Rheumatiod Factor isotype in Rheumatiod Arthritis patients .

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Summary

Background: *Rheumatiod factor in patients with Rheumatoid arthritis (RA) could be of IgM, IgG, or IgG isotypes.*
Aim*: To study the occurance of each or all these isotypes in RA patients .*
Methods: *Enzyme linked Immune Sorbent Assay (ELISA) & Latex agglutination test were used to asses RF in 74 patients with RA.*
Results: *Using ELISA, 58 (78.4%) patients had positive RF (IgM 48.6%, IgG in 47.3% & IgA in 54.1%), while only 43 (58.1) patients were positive by AG .*
Conclusion *All RF isotypes should be assessed in patients with RA.*
Key words *: RA, RF, IgG, IgM, IgA, ELISA, AG.*

Introduction :

RA is a systemic inflammatory disease that predominantly affects synovial membrane of diarthridal joints (1). One of the characteristic features of this disease is the production of autoantibodies against Fc portion of immunoglobulin G. These autoantibodies are generally known as RF and may be IgA, IgG, or IgM isotypes and it might be present all three together or only two types or just one.

Patients and Methods

Patients: Seventy four patients (19 male, 55 female) with RA who met the American College of Rheumatology (ACR)1987revised criteria (2) attending the rheumatology consultation clinic or admitted to Baghdad Teaching Hospital in a period between November 2001 and February 2002.

Laboratory investigation:

RF was detected using the latex test which has been supplied by Biokit company, Spain, and results were expressed in international unit / ml (IU / ml). The ELISA technique used human IgG Fc as the antigen (Sigma, St. Louis, Mo.) coated the microwells plate and isotype-specific horse antibodies coupled to radish peroxidase; result were expressed as the optical density. A level>20 IU/ ml was considered positive .

Results

The male to female ratio was 1:2.9 with the mean age 42.1±11.3 as shown in table 1&2.
Rheumatoid factor Fourty three patients were RF positive (58.1%), while the rest (41.9%) were negative these detected by latex agglutination test where 10 IU/ml was the best cutoff with sensitivity 58.1%, while by ELISA technique 25 IU/ml was the best cutoff with sensitivity of 78.4% as shown in table 3.

In relation to RF isotypes as expressed in the same table where IgA, IgG & IgM RF was 20 IU/ml the best cutoff with sensitivity 54.1, 47.3 & 48.6% respectively.

Considering RF concentration for positive cases that the median was 63 IU/ml; range 25-600 IU/ml as shown in table 4.

Table 5 shows that IgA RF concentration that median was 96 IU/ml; range 27-600 IU/ml. It has been noticed that the median concentration of IgG RF was 160 IU/ml; range 27-600 IU/ml. Considering IgM RF concentr- ation the median was 310 IU/ml; range 21-600 IU/ml.

Table 1 : Age distribution of RA patients

	RA	
Age in years	**N**	**%**
<20	1	1.4
20-29	9	12.2
30-39	23	31.0
40-49	19	25.7
50-59	16	21.6
60+	6	8.1
Total	**74**	**100**
Range	18-67	
Mean	42.1	
SD	11.3	

Table 2: Distribution of patients by gender

	RA	
	N	**%**
gender		
Female	55	74.3
Male	19	25.7
Total	74	100

Table 3 : Detection of RF and RF isotypes

Test	RA	Sensitivity
RF by latex		
Negative	31	
Positive >10	43	58.1%
RF by ELISA		
Negative (<25)	16	
Positive (>25)	58	78.4%
RF- IgA type by ELISA		
Negative (<20)	34	
Positive (>20)	40	54.1%
RF- IgG type by ELISA		
Negative (<20)	39	
Positive (>20)	35	47.3%
RF- IgM type by ELISA		
Negative (<20)	38	
Positive (>20)	36	48.6%

Table 4 : Median serum RF concentration (IU/ml) in RA patients.

* Rheumatoid factor	RA
RF by ELISA	
Range	25-600
Mean	194.9
Median	63
SD	233.9
N	58

***Detect by ELISA positive > 24 IU/m**

According to the frequency distribution of RF isotypes number table 6 revealed that 10.8% has one type either IgA or IgM RF in 6 (8.1%) and 2 (2.7%) patients respectively . Presence of two types of RF together Were 23% either (IgA+IgM) , (IgA+IgG) or (IgG+IgM) were found in 5 (6.8%) , 6(8.1%) and 6(8.1%) respectively . Finally, the combination of three RF isotypes was found in 23 (31.1%).

* RF isotypes	RA
IgA	
Range	27-600
Mean	171.3
Median	96
SD	188
N	40
IgG	
Range	27-600
Mean	309.8
Median	160
SD	261.5
N	35
IgM	
Range	21-600
Mean	379.6
Median	310
SD	223.8
N	36

*** Detect by ELISA**

Table 6: Frequency distribution of RF and RF isotypes among RA patients

RF isotypes	RA	
	N	%
Negative for all Ig types	26	35.1
IgA + IgG + IgM	23	31.1
IgA + IgM	5	6.8
IgA + IgG	6	8.1
IgG + IgM	6	8.1
IgA	6	8.1
IgM	2	2.7
Total	**74**	**100**

Discussion

The male to female ratio in this study was 1:2.9 which is somewhat comparable to 1:2.7 reported by Ubaid (3) locally & canstantine (1:3.4) abroad (4), and higher than Farhat (1:2.1) & Saraux (1:2.1) (5,6),this is well accepted that females are more prone to have autoimmune disease than males & that simply might be related to sex hormone e.g. estrogen.

It is generally accepted that RF have been widely used as an immune marker, hence Latex agglutination test was 58.1% shown to be less than other Iraqi studies where 72.6%, 75.3% as had been reported by Ubaid, & Al-Rawi, respectively (3,7) while abroad studies showed 56.6% and 70% which were reported by Adhya, & Tighe and Carson, respectively (8,9).

Unlike agglutination tests which failed to detect other RF isotypes rather than IgM, the other technique, ELISA did this job quite well. Moreover this technique usually discriminates RF isotypes where (45.1,47.3, & 48.6%) showed positivity for IgA, IgG & IgM respectively compared with other studies abroad where (44,59, & 65%) and other study (44,72,& 69%) for IgA, IgG & IgM respectively (5,10), these differences may be related to the source of the kit or some vague other reasons which need further studies.

In spite of IgM RF which was regarded as the classical one that detected by latex and found in higher rate than the other two RF types in many abroad studies (10). Yet other studies suggested that IgG and IgA RF may be more specific than IgM RF and may assist in the diagnosis (11), in this study presence of these RF isotypes where nearly to be equal to each other.

In relation to frequency distribution of RF isotypes number was showed that the combination of (IgA+IgG+IgM) with 31.1% higher than 23% and 10.8% for two and one type of RF isotypes.

References:

1.ope RM. Rheumatoid Arthritis: Pathogenesis and Early Recognition . Am J Med 100 Suppl+ 2A.:35-95,1996.

2- Arnett FC, Edworthy SM, Bloch DA, Mc.Shane DJ, Fries JF, Cooper NS. et al . The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis . Arthritis Rheum 1988;31:315-24.

3- Ubaid AH: Formal education level as a marker of clinical status in RA among Iraqis. A thesis submitted to the college of Medicine, University of Baghdad for the partial fulfillment of the Master Degree in Community Medicine (1996).

4- Farhat HF: Antiphospholipid antibodies in Rheumatoid arthritis. Clinical and Laboratory correlations. A thesis submitted to the college of Medicine, University of Baghdad in Partial Fulfillment of the Requirements for the Degree of Master of Science in pathology. (2000).

5- Saraux A, Berthelot JM, Charles G, et al. Value of laboratory Tests in Early Prediction of Rheumatoid Arthritis. J, Arthi & Rheum. 2002; 47(2):155-65.

6- Constantin A, Cances VL, Navaux F, et al. Stromelysin 1 (Mafrix Metalloproteinase 3) and HLA-DRB1 Gene Polymorphisms- J. Arth. & Rheum. 2002; 46(7):1754-62.

7- AL-Rawi ZS, Al Azzawi AJ, Al Ajili FM, Al Wakil, R. "Rheumatoid arthritis in population samples in Iraq "Ann Rheum. Dis. 1978;37:73-75.

8- Adhya S, Chakraborty G, Hajra B, Bhattacharya S, Sikdar Pk, Sinha S, Banerjee PP, Ghosh E. Serology and Immunoglobulin profile in rheumatoid arthritis. Indian -J-Pathol-Microbid. 1998; 41(1):43-7.

9- Tighe H, Carson DA: Rheumatoid Factors In: Kelly W.N; Ruddy S: Harris ED, and Sledge, CB, Textbook of rheumatology (5th ed). Sanders, W.B. Company. 1997: 241-49.

10- Visser H, Gelink LBS, Kaamphraath AH, Breedvald FG, Hazes JMW. Diagnostic and prognostic characteristics of the enzyme linked immunosorbent rheumatoid factors assays in rheumatoid arthritis. Ann Rheum Dis. 1999; 55:157-61.

11- Jonsson T, Steinsson K, et al. Combined elevation of IgM and IgA rheumatoid factor has high diagnostic specificity for rheumatoid arthritis, Rheumatoid. Int. 1998; 18(3):119-22.