The Association Between Certain Immunological Markers And Clinical Manifestation Of SLE In Iraqi Arab Patients

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Summary:

The present study was conduction to have a clearer integrative idea on the impact of immunological abnormalities including a set of auto antibodies on the clinical expression of lupus among Iraqi Arab patients, compared with a normal population matched in ethnic background. A total of (39) well diagnosed patients with lupus attending the rheumatology clinic of medical city in Baghdad (from Jun–2005 to October–2006) have been studied compared with (40) normal individuals of a blood bank donors as a general control.

Indirect immunofluorescent technique was used to assess the prevalence of antinuclear antibody among subjects group, while other auto antibodies including anti–ds DNA, anti–Sm, anti–Ro, anti–La, anti–Sm RNP, and anti- cardiolipin antibodies were detected with enzyme immuno assay (EIA) and rheumatoid factor with latex agglutination.

Patient's group reported prevalence of all the eight sero immunological abnormalities in a statistically significant way, compared to general control. The risk for having a positive immunological marker for cases (represented by odds ratio) ranged between (7.5) for rheumatoid factor to (61.2) for antinuclear antibodies. Besides, selected auto antibodies were significantly associated with particular manifestation. Patients testing positive for rheumatoid factor had a significant risk of having malar rush (OR = 11.0 , $P< 0.05$) and those how had positive results for anti–ds DNA and anti–Sm antibodies had a significant risk of having renal involvement (OR = 4.7 and 4.3 respectively , $P< 0.05$) , while having anti–Ro antibodies decrease the risk of developing arthropathy (OR=0.2, $P< 0.05$). Nonetheless, present

study composed a model of correlation between autoimmune finding and clinical manifestation, that may explain partly the clinical heterogenicity of patients with lupus.

Introduction:

During the years, a wide attention has been directed towards studying the autoimmune diseases which have been classified into organ specific disease and non organ specific disease which represented by the classical example, systemic lupus erythematosus (SLE).This classification depends on whether autoimmune responses are directed to an antigen confined to a particular organ or to that which was widely distributed in the body (Mackay, 1998 and D'Cruz ,2006).

Systemic lupus eythematosus represented by a diverse spectrum of clinical manifestation with variable courses characterized by exacerbation and remission, marked serologically by both humoral and cellular immunologic abnormalities including multiple auto antibodies directed against non organ specific, selected intracellular antigens, mostly against the cell nucleus components (Hahn, 1997 and Riemekasten and Hahn,2005). Several dozen of nuclear antigens have been characterized and shown to react with auto antibodies from SLE patients and other collagen diseases (Senecal et al.,2000 and Kelleher et al.,2004) . The combination of research efforts in different branches of science established SLE as an extraordinary, complex autoimmune disease that touches on nearly all medical specialties, with an equally complex pathogenesis that vary from patient to patient. This diverse expression of the common lupus syndrome may result from variable abnormalities in intersecting genetic, immunologic, hormonal and environmental pathways (Boumpas et al.,1995 and Cooper et al., 1998).

Studies showing an association between a particular clinical finding and auto antibody present an attractive concept for explaining the pathogenesis of the clinical illness of lupus. Moreover, to racial variation in the incidence of SLE, race and genetic background seem to influence both the clinical manifestation and auto antibody expression (AL – Attia et al., 1998 and Arbuckle et al.,2003).

With this in mind, accompanied by the increased prevalence of this disease in Iraq and the absence of other studies regarding the effect of immunological abnormality on expression of SLE among Iraqi Arab patients, prompted us to carry out this study in an attempt to shed some

light on correlation between laboratory finding and the clinical expression of this disease, that may help in clarifying the pathogenesis of clinical illness of lupus.

Materials and Methods:

♦ Patient and control study group:

Thirty nine Iraqi Arab patients with SLE were subjected for a questionnaire on the disease manifestation, and their medical histories reviewed for clinical features and previous serological findings. Their ages ranged from (9 – 52) years with an average age of (30.0 ± 8.0) years. Healthy individuals, age, sex & ethnicity matched from a blood bank donors were used as a control.

From each subject, (10) ml blood were aspirated, centrifuged and the separated serum was divided into several (0.25) ml aliquots and immediately frozen at ($-20c^{o}$) till used.

♦ Kits and Methods:

a – Detection of antinuclear antibody (ANA):

Kallested^{TM} Quantafluor kit (Utilize tissue culture cells as a substrate of ANA detection , Sanofi Diagnostic Pasteur- France) has been used for ANA detection by (IFA) technique. According to the method auto antibodies in the test sample bind to antigen in the substrate. After washing to remove excess serum from the substrate, fluorescein conjugated (FITC) antiserum added to the substrate to give a three - part complex which emits in the fluorescent microscope. Observation of a specific fluorescent pattern on the substrate indicates the presence of auto antibodies in the test sample.

b – Detection of auto antibodies [anti – ds DNA, anti – ENA and anti – cardiolipin antibodies (ACL)]:

This test is performed as a sandwich ELISA assay. Kallested^{TM} microplate EIA kits (Sanofi Diagnostic Pasteur- France) have been used for the qualitative determination of auto antibodies in human serum. A diluted sample is added to the microtiter well with incubation. Upon washing, a specific antibody present in the sample bind to the highly purified antigen coated on the microtiter wells. Then a conjugate of enzyme – labeled monoclonal antibody to human IgG bind to the surface bound antibodies in the second incubation. After a further washing step remove unbound conjugated antibody, a specific antibodies are traced by incubation with substrate solution. Addition of

the stopping solution terminate the reaction. The amount of conjugate bound is measured in term of absorbance units and this amount in the presence of unknown sample is compared with that bound in the presence of a known concentration specific antibody in a single reference control.

c – Detection of Rheumatoid Factor (RF):

The latex regent is suspension of polystyrene latex particles of a uniform size coated with a human gamma – globulin, which allowed visual observation of the antigen – antibody reaction. If the reaction took place, a clear agglutination become evident due to the reaction of RF present in the serum with the IgG coated to the latex particles, staring the formation of a web between them if the serum contain more than (10) IU/ml of RF. Kits that were used in test were supplied from (Biokit – Spain).

Results:

Comparing with a general control eight immunological markers have been tested for unvaried association with disease status. For each immunological marker the odds of being a case against the odds of being a control (odds ratio) was used as an approximation for the relative risk of having the disease when a specific marker was present. When a marker was absent in either cases or control group, a modified formula for calculating the odds ratio (OR2) was used. A calculated OR was considered statistically significant if its X^2 value was higher than (3.84), reflecting (P) value less than (0.05).

In general SLE cases had a significantly higher positivity rate for the seven auto antibodies and rheumatoid factor compared to control. The odds ratio (risk) for having a positive immunological marker for cases ranged between (7.5) for rheumatoid factor to (61.2) for antinuclear antibodies, (table -1).

Table-1: Positivity rates for certain indices and the odds ratio of having appositive result for each of the indices in SLE cases compared to a general population control.

Immunological marker		General Control		Case					
		N	%	N	%	OR1	X^2	OR2	X^2
1. Antinuclear antibody	:Negative	36	90.0	5	12.8				
	:Positive	4	10.0	34	87.2	61.2	48.70	**	**
2. Anti-ds-DNA antibody	:Negative	38	95.0	12	30.8				
	:Positive	2	5.0	27	69.2	42.8	35.50	**	**

Immunological marker		General Control		Case					
		N	%	N	%	OR1	X^2	OR2	X^2
3. Anti-Sm antibody	:Negative	39	97.5	32	82.1				
	:Positive	1	2.5	7	17.9	8.5	5.23	**	**
4. Anti-Ro antibody	:Negative	40	100	31	79.5				
	:Positive	0	0.0	8	20.5	**	**	40.3	11.78
5. Anti-La antibody	:Negative	39	97.5	31	79.5				
	:Positive	1	2.5	8	20.5	10.1	7.30	**	**
6. Anti-Sm-RNP	:Negative	40	100	35	89.7				
antibody	:Positive	0	0.0	4	10.3	**	**	18.7	6.89
7. Anti-Cardiolipen	:Negative	39	97.5	27	69.2				
antibody	:Positive	1	2.5	12	30.8	17.3	12.78	**	**
8. Rhomatoid factor	:Negative	38	95.0	28	71.8				
	:Positive	2	5.0	11	28.2	7.5	8.62	**	**
Total		40		39					

The eight immunological markers were tested in the SLE cases group for possible invariant association with clinical criteria that were important in the diagnosis of SLE cases. Although none of the immunological markers had a statistically significant association with having oropharyngial ulcer, having anti–Sm antibodies or rheumatoid factor and being positive for anticardiolipin antibodies increased the risk of having such a symptom by (4.5 and 3.2) times respectively. Testing positive for anti – Sm RNP antibodies decreased the risk of having a symptom by more than five times (OR=0.2), as shown in table (2).

Table-2: The odds ratio of having oropharyngial ulcer when specific immunological marker is positive.

Immunological marker		Negative		positive					
		N	%	N	%	OR1	X^2	OR2	X^2
1. Antinuclear antibody	:Negative	11	42.3	15	57.7				
	:Positive	5	38.5	8	61.5	1.2	0.25	**	**
2. Anti-ds-DNA antibody	:Negative	4	40.0	6	60.0				
	:Positive	12	41.4	17	58.6	0.9	0.02	**	**
3. Anti-Sm antibody	:Negative	14	50.0	14	50.0				
	:Positive	2	18.2	9	81.8	4.5	1.69	**	**
4. Anti-Ro antibody	:Negative	6	37.5	10	62.5				
	:Positive	10	45.5	12	54.5	0.7	0.27	**	**
5. Anti-La antibody	:Negative	5	33.3	10	66.7				
	:Positive	11	45.8	13	54.2	0.6	0.23	**	**
6. Anti-Sm-RNP	:Negative	13	38.2	21	61.8				
antibody	:Positive	3	75.0	1	25.0	0.2	1.65	**	**
7. Anti-Cardiolipen	:Negative	15	44.1	19	55.9				
antibody	:Positive	1	20.0	4	80.0	3.2	2.80	**	**
8. Rhomatoid factor	:Negative	14	50.0	14	50.0				
	:Positive	2	18.2	9	81.8	4.5	3.30	**	**
Total		16	41.1	23	58.9				

On the other hand, only the presence of anti – Ro antibodies had a statistically significant negative association with complaining of

arthrpathy. Patients testing positive for anti – Ro antibodies had five times lower risk to complaining of this manifestation (OR = 0.2 , P< 0.05). The remaining immunological markers had no statistically significant association with this symptom, (table -3).

Table-3: The odds ratio of having arthropathy when specific immunological marker is positive.

Immunological marker		Negative		positive					
		N	%	N	%	OR1	X^2	OR2	X^2
1. Antinuclear antibody	:Negative	8	24.2	25	75.8				
	:Positive	1	16.7	5	83.3	1.5	0.14	**	**
2. Anti-ds-DNA antibody	:Negative	8	28.6	20	71.4				
	:Positive	1	9.1	10	9.9	4.0	2.6	**	**
3. Anti-Sm antibody	:Negative	8	24.2	25	75.8				
	:Positive	1	16.7	5	83.3	1.5	0.14	**	**
4. Anti-Ro antibody	:Negative	5	16.7	25	83.3				
	:Positive	4	50.0	4	50.0	0.2	3.86	**	**
5. Anti-La antibody	:Negative	4	21.1	15	78.9				
	:Positive	5	25.0	15	75.0	0.8	0.14	**	**
6. Anti-Sm-RNP	:Negative	8	23.5	26	76.5				
antibody	:Positive	1	25.0	3	75.0	0.9	0.02	**	**
7. Anti-Cardiolipen	:Negative	2	13.3	13	86.7				
antibody	:Positive	7	29.2	17	70.8	0.3	1.45	**	**
8. Rhomatoid factor	:Negative	6	21.4	22	78.6				
	:Positive	3	27.3	8	72.7	0.7	0.20	**	**
Total		9	23.1	30	76.9				

Furthermore the presence of anti – ds – DNA and anti – Sm antibodies increased the risk of renal involvement (4.7 and 4.3) times respectively, with a statistically significant and highest x^2 value among other markers. Three other markers were associated with a positive risk of this symptom greater than (2), however they were not reached the statistically significant value. On the other hand having anti-La antibodies decreased the risk of developing renal involvement by two times with a statistically insignificant association , as shown in table (4).

Table-4: The odds ratio of having renal involvement when specific immunological marker is Positive.

Immunological marker		Negative		positive					
		N	%	N	%	OR1	X^2	OR2	X^2
1. Antinuclear antibody	:Negative	7	58.3	5	41.7				
	:Positive	10	37.1	17	62.9	2.4	2.30	**	**
2. Anti-ds-DNA antibody	:Negative	13	59.1	9	40.9				
	:Positive	4	23.5	13	76.5	4.7	3.87	**	**
3. Anti-Sm antibody	:Negative	15	51.7	14	48.3				
	:Positive	2	20.0	8	80.0	4.3	3.84	**	**

Immunological marker		Negative		positive					
		N	%	N	%	OR1	X^2	OR2	X^2
4. Anti-Ro antibody	:Negative	9	50.0	9	50.0				
	:Positive	8	40.0	12	60.0	1.5	0.35	**	**
5. Anti-La antibody	:Negative	10	38.5	16	61.5				
	:Positive	7	53.8	6	46.2	0.5	1.00	**	**
6. Anti-Sm-RNP	:Negative	16	47.1	18	52.9				
antibody	:Positive	1	25.0	3	75.0	2.7	0.67	**	**
7. Anti-Cardiolipen	:Negative	11	55.0	9	45.0				
antibody	:Positive	6	33.3	12	66.7	2.4	1.59	**	**
8. Rhomatoid factor	:Negative	12	48.0	13	52.0				
	:Positive	5	50.0	5	50.0	0.7	0.58	**	**
Total		17	43.6	22	56.4				

Table (5) shows that only the rheumatoid factor had a statistically significant association with the presence of malar rash ($P< 0.05$). The results verified that patients testing positive for rheumatoid factor had (11) times the risk of having malar rash compared to patients who were negative for rheumatoid factor. The remaining markers, failed to reach the level of statistical significance. Additionally non of the immunological markers had a statistically significant association with having discoid rash, (table – 6).

Table-5: The odds ratio of having malar rash when specific immunological marker is positive.

Immunological marker		Negative		positive					
		N	%	N	%	OR1	X^2	OR2	X^2
1. Antinuclear antibody	:Negative	4	15.4	22	84.6				
	:Positive	5	38.5	8	61.5	0.3	2.56	**	**
2. Anti-ds-DNA antibody	:Negative	1	8.3	11	91.7				
	:Positive	8	29.6	19	70.4	0.2	1.75	**	**
3. Anti-Sm antibody	:Negative	6	18.8	26	81.2				
	:Positive	3	42.9	4	57.1	0.3	0.48	**	**
4. Anti-Ro antibody	:Negative	7	23.3	23	76.7				
	:Positive	2	25.0	6	75.0	0.9	0.04	**	**
5. Anti-La antibody	:Negative	6	23.1	20	76.9				
	:Positive	3	23.1	10	76.9	1.0	0.00	**	**
6. Anti-Sm-RNP	:Negative	8	23.5	26	76.5				
antibody	:Positive	1	25.0	3	75.0	0.9	0.02	**	**
7. Anti-Cardiolipen	:Negative	8	30.8	18	69.2				
antibody	:Positive	1	7.7	12	92.3	5.3	2.08	**	**
8. Rhomatoid factor	:Negative	9	32.1	19	67.9				
	:Positive	0	00.0	11	100	**	**	11.0	4.60
Total		9	23.1	30	76.9				

Table-6: The odds ratio of having discoid rash when specific immunological marker is positive.

Immunological marker		Negative		positive					
		N	%	N	%	OR1	X^2	OR2	X^2
1. Antinuclear antibody	:Negative	20	80.0	5	20.0				
	:Positive	12	85.7	2	14.3	0.7	0.38	**	**

Immunological marker		Negative		positive					
		N	%	N	%	OR1	X^2	OR2	X^2
2. Anti-ds-DNA antibody	:Negative	21	80.8	5	19.2				
	:Positive	11	84.6	2	15.4	0.8	0.27	**	**
3. Anti-Sm antibody	:Negative	26	78.8	7	21.2				
	:Positive	5	83.3	1	16.7	0.7	0.05	**	**
4. Anti-Ro antibody	:Negative	24	80.0	6	20.0				
	:Positive	7	87.5	1	12.5	0.6	0.35	**	**
5. Anti-La antibody	:Negative	28	82.4	6	17.6				
	:Positive	3	75.0	1	25.0	1.6	0.07	**	**
6. Anti-Sm-RNP	:Negative	24	80.0	6	20.0				
antibody	:Positive	7	87.5	1	12.5	0.6	0.35	**	**
7. Anti-Cardiolipen	:Negative	21	80.8	5	19.2				
antibody	:Positive	11	84.6	2	15.4	0.8	0.25	**	**
8. Rhomatoid factor	:Negative	23	82.1	5	17.9				
	:Positive	9	81.8	2	18.2	1.0	0.05	**	**
Total		32	82.1	7	17.9				

Finally, table (7) shows that none of the studded immunological markers had a statistically significant association with having neurological manifestation. Yet, all patients with no neurological manifestation have negative results for ANA and anti – ds – DNA antibodies and positive results for anti-Sm antibodies.

Table-7: The odds ratio of having neurological manifestation when specific immunological marker is positive.

Immunological marker		Negative		positive					
		N	%	N	%	OR1	X^2	OR2	X^2
1. Antinuclear antibody	:Negative	6	100	0	0.0				
	:Positive	30	90.9	3	9.1	**	**	1.5	0.20
2. Anti-ds-DNA antibody	:Negative	12	100	0	0.0				
	:Positive	24	88.9	3	11.1	**	**	3.4	1.21
3. Anti-Sm antibody	:Negative	30	90.9	3	9.1				
	:Positive	6	100	0	0.0	**	**	0.7	0.10
4. Anti-Ro antibody	:Negative	18	94.7	1	5.3				
	:Positive	17	89.5	2	10.5	2.1	0.35	**	**
5. Anti-La antibody	:Negative	18	94.7	1	5.3				
	:Positive	18	90.0	2	10.0	2.0	0.37	**	**
6. Anti-Sm-RNP	:Negative	32	94.1	2	5.9				
antibody	:Positive	3	75.0	1	25.0	5.3	1.60	**	**
7. Anti-Cardiolipen	:Negative	29	93.5	2	6.5				
antibody	:Positive	7	87.5	1	12.5	2.1	0.35	**	**
8. Rhomatoid factor	:Negative	25	92.6	2	7.4				
	:Positive	11	91.7	1	8.3	1.4	0.08	**	**
Total		36	92.3	3	7.7				

Discussion:

Advances in immunology and hematology have refined our understanding of the pathogenesis of systemic lupus erythematosus and its diverse disease expression, reporting the production of auto antibodies to the cellular macromolecules as the central immunologic disturbance in SLE . In general , auto antibodies participate in tissue

injury by an immune-complex mediated inflammatory response (such as glomerulonephritis) or by auto antibody mediated cellular dysfunction (Hahn , 1997 and D'Cruz ,2006).

The present work stated ANA among patients group as the most prominent marker compared to the general population . It was found in (87.2%) of patients which is comparable to that reported by Al-Attia and George (1995) on lupus patients of united Arab Emirate (U.A.E) .However , when disease activity was considered , ANA positivity may increase to be more than (95%) according to Tan et al. (1997) and Arbuckle et al.(2003) .It is of interest the association of ANA with renal involvement (OR = 2.4) however, without a statistically signification value , that may be related to the more specific lupus antibodies than ANA (anti-ds-DNA and anti–Sm antibodies) which is also shown on present study. This proposal accompanied by the fact that ANA may occur in some normal individual , auto – immune disease , viral infection , chronic inflammatory process and several induced ANA cases (Tan et al, 1997 and Kelleher et al.,2004).

The results in present study showed that Anti – ds -DNA auto antibodies are highly prevalent among Iraqi patients , they were occur in (69.2%) of them . Nevertheless , widely varying prevalence of anti-ds-DNA antibodies in different population are not unusual. Feng and Boey (1982) , reported a rate of (100%) among Chinese in Singapore study , and Taylor and Stein (1986) reported these antibodies in (99%) among Zimbabwe patients . Rates as low as (33%) and (35%) were observed in Brazillian male and female respectively (Feng and Boey ,1982). Anti –ds-DNA antibodies were in highly positive correlation with a renal involvement in the present results, the presence of this marker increased the risk of having renal involvement more than five and a half time, which was the highest among other immunologic markers. Further verification of their true value could , however be measuring their titer and avidities .

Comparing with some studies , this work demonstrated a less prevalence of anti-Sm antibodies among patients , however patients with anti–Sm antibodies appeared to have significant increased prevalence of anti ds-DNA antibodies, thereby indicating the activity of disease. The rate of anti –Sm antibodies (17.9%) was comparable to that in Brazillian female patients (18%) by Costallate and Coimbra (1993). Besides ,it

was lower than the Indian (25%) (Malaviya et al.,1998).This variation reflect the effect the ethnic origin in patients population, further to differences in the serological test used to detect the presence of these antibodies. Furthermore, the low frequency of anti – Sm auto antibodies may account for the absence of statistically significant correlation with the clinical findings reported among patients. yet, this marker increased the risk of having renal involvement (4.3) times among cases , which was comparable to the risk of anti ds-DNA antibodies (OR= 4.7) . These results may confirms the association of these two types of auto antibodies with lupus pathogenicity.

A low frequency of anti-Ro (SS – A) antibodies (20.5%) in this study was not comparable to that observed in Brazillian female which were (63%) (Costallate & Coimbra ,1993) and Indian series that were (35%) (Malaviya et al.,1998). Furthermore , anti – Ro accompanied by anti – La antibodies reported in (20-30%) of lupus patients (Baron et al.,1993).

Though the primary association in this study was an inverse relationship between renal involvement and anti – La antibodies. It was absent in (61.5%) of patients with nephropathy, comparable to the results of Harely (1989), however with a less level of statistical significance . Moreover, anti – Ro and anti – La antibodies have been linked with distinguishable subsets of SLE. It is occur in (62%) of ANA negative lupus patients (Maddison et al .,1981), this report may account for the reported low presence of these antibodies in the present data, since ANA positively rate was (87.2%) among cases group .

Previous report dealing with ACL antibodies and SLE recorded as average prevalence of (44%), however, Malabery and Colleagues (1998) reported a higher prevalence of (55%) of APL antibodies regardless its type , while this work detected a less prevalence of these antibodies in Iraqi patients (30.8%), Yet it was more than reported by AL-Attia and George (1995) .

The frequency of RF among Iraqi patients was comparable with Garacia (1996) .Interestingly the occurrence of this marker in an obscure manner among all patient that were positive for a malar rash .

In conclusion , present data composed a model from autoimmune serological finding and clinical manifestation, which demonstrated presence of a significant positive correlation between anti-ds-DNA and

anti–Sm auto antibodies with renal involvement as well as between Rhomatoid factor and malar rash, in addition to the negative correlation between anti-Ro antibodies and arthropathy. Longitudinal studies will be required to determine whether auto antibodies sero - negative individuals will subsequently develops a lupus or lupus related symptoms .

الخلاصة:

أجريت هذه الدراسة للحصول على مزيد من الإيضاحات حول دور بعض الاضطرابات المناعية والمصلية وبضمنها مجموعة الأضداد الذاتية في حدوث الإصابة بداء الذئاب ألاحمراري ألجهازي بين مجموعة من المرضى العراقيين العرب بالمقارنة مع الأصحاء من نفس القومية .وقد شملت الدراسة (39) مريضا من الذين سبق وان شخص المرض لديهم من قبل الأخصائيين في العيادة الاستشارية لأمراض المفاصل في مستشفى مدينة الطب للفترة من حزيران/ 2005 لغاية تشرين الأول / 2006 إضافة إلى (40) شخصا من الأصحاء ظاهريا من متبرعي مصرف الدم كسيطرة .

أستخدمت تقنية ألومضان ألمناعي غير المباشر لاختبار وجود وانتشار أضداد ضد الأنوية (ANA) لدى عينات البحث في حين تم تحديد وجود أضداد : (anti - ds DNA) ، (anti – Sm) ، (anti - Ro) ، (anti - La) ، (anti – Sm) anti – RNP /) وأضداد (anti - cardiolipin) باستخدام تقنية الاختبار المناعي بالأنزيم (EIA)، وكذلك وجود العامل الرثياني (RF) باستخدام فحص ألتلازن.

برهن التحليل الإحصائي للنتائج على تسجيل زيادة معنوية في وجود ألاضطرابات المصلية والمناعية أعلاه لدى مجموعة المرضى مقارنة بالأصحاء ، حيث تراوحت الخطورة لوجود عامل (RF) وأضداد (ANA) لدى مجموعة المرضى بين (7.46)

و (61.2) مرة على التوالي، وبشكل معنوي حيث (P<0.05) . علاوة على ذلك أثبتت النتائج وجود ارتباط معنوي لأضداد ذاتية نوعية مع أعراض سريرية محددة ، حيث ثبت إن المرضى الذين يظهرون نتائج موجبة لعامل (RF) لديهم خطورة معنوية (P<0.05) لامتلاك أعراض التقلصات الوجنية والفشل الكلوي بما يعادل (11) مرة ، واللذين لديهم نتائج موجبة للأضداد الذاتية (anti - ds DNA) و (anti – Sm) يكونوا معرضين لخطورة الإصابة بأعراض الفشل الكلوي بما يعادل (4.7 و 4.3) مرة على التوالي . في حين وجد أن النتائج الموجبة لأضداد (anti – Ro) تخفض خطورة تطور أعراض الاعتلال المفصلي بشكل معنوي (P<0.05) ولخمس مرات (OR=0.2).أخيرا يمكن القول أن البيانات المستخلصة من هذه الدراسة يمكن أن تساهم في اقتراح نموذج للعلاقة بين العوامل المناعية والأعراض السريرية بما قد يفسر ولو بشكل جزئي التباين الواسع في الأعراض السريرية للمصابين بداء الذئاب ألاحمراري ألجهازي.

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