Assessment the Role of Erythrocyte Sedimentation Rate and C-Reactive Protein Tests For Prediction Of Rheumatoid Arthritis Activity In Misan Province

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Abstract Rheumatoid Arthritis (RA) activity was assessed based on erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) tests. The ESR and CRP tests were monitored in 25 Rheumatoid Arthritis diagnosed patients and 25 healthy approved cases of suspected patients from Missan Province. The sample comprised of 25 male and 25 females with ages varied from 21-68 years and body weights from 45 – 112 kg. ESR readings in RA diagnosed patients varied between 22 – 116 averaged 46.8 mm/h in patients case while those recorded in the healthy approvrd cases ranged between 4-18 averaged 8.4 mm/h. Differences between patients and control cases were statistically significant ($P < 0.05$). This approved that measuring ESR is a valid tool to predict RA among Missan population. CRP test showed only 2 negative results among RA patients compared with 15 negative results in healthy approved cases. CRP values in patients sample ranged between 10 mg/dl in 11 cases and 24 – 48 mg/dl in another 11 cases with only one highly extreme value of 96 mg/dl. In he healthy approved cases, CRP values ranging from 6-12 mg/dl were recorded in 10 cases and negative results in the rest 15 cases. differences were highly significant ($p < 0.01$) indicating the validity of CRP test to predict RA cases. Both parameters varied among various age groups, gender and body weight classes. Apparantly both ESR and CRP tests may help to find or monitor inflammation in acute or chronic conditions of rheumatoid arthritis.

1. INTRODUCTION

Rheumatoid arthritis RA is a chronic inflammatory autoimmune disease where the patient's immune system attacks the body's own tissues. Symptoms usually include pain, swelling and stiffness with some functional impairment. More general symptoms such as fatigue, loss of appetite and low-grade fever can also be observed in many patients (Harris 2005). The American College of Rheumatology (2002) stated that the age of RA onset is between 30 and 55 years and it affects women more than men (ratio 3:1) with prevalence varies from 0.5% to 1.5% of the population. According to Duhme (2018) there are many rheumatic disorders, with similar signs and symptoms which may overlap and need expert for diagnosis and treatment. RA patients are often at a higher risk for anxiety and depression (Arnett, 1988). In addition to causing peripheral symptoms, RA may also involve the cervical spine, causing pain in the neck and occipital headache (Goekoop-Ruiterman, 2005). Extra-articular features are common and may involve multiple organs, including the skin, eyes, lungs, and blood vessels. (Van-Gaalen, 2004). Physical therapy is effective in management of rheumatoid arthritis; there is evidence to support aerobic and strengthening exercises, transcutaneous electrical nerve stimulation, and ultrasound (Majithia, and Geraci, 2007).

Different measures are used for evaluating disease activity in rheumatoid arthritis. Laboratory tests such as the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) have been used as markers of inflammation, although there is still no clear consensus on when to use one, the other, or both (Kennnan et al. (2008) . Among these tests CRP had become the more preferred serological marker for evaluating acute disease activity (Skogh et al., 2003). People with rheumatoid arthritis often have an elevated ESR, or CRP levels, which may indicate the presence of an inflammatory process in the body as reported by Mayo Clinic Staff (2021).

The present study aims at measuring the activity of Rheumatoid Arthritis (RA) disease among patients in Misan Province based on erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).

2. MATERIALS AND METHODS

2.1. Sampling

The ESR and CRP tests were monitored in 25 Rheumatoid Arthritis diagnosed patients and 25 healthy approved cases of

suspected patients. The patients sample comprises of 15 male and 10 females. While the control sample comprised of 15 female and 10 males. The age of healthy sample varied between 21 – 55 year, those of the patients sample between 22-68 year. The weight of the healthy sample 45 – 87 kg and for patients 65 – 112 kg. Blood samples were collected and analyzed according to standard methods ESR by Westergren method and CRP by ELISA method, as follows:

2.2. ESR Analysis Method

This method was developed by Westergren (1981-1968). The most acceptable and indicative method of inflammation. Four ml of venous blood is required and filled the Westergren tube to the 0 mark. Mix with sodium citrate anticoagulants and place the tube in the rack at room temperature. Readings were taken exactly 1 hour later and read the millimeters from the top surface of the column to the top of the RBC deposit.

2.3. CRP Analysis Method

0.5 mL of serum is to be diluted at 1:2 for a semi-quantitative CRP test. It is necessary to dilute the serum until a positive

agglutination reaction is observed. the serum is diluted in a serial double dilution. The serial double dilution procedure used up to the sixth tube. Determine the thinning and dilution factor for each tube. Prepare 6 groups of tubes. To tube #1 add 0.5 mL of serum and 0.5 mL of NSS. A positive CRP test indicates a medical condition and can help the clinician in resolving the patient's health condition.

3. RESULTS & DISCUSSION

3.1 ESR in Rheumatoid Arthritis Patients

ESR readings in Rheumatoid Arthritis (RA) patients compared with the healthy cases from Misan province are shown in Tables (1 & 2) respectively. It has been noted that ESR readings ranged between 22 – 116 mm/h in 21 patients case (Table 1). These values are significantly ($P < 0,05$) higher than those recorded in the healthy case which ranged between 4-18 mm/h (Table 5). The extreme values of 71 & 116 mm/h were recorded in two patients only. The highest frequency (12 patients) occurred in the range of 15- 30 (av. 22.5) mm/h (Table, 1). As for the healthy cases (Table 5), the high frequency occurred within the range 1 – 15 mm/h with an average value of 4-12 mm/h. Only one case has shown a high value of 18 mm/h for the healthy case.

Table (1) Frequency of occurrence of ESR readings (mm/h) with average values among RA patients in Missan Province

ESR range	NO	Average
30-15	12	22.5
45-30	5	37
60-45	2	57
75-60	1	71
90>	1	116

Table (2) Frequency of occurrence of ESR (mm/h) with average values among healthy cases in Missan Province

ESR range	NO	Average
5-1	7	3.71
10-5	8	7.87
15-10	8	12.5
15>	1	18

A high ESR test result may be from a condition that causes inflammation, such as: Arteritis – Systemic vasculitis - Polymyalgia rheumatica - Inflammatory bowel disease - Kidney disease – Infection - Rheumatoid arthritis - Heart disease - Certain cancers and other autoimmune diseases (Mayo Clinic Staff, 2021). To compare our results in Missan province with those for RA patients published by Mayo Clinic in 2021 in which ESR values averaged 30 mm/h in patients and 12 mm/h in the control group. Our results are comparable with Mayo clinic values for healthy cases, the patients values,

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however, were lower (22 mm/h) in 12 cases and higher (47 mm/h) in 9 cases. This approved that measuring ESR is a valid tool to predict RA among Missan population. The above results are also comparable to those obtained by Yousef et al. (2015) in Egypt who found ESR ranged from 10 to 150 mm/h in first hour (Mean ± SD 52.9 ± 33.9).

A low ESR test result such as those recorded in our control cases (3-7 mm/h) means that red blood cells sank more slowly than normal. This may be caused by conditions such as: A blood disorder (Polycythemia , Sickle cell disease, Leukocytosis, a very high white blood cell count)in addition to other diseases such as Heart failure or certain kidney and liver problems Silva (2010). The ESR up-normal results doesn't always mean a medical condition that needs treatment. Silva (2010) pointed out that, pregnancy, a menstrual cycle, aging, obesity, drinking alcohol regularly, and exercise can affect ESR results. Certain medicines and supplements may also affect your results, so be sure to tell your provider about any medicines or supplements you are taking.

3.2 CRP in Rheumatoid Arthritis Patients

Results concerning the relationship between CRP and Rheumatoid Arthritis are shown in Table (3) and (4). As for RA

patients in Missan CRP values ranged between 10 mg/dl as mild value in 11 patients to moderate values of 24 – 48 mg/dl occurred in 11 cases and a single extreme value of 96 mg/dl (Table, 3). The above results are comparable to those obtained by Yousef et al. (2015) in Egypt who found positive CRP test in 54 RA patients but negative in 26 patients (67.5% versus 32.5%), the CRP values ranged from 0.6 to 65 mg/dl (Mean ± SD 18.1 ± 15.8).

The above results indicates that higher CRP levels are associated with greater RA disease activity. Indeed, CRP levels are widely used for monitoring systemic inflammation and disease activity in RA patients. CRP level is a component of several composite disease activity measures as suggested by Dessein et al. (2004).

As for the healthy control samples (Table 4), values ranged between 6 – 12 mg/dl in 10 cases while 15 cases showed negative results. To compare CRP values with patients cases (10 – 48 mg/dl), differences were highly significant (p< 0.01) indicating the validity of CRP test to predict RA cases in Missan Province. According to Silva (2010), CRP test may be used to help find or monitor inflammation in acute or chronic conditions of rheumatoid arthritis.

Table (3): Frequency of occurrence and average CRP readings (mg/dl) for RA Patients in Missan Province

CRP	NO	AV
-ve	2	-
5-15	11	10.4
15-25	5	24
55-45	6	48
> 55	1	96

Table (4): Frequency of occurrence and average CRP readings (mg/dl) for healthy cases in Missan Province

CRP	NO	Average
10-5	5	6
25-10	5	12
negative	15	_

3.3 Impact of Gender on ESR Readings

Data of Table (5) showed that ESR values in patients (averaged 46.8 mm/h) are high compared with those in healthy cases (averaged 8.4 mm/h). Differences are highly significant (p<0.01). As for the effect of gender, ESR values in male

patients (34.5 mm/h) were less than those of females patients (59.1 mm/h). Differences between male and female patients were significant (p<0.05). On contrary ESR values in healthy males and females are nearly similar and differences are not significant (p>0.05), they varied between 8.1 - 8.8 mm/h.

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Table (5): Comparison of ESR values between males and females

Patients	Gender	No.	Av. (mm/h)
	Male	15	**34.5**
	Female	10	**59.1**

Healthy	Gender	No.	Av. (mm/h)
	Male	10	8.1
	Female	15	8.8

3.4 Impact of Age on ESR Readings

It can be seen from the below data that ESR values increased with age in both RA patients but not with the control. However, patients with old ages recorded the highest ESR values 97.3 mm/h. As for comparison between ages, at the 50-59 years age group the patient recorded an average ESR 45.2 mm/h compared with only 9.0 mm/h in the control indicating the impact of age in increasing ESR and RA disease in turn (Table 6). Values of all age groups in patients are significantly ($p<0.05$) different from ESR of the same age group in the control sample.

Table (6): Comparison of ESR values on the basis of ages in RA patients and control healthy cases

Age (year) Patients	NO	Av. ESR	Age (year) Healthy	NO	Av. ESR
29-20	4	21.5	29-20	9	8.7
39-30	5	25.4	39-30	7	8.7
49-40	9	46.9	49-40	3	9.0
59-50	4	45.2	59-50	5	9.0
69-60	3	97.3	-	-	-

3.5 Impact of Weight on ESR Readings

For healthy (control) sample increasing weight has not led to a corresponding increase in ESR values. Correlation was weak ($r^2 = 0.4530$) (Table 7). On the other hand, ESR values in RA patients showed a clear ascending trend with the increase of body weight ($r^2 = 0.8631$). These data indicate the possibility of suffering from RA in overweight people

.Table (7): Comparison of ESR values on the basis of weight in RA patients and control healthy cases

Patients Body Wt. (kg)	No.	Av. ESR (mm/h)
60-69	4	22.5
70-79	5	27.4
80-89	6	45.8
90-99	7	47.5

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100>	3	77.0
Healthy Body Wt. (kg)	No.	Av. ESR (mm/h)
40-49	2	6.5
50-59	8	10.4
60-69	4	5.7
70-79	8	9.7
880-89	3	5.3

4. Conclusions

i. The significant correlation between ESR and CRP tests with Rheumatoid arthritis activity indicated the importance of performing both tests for evaluation .

ii. Both measures are useful for assessing RA activity and may enable physicians to easily assess the disease activity .

iii. Factors such as age, gender and body weight are essential for monitoring in RA patients.

REFERENCES

[1] American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines (2002). Guidelines for the management of rheumatoid arthritis: update. *Arthritis Rheum*. 2002;46:328-346.

[2] Arnett F.C., Edworthy S.M., Bloch DA, McShane D.J., Fries J.F., Cooper N.S., Healey L.A., Kaplan SR, Liang M.H,, Luthra H,S. (1988). The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum; 31:315–24.

[3] Deighton C, O'Mahoney R, Tosh J, Turner C, Rudolf M (2009). Guideline Development Group. Management of rheumatoid arthritis: summary of NICE guidance. BMJ;338:710–2.

[4] Dessein P.H. , Joffe B.I. , Stanwix A.E. (2004). High sensitivity C-reactive protein as a disease activity marker in rheumatoid arthritis. J Rheumatol, 31 (2004), pp. 1095-1097.

[5] Firestein GS. (2005). Etiology and pathogenesis of rheumatoid arthritis. In: *Kelley's Textbook of Rheumatology*, 7th ed. Philadelphia, PA: W.B. Saunders : 996-1042.

[6] Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, van Zeben D, Kerstens PJ, Hazes JM, Zwinderman AH, Ronday HK, Han KH, Westedt ML, et al. (2005). Clinical and radiographic outcomes of four different treatment strategies in patients with early rheumatoid arthritis : a randomized, controlled trial. Arthritis Rheum, 52:3381–90.

[7] Harris ED. (2005). Clinical features of rheumatoid arthritis. In: *Kelley's Textbook of Rheumatology,* 7th ed. Philadelphia, PA: W.B. Saunders; 1043-1078.

[8] Keenan R.T, Swearingen C.J, Yazici Y (2008): Erythrocyte sedimentation rate and C-reative protein levels are poorly correlated with clinical measures of disease activity in rheumatoid arthritis, systemic lupus erythematosus and osteoarthritis patients. Clinical and Experimental Rheumatology; 26: 814-819. 3.

[9] Lawrence RC, Helmick CG, Arnett FC, Deyo RA Felson DT, Giannini EH, Heyse SP, Hirsch R, Hochberg MC, Hunder GG, et al. (1998). Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. Arthritis Rheum , 41:778–99.

[10]   Majithia, V. and Geraci, S. A. (2007). Rheumatoid Arthritis: Diagnosis and Management. The American Journal of Medicine (2007) 120, 936-939.

[11]   Mayo Clinic Staff (2021) Departments & Centers. Medical Departments & Centers Rheumatology. Inflammatory Arthritis Clinic.

[12]   Pope. J.E. and Choy, E. H. (2021). C-reactive protein and implications in rheumatoid arthritis and associated comorbidities. Seminars in Arthritis and Rheumatism , 51, (1) : 219-229

[13]   Skogh T, Gustafsson D, Kjellberg M and Husberg M (2003): Twenty eight joint count disease activity score in recent onset rheumatoid arthritis using C reactive protein instead of erythrocyte sedimentation rate. Ann Rheum Dis.; 62: 681-82

[14]   Sluka KA. Osteoarthritis and rheumatoid arthritis. In: Sluka KA, editor. Mechanisms and management of pain for the physical therapist. Seattle: IASP Press; 2009. p. 349–360.

[15]   Van-Gaalen FA, Linn-Rasker SP, van Venrooij WJ. (2004). Autoantibodies to cyclic citrullinated peptides predict progression to rheumatoid arthritis in patients with undifferentiated arthritis: a prospective cohort study. *Arthritis Rheum*. 50(3):709-715.

[16]   Yousef, M.E. , Elshabacy, F.A. , Abdelrahman, S. K. , Mohamed.T. F. (2015). Comparison between ESR and C-Reactive Protein(CRP) as a Marker of Disease activity in Patients with Rheumatoid Arthritis. Egypt J Rheumatology & Clinical Immunology, 2015; 3(1): 77-81.