocyte Sediment Level and C-reactive Protein Level in Rheumatoid Arthritis Patients Receiving Anti-Tumor Necrosis Factor Alpha Treatment. *EJMO*, 2017; 1(2): 69-75.
29. Gulhar R, Ashraf MA, Jialal I. Physiology, Acute Phase Reactants. In: *StatPearls*. Treasure Island (FL): StatPearls, 2021.