

HAEMOGLOBIN LEVEL AND PLATELETS COUNT IN ACTIVE RHEUMATOID ARTHRITIS

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ABSTRACT

Aim of the Study: To assess the level of the haemoglobin and the platelet count in patients with active rheumatoid arthritis. **Subjects and Material:** In this study and during a period of eight months, sixty patients with active rheumatoid arthritis, (50) females and (10) males, attending Ibn-Sina teaching hospital in Mosul / the rheumatology department were included. Their ages were ranging between (19-70) years, with the mean of (45.15) years, those patients were diagnosed to have rheumatoid arthritis according to the criteria of the American College of Rheumatology (ACR), and patients were considered to have an active disease according to parameters of assessing disease activity. This study includes clinical evaluation of disease activity depending on the number of inflamed joints and pain intensity (score), assessing the haemoglobin level and the platelet count. **Results:** There was a significant negative correlation between haemoglobin and platelet count and a significant increase in platelet count with disease activity. **Conclusion:** 76.6% were in fourth-sixth decades of life with a female predominance. Anaemia was found in (46.7%) of cases and the degree of anaemia increased with disease activity. The anaemia was mostly of normochromic normocytic type (82.14%). Thrombocytosis was found in (63.3%) of patients and it had a significant positive correlation with Ritchie index ($p \leq 0.05$).

KEYWORDS: Rheumatoid Arthritis, Haemoglobin, Anemia, Platelet, Thrombocytosis.

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic inflammatory connective tissue disease with polyarthritis as a prominent feature. However, extra-articular symptoms and signs are always present. The prevalence of the disease in women is about 1% and in men about 0.5%.^[1] The disease can occur at any age but according to common age of occurrence the disease can be categorized into a young-onset RA (YORA) which usually begins between 30 and 40 years of age, whereas RA developing after 60 to 65 years of age is usually called late-onset RA (LORA).^[2] With female to male ratio of 3:1.^[3]

The diagnosis of the RA is made by clinical observation of the patients, that is depend on the presence of sufficient number of criteria as defined by the American College of Rheumatology (ACR).^[4] Anaemia is often present in patients with active RA.^[5-7] It is the most common extra-articular manifestation,^[8] and the degree of anaemia in RA is related to the activity of the

underlying disease and inflammation.^[9] Treatment of the underlying activity will usually improve the anaemia.^[10,11] It has been reported that RA patients with anemia seemed to have a more serious course and physical disability than those without anemia.^[12,13] The most common type of anaemia seen in rheumatoid patients is anaemia of chronic disease (normochromic normocytic) (60–90%) followed by (hypochromic microcytic)(8–30 %).^[14,15] The mechanism resulting in anaemia has attracted the attention of numerous investigators.^[16] Mild haemolytic tendency of an extra-corporeal type has been confirmed but it is insufficient to explain the associated anaemia in the presence of adequate marrow compensation.^[17] Expanded plasma volume with secondary haemodilution may play a minor role.^[18]

Other causes of anaemia are impairment of the release of iron from the reticuloendothelial tissue,^[19] sequestration of iron in the inflamed synovial tissue,^[20] impairment of iron utilization due to increased lactoferrin which binds

and lowers serum iron, reduced erythropoietin levels, also the increased production of inflammatory cytokines (e.g. tumor necrosis factor) that is observed in RA is linked to a cytokine-mediated decrease bone marrow response to erythropoietin,^[16,20] drug associated anaemia specially non-steroidal anti-inflammatory drugs (NSAIDs) induced bleeding and secondary iron deficiency and bone marrow suppression from drug therapy like gold, penicillamine, methotrexate.^[14,21] Still other causes of anaemia are intercurrent infection.^[17] Decreased iron absorption, where investigations of the upper gastrointestinal tract by endoscopy showed that acute macroscopic lesions are infrequently associated with anaemia.^[22]

Thrombocytosis has often been found in association with active RA.^[23] Also an association appeared to exist between thrombocytosis and extra-articular manifestation of RA.^[24] The Exact pathogenic mechanism(s) that cause increased platelet counts in RA are still unknown. Recent investigations indicate that proinflammatory cytokines of RA have megakaryocytopoietic / thrombopoietic properties. Moreover, several hematopoietic cytokines can also act as acute phase responders and contribute to the inflammation.^[25] Thrombopoietin (TPO) is the major regulator of growth and differentiation of megakaryocytes. Recent studies have shown that TPO may also act as an acute-phase reactant, and it has been suggested as a component of inflammatory reactions.^[26]

METHODS AND SUBJECTS

Sixty patients with active rheumatoid arthritis (according to the criteria of the American College of Rheumatology), (10) males, (50) females, aged between (19-70) years, with mean (45.15) years, and the disease duration was (1-27) years with mean (6.38) years under treatment, attending Ibn-Sina Teaching Hospital in Mosul were studied during a period of eight months. Patients were considered to have an active disease according to the parameters of assessing disease activity.^[11]

Blood Sampling and Processing

A two ml of venous blood sample were obtained and added to EDTA tube to be used for performing haemoglobin level and platelet count.^[27]

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 showing full clinical and hematological data of the patients as demonstrated in the Table1 below with their relevant statistical analysis Fig. 1, Fig. 2, and Fig. 3.

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
Haemoglobin (g/L)	119.23	14.41	80.00-155.00
Platelet x 10 ⁹	435.55	113.08	173.00-775.00

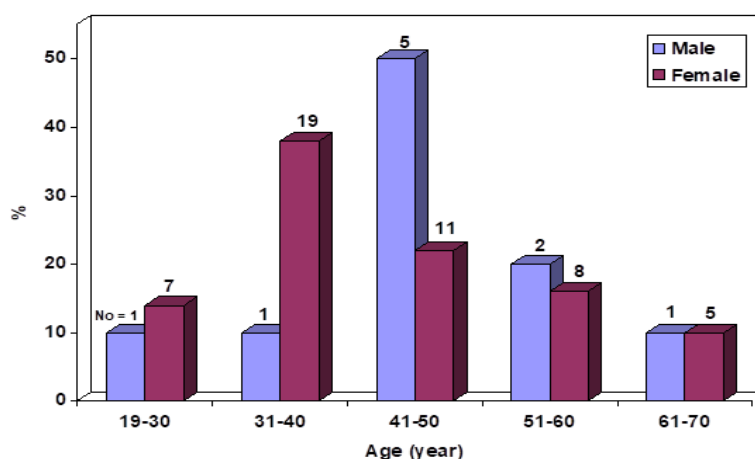


Figure (1): Age and sex distribution of patients.

There was a significant negative correlation between haemoglobin and platelet count as seen in Fig. 2

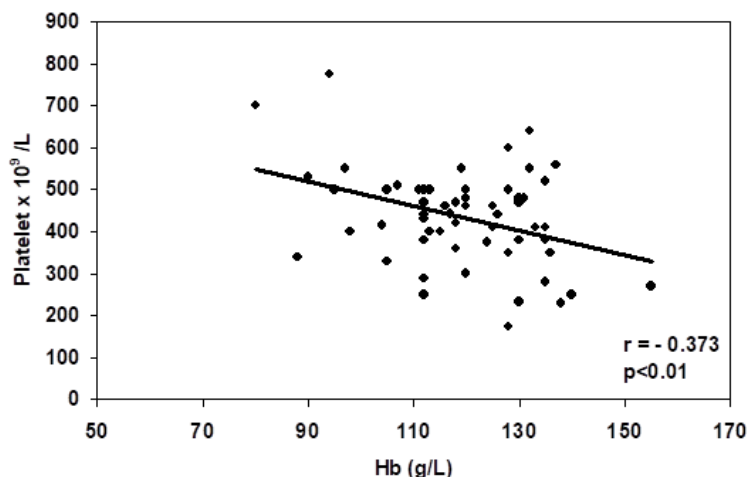


Figure (2): Scatter diagram between haemoglobin and platelet count of patients.

There was a significant increase in platelet count with the increase in the disease activity as shown in Fig 3.

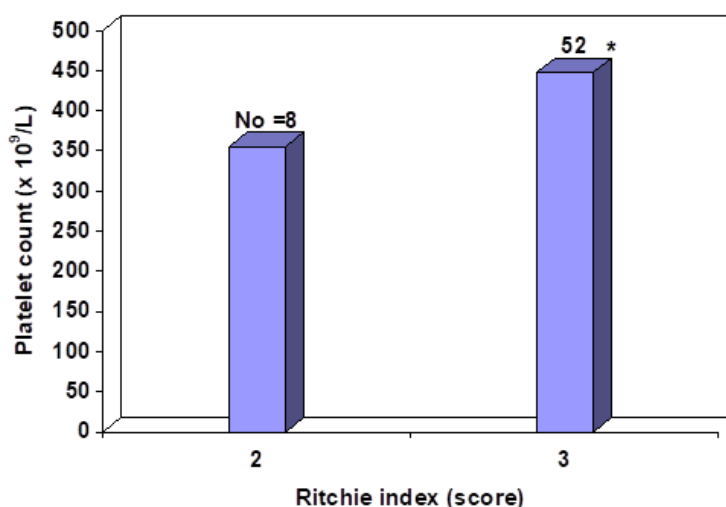


Figure (3): Effect of disease activity (Ritchie index) on platelet count in patients.

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.^[10,28] The age range of the patients are between (19 to 70) years, with mean of (45.15) years, (76.6 %) of them were in the fourth to sixth decades of life. This is similar to other studies as RA is more frequent in this period of life.^[29] The gender variation shows female to male ratio is 5 to 1 and this distribution of sex agrees with that reported in other studies which revealed that females affected 5 times more than males.^[30] Anaemia was found in (46.7%) of our patients, (17.86%) of them had hypochromic microcytic anaemia, while the other (82.14%) had normochromic normocytic anaemia. This agrees with that reported in other studies

which stated that anemia develops in 30-70% of patients with RA and the most common type of anaemia seen in rheumatoid patients is anaemia of chronic disease (normochromic normocytic) (60-90%), followed by hypochromic microcytic (8-30%).^[7,31] The cause for normochromic normocytic anaemia may be due to reduced erythropoietin levels or decreased bone marrow response to erythropoietin, or may be drug associated specially non-steroidal anti-inflammatory drugs, while the cause of hypochromic microcytic anaemia may be due to impairment of the release of iron from the reticuloendothelial tissue.^[17,32] Thrombocytosis was found in (63.3%) of patients, and this agrees with the results of other workers which may be due to proinflammatory cytokines which have megakaryocytopoietic / thrombopoietic properties. Thrombocytosis was shown with the increase of disease activity which is reflected by

Ritchie index, and this is similar to what is reported in some other studies.^[33]

CONCLUSION

- 1) 76.6% of patients were in fourth to sixth decades of life, with male to female ratio of 1:5.
- 2) Anaemia was found in 28/60 (46.67%) of cases, and it is associated more with disease activity. Anaemia was mostly of normochromic normocytic type (82.14%) and of hypochromic microcytic type in (17.9%).
- 3) Thrombocytosis was found in (63.3%) of cases and it is correlated negatively with haemoglobin, and also thrombocytosis associated with disease activity as seen from positive correlation between platelet count and Ritchie index score.

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REFERENCES

1. Symmons DP. Epidemiology of rheumatoid arthritis: determinants of onset, persistence and outcome. *Best Pract Res Clin Rheumatol*, 2002; 16(5): 707-722.
2. Krams T, Ruysen-Witrand A, Nigon D, Degboe Y, Tobon G, Fautrel B, Berenbaum F, Cantagrel A, Constantin A. Effect of age at rheumatoid arthritis onset on clinical, radiographic, and functional outcomes: The ESPOIR cohort. *Joint Bone Spine*, 2016; 83(5): 511-515.
3. Al-Shukaili AK, Al-Jabri AA. Rheumatoid arthritis, cytokines and hypoxia. What is the link? *Saudi Med J*, 2006; 27(11): 1642-1649.
4. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, Birnbaum NS, Burmester GR, Bykerk VP, Cohen MD, Combe B, Costenbader KH, Dougados M, Emery P, Ferraccioli G, Hazes JM, Hobbs K, Huizinga TW, Kavanaugh A, Kay J, Kvien TK, Laing T, Mease P, Ménard HA, Moreland LW, Naden RL, Pincus T, Smolen JS, Stanislawski-Biernat E, Symmons D, Tak PP, Upchurch KS, Vencovský J, Wolfe F, Hawker G. Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum*, 2010; 62(9): 2569-2581.
5. Freireich EJ, Miller A, Emerson CP, Ross JF. The effect of inflammation on the utilization of erythrocyte and transferrin bound radioiron for red cell production. *Blood*, 1957; 12(11): 972-983.
6. Mowat A. Haematological abnormalities in rheumatoid arthritis. *Semin Arthritis Rheum*, 1971; 1: 383-390.
7. Nikolaisen C, Figenschau Y, Nossent JC. Anemia in early rheumatoid arthritis is associated with interleukin 6-mediated bone marrow suppression, but has no effect on disease course or mortality. *J Rheumatol*, 2008; 35(3): 380-6.
8. Hollander JL, McCarty DJ. *Arthritis and Allied Conditions*. 10th ed. Lea and Fabiger: Philadelphia, 1985; 620.
9. Yunt ZX, Solomon JJ. Lung disease in rheumatoid arthritis. *Rheum Dis Clin North Am*, 2015; 41(2): 225-36.
10. Dennis L. Kasper, Anthony S. Fauci, Stephen L. Hauser, Dan L. Longo, J. Larry Jameson, Joseph Loscalzo. *Harrison's Principles of Internal Medicine*. 20th ed. New York; McGraw Hill Education, 2018; 2527-2540.
11. Stuart H Ralston, Ian D Penman, Mark WJ Strachan, Richard P Hobson. *Davidson's Principles and Practice of Medicine*. 23rd ed. Edinburgh; Elsevier, 2018; 1021-1026.
12. Van Steenberg HW, van Nies JA, van der Helm-van Mil AH. Anaemia to predict radiographic progression in rheumatoid arthritis. *Ann Rheum Dis*, 2013; 72(7): 16.
13. Möller B, Scherer A, Förger F, Villiger PM, Finckh A; Swiss Clinical Quality Management Program for Rheumatic Diseases. Anaemia may add information to standardized disease activity assessment to predict radiographic damage in rheumatoid arthritis: a prospective cohort study. *Ann Rheum Dis*, 2014; 73(4): 691-696.
14. Fitzsimons EJ, Sturrock RD. The chronic anaemia of rheumatoid arthritis: iron banking or blocking? *Lancet*, 2002; 360(9347): 1713-1714.
15. Wahle M. Anämie bei Patienten mit rheumatoider Arthritis [Anemia in patients with rheumatoid arthritis]. *Z Rheumatol*, 2012; 71(10): 864-868.
16. Agrawal S, Misra R, Aggarwal A. Anemia in rheumatoid arthritis: high prevalence of iron-deficiency anemia in Indian patients. *Rheumatol Int*, 2006; 26(12): 1091-1095.
17. Porter DR, Sturrock RD, Capell HA. The use of serum ferritin estimation in the investigation of anaemia in patients with rheumatoid arthritis. *Clin Exp Rheumatol*, 1994; 12(2): 179-182.
18. Jeffrey MR. Haemodilution in rheumatoid disease. *Ann Rheum Dis*, 1956; 15(2): 151-159.
19. Means RT Jr, Krantz SB. Progress in understanding the pathogenesis of the anemia of chronic disease. *Blood*, 1992; 80(7): 1639-1647.
20. Dabbagh AJ, Trenam CW, Morris CJ, Blake DR. Iron in joint inflammation. *Ann Rheum Dis*, 1993; 52(1): 67-73.
21. Sosin M, Handa S. Low dose methotrexate and bone marrow suppression. *BMJ*, 2003; 326(7383): 266-267.
22. Doube A, Davis M, Smith JG, Maddison PJ, Collins AJ. Structured approach to the investigation of anaemia in patients with rheumatoid arthritis. *Ann Rheum Dis*, 1992; 51(4): 469-472.
23. Gudowska M, Gruszevska E, Wrona A, Gindzienska-Sieskiewicz E, Domyslawska I, Lipartowska-Klimuk K, Cylwik B, Sierakowski S, Chrostek L. The Profile of Serum Transferrin

- Isoforms in Rheumatoid Arthritis. *J Clin Rheumatol*, 2019; 25(4): 159-162.
24. Hutchinson RM, Davis P, Jayson MI. Thrombocytosis in rheumatoid arthritis. *Ann Rheum Dis*, 1976; 35(2): 138- 142.
 25. Ertenli I, Kiraz S, Oztürk MA, Haznedaroğlu Ic, Celik I, Calgüneri M. Pathologic thrombopoiesis of rheumatoid arthritis. *Rheumatol Int*, 2003; 23(2): 49-60.
 26. Kiraz S, Ertenli I, Oztürk MA, Haznedaroğlu IC, Celik I, Kirazli S, Calgüneri M. Bloodstream thrombopoietin in rheumatoid arthritis with thrombocytosis. *Clin Rheumatol*, 2002; 21(6): 453-456.
 27. Bain BJ, Bates I, Laffan MA. *Dacie and Lewis Practical Haematology*. 12th ed. London; Elsevier, 2017; 1-7: 30-45.
 28. Adam Feather, David Randall, Mona Waterhouse. Kumar and Clark's *Clinical Medicine*. 10thed. London; Elsevier, 2021; 437-447.
 29. Slimani S, Abbas A, Ben Ammar A, Kebaili D, Ali el H, Rahal F, Khamari MC, Baltache A, Khider I, Chiheub R, Khelif K, Akbi S, Rahmani S, Dahou-Makhloufi C, Brahimi-Mazouni N, Abtroun-Benmadi S, Ladjouze-Rezig A. Characteristics of rheumatoid arthritis in Algeria: a multicenter study. *Rheumatol Int*, 2014; 34(9): 1235-1239.
 30. Nesreen SA, Ibrahim MS, Amira MM. Gender Impact on Rheumatoid Arthritis Disease Characteristics in A Cohort of Egyptian Patients. *Med J Cairo Univ*, 2019; 87(63): 1895-1899.
 31. Peeters HR, Jongen-Lavrencic M, Raja AN, Ramdin HS, Vreugdenhil G, Breedveld FC, Swaak AJ. Course and characteristics of anaemia in patients with rheumatoid arthritis of recent onset. *Ann Rheum Dis*, 1996; 55(3): 162-8.
 32. Theurl I, Mattle V, Seifert M, Mariani M, Marth C, Weiss G. Dysregulated monocyte iron homeostasis and erythropoietin formation in patients with anemia of chronic disease. *Blood*, 2006; 107(10): 4142-8.
 33. Zhou Z, Chen H, Ju H, Sun M, Jin H. Platelet indices in patients with chronic inflammatory arthritis: a systematic review and meta-analysis. *Platelets*, 2020; 31(7): 834-844.