Some Immunological Profile of Rheumatoid Arthritis

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Summary:

Seventy- four cases of clinically diagnosed Rheumatoid Arthritis (RA), fifty cases of systemic lupus erythematosus (SLE), and thirty healthy normal controls were investigated for detection of rheumatoid factor (RF), total serum immunoglobulins (Igs), antinuclear antibody (ANA), and ANA subtype anti-double stranded DNA (anti-ds DNA).

Patients with RA showed 58.1% positive for RF comparable with 14% positivity in SLE patients and 6.6% in normal individuals. Serum Igs (IgA,IgG) were found to be elevated in RA and SLE patients (62.2% , 36.5%) (54% , 38%) respectively. This study revealed that ANA is found in 88% of SLE patients sera and 78% of these ANA is ds DNA in comparison with only 6.8% of RA sera were found positive for ANA.

Introduction:

RA is a chronic systemic inflammatory autoimmune disorders of mysterious aetiology, which is dominated by joint inflammation accompanied by several peripheral inflammatory manifestations .

In this disease patients develop distinct immuno abnormalities espe-cially autoantibodies, among these antibodies is RF which is a major immunological abnormality in RA and regarded as one of the diagn-ostic criteria of RA which is inc-luded in the American College of it may occur even in some normal individuals (4).

It is well accepted that anti-ds DNA antibodies are rather specific to SLE with occurance in 70% but detected in less than 5% in RA patients (5). RF, ANA and anti-ds DNA appear in RA as well as SLE patients sera.

Patients and methods

Study population : The study cohort comprised 74 sera samples for patients (19male and 55 female), their age range (18-67 years) with RA who met (ACR) 1987 reversed criteria (1) attending the Rheumatology Consultation Clinic or admitted to Baghdad Teaching Hospital in the period between November 2001 and February 2002.

- Control group: were sex and age matched. They were included :-

- Patient control group of 50 sera samples for clinically diagnosed SLE patients according to ACR criteria 1997 for classification of SLE (6).
- Healthy control group of thirty healthy individuals collected from the blood banking donors.

All these sera samples have been collected and stored at-20C° for analysis. Laboratory investigations : RF was detected using the latex test Rheumatology(ACR)1987 reversed criteria (1), though non specific because present in 5% of healthy individuals and in many auto immune rheumatic diseases in addition in some chronic bacterial infections (2), while ANA was directed against a variety of nuclear antigens has been identified in the serum of patients with many rheumatic and non rheumatic diseases (3). Moreover; several studies denote that these antibodi-es are not specific for the disease, supplied by Biokit company, Spain and results were expressed in international units (IU/ml) .

Total Igs concentration were estimated by single radial immuno diffusion (SRID)test (Biomaghreb), and results were expressed in mg/dl.

ANA and anti-ds DNA were performed by enzyme-linked immunesorbent assay (ELISA) using purified antigens (extracted from the Hep-2 nucleus) are bound to microwells.The results expressed in IU/ml.

In addition to that ANA was detected by immunofluorescence antibody test (IFAT) as well as using substrate (Mouse kidney).

Results :

From 74 RA patients the maximum incidence of the disease was observed among age 30-49 years, with mean age 42.1±11.3. There were 55 females and 19 males with a female to male ratio 2.9:1 as shown in table 1&2.

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- Among the laboratory tests performed.

 Rheumatoid factor: 43 patients were RF positive (58.1%), while the rest (41.9%) were negative, while in SLE patients only 7 patients were RF positive (14%) as observed in table 3.

Table 1: Age distribution of studied groups.

	RA		SLE		Healthy control	
Age in years	**N**	**%**	**N**	**%**	**N**	**%**
<20	**1**	**1.4**	**4**	**8.0**	**2**	**6.7**
20-29	**9**	**12.2**	**18**	**36.0**	**6**	**20.0**
30-39	**23**	**31.0**	**17**	**34.0**	**13**	**43.3**
40-49	**19**	**25.7**	**10**	**20.0**	**7**	**23.3**
50-59	**16**	**21.6**	**1**	**2.0**	**2**	**6.7**
60+	**6**	**8.1**				
Total	**74**	**100.0**	**50**	**100.0**	**30**	**100.0**
Range	**18-67**		**9-59**		**18-56**	
Mean	**42.1**		**30.6**		**33.8**	
SD	**11.3**		**10.1**		**9.4**	
P (ANOVA) < 0.001						

Table 2: Distribution of the studied groups by gender.

	RA		SLE		Healthy control	
	N	**%**	**N**	**%**	**N**	**%**
Gender						
Female	**55**	**74.3**	**44**	**88**	**23**	**76.7**
Male	**19**	**25.7**	**6**	**12**	**7**	**23.3**
Total	**74**	**100**	**50**	**100**	**30**	**100**

 Total concentration of immuno-globulins level (IgA, IgG, and IgM): The serum of IgA and IgG level in RA patients were significantly higher than those in healthy control group, while there was no difference in comparison to SLE patients, where as IgM level was normal in all studied groups.

Auto antibodies such as ANA and ds-DNA: Were not present in RA patients except in few cases in comparison to patients control with highly significant difference P<0.001 as clearly shown in table 3.

While in table 5 The data showed that these Abs were detected by 2 different methods, either by ELISA as showed in 5 (6.8%) RA patients cases as compared to 44 (88%) in SLE patients, or by IFAT was revealed in 4 (5.5%) RA patients in comparison to 39 (78%) SLE patients

Table 3: The difference in positivity rate of different parameters measurement between RA patients and control groups.

		RA		SLE		Healthy control		P (Fisher's exact) for the difference between RA and	
		N	**% (n=74)**	**N**	**% (n=50)**	**N**	**% (n=30)**	**Controls**	**SLE**
	RF by latex	**43**	**58.1**	**7**	**14.0**	**2**	**6.7**	**<0.001**	**<0.001**
**	**High serum immunoglobulins level**								
	Serum IgA	**46**	**62.2**	**27**	**54.0**	**5**	**16.7**	**<0.001**	**0.24[NS]**
	Serum IgG	**27**	**36.5**	**19**	**38.0**	**1**	**3.3**	**<0.001**	**0.51[NS]**
	Serum IgM	**6**	**8.1**	**1**	**2.0**	**0**	**.0**	**0.12[NS]**	**0.15[NS]**
	Positive autoantibodies								
*	**ANA**	**5**	**6.8**	**44**	**88.0**	**0**	**.0**	**0.17[NS]**	**<0.001**
*	**Anti ds DNA antibodies**	**0**	**.0**	**39**	**78.0**	**0**	**.0**	*******	**<0.001**

** Detected by ELISA*
*** Detected by SRID*

Table 4 : The difference in mean serum Immunoglobulin concentration (mg/dl) between studied groups.

	Serum Igs (mg/dl)	RA (n=74)	SLE (n=50)	Healthy control (n=30)	P (ANOVA)
*	Serum IgA				<0.001
	Range	62.3-633.3	48-633.3	90-540	
	Mean	350.9	358.3	208.8	
	SD	129.3	174.7	105.9	
*	Serum IgG				0.006
	Range	643.7-2965.9	295.9-3042.3	700-1614.6	
	Mean	1462.8	1481	1114.5	
	SD	515.9	728.2	282.9	
*	Serum IgM				0.43[NS]
	Range	48.1-277.3	40.8-277.3	93.2-205.2	
	Mean	151.6	140.5	146.1	
	SD	48.9	49.9	33.1	

**** Normal range of Igs***
IgA: 90-540 mg/dl
IgG: 700-1620 mg/dl
IgM: 50-250 mg/dl

Table 5: The difference in positivity rate of ANAs cases detected using two different parameters.

	RA		SLE	
Technique	N	%	N	%
ELISA				
Positive	5	6.8	44	88
Nagative	69	93.2	6	12
Total	74	100	50	100
IFA				
Positive	4	5.5	39	78
Nagative	70	94.5	11	22
Total	74	100	50	100

Discussion

Now as ever, autoimmune diseases constitute one of the main problem in human clinical medicine. This is because our knowledge of their aetiology and pathogenesis is still not sufficient enough to provide concepts toward specific therapy, moreover it's importance resides not only from the fact that it is fairly prevalent but rather because the victims are usually young, and economically active people.

It is generally accepted that the incidence of RA is usually at the fourth decade of life,which is rather consistent with Iraqi studies (7,8), and abroad studies (2,9). However, in the present study, the maximum incidence of the disease observed among 30-49 with a mean age 42.1±11.3 years and predominantly female. Thus our patients are younger than those in most westren and American countries, where their range was 44-67 years (10,11). This might be related to the increased average of middle age in these countries due to advanced health education services, or probably related to environmental influence during the last decade. However female to male ratio in this study was 2.9:1 which is somewhat comparable to 2.7:1 reported by Ubaid, and higher than Farhat, 2.1:1(12). However abroad studies showed the ratio of 2.1:1, and 3.4:1 had been reported by Saraux, and Constantin, respectively (11,13) and this is generally accepted to be related to sex hormones e.g. estrogen.

It is generally agreed that RFs have been widely used as a immunologic marker. Latex agglutination test was showed 58.1% that showed to be less than other Iraqi studies where 72.6%, 75.3% had been reported by Ubaid, AL-Rawi, respectively (8,14), while abroad studies 56.6%,and 70% that had been reported by Adhya, and Tighe and Carson, respectively (15,16).

Regarding immunoglobulins (IgA, IgG, and IgM) concentration levels; our results were similar to abroad study (19), which denote no correlation in between Igs themselves and different RF isotype and their concentrations. Related to this study, the concentration levels of IgA & IgG were significantly higher in RA patients compared to

control groups, possible explanation of the above data propose that high level of IgG related to denaturation of IgG during initiation phase, while IgA concentration is proportionally associated with it's consumption in the synovium due to alternative pathway complement activation.

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