SYSTEMIC LUPUS ERYTHEMATOSUS; CORRELATION OF AUTOANTIBODIES WITH CLINICAL MANIFESTATIONS

Belmokhtar Naima Rania[1], Zemri Khalida[2], Kanoun Khedoudja[3], Harir Noria[4], Bachaoui B.M[5], Hebri Sid Tadj[6]

[1-4]Molecular Microbiology, Proteomics and Health Laboratory, Faculty of Natural and Life Sciences, Djillali Liabès University of Sidi Bel Abbés, Algeria - Algeria.
[5]Department of Internal Medicine, Diabetes, Etablissement Hospitalier Universitaire d'ORAN - Algeria.
[6]Department Internal Medicine, University Hospital Centre CHU Dr. Hassani Abdelkader, Sidi Bel Abbes - Algeria.
Address for correspondence:
Belmokhtar Naima Rania
Faculty of Natural and Life Sciences, Djillali Liabès University of Sidi Bel Abbés - Algeria.
E-mail: avril_lavignerockstar@hotmail.fr
Date Received: July 7, 2020
Date Revised: September 20, 2020
Date Accepted: September 25, 2020

ABSTRACT

Objective: To correlate positivity of auto-antibodies with clinical manifestations of systemic lupus erythmatosus in Algerian population.

Methodology: This retrospective multicenter study was carried out on 203 Algerian patients with systemic lupus erythmatosus, diagnosed according to the American College of Rheumatology and SLICC criteria, from January 2006 to December 2019 in the University Hospital of ORAN region (EHUO) and the Abdelkader Hassani University Hospital of Sidi Bel Abbes region (CHU-SBA), west of Algeria. The study assessed the clinical characteristics and the profile of the auto-antibodies. The detection of antinuclear antibodies was carried out by indirect immune-fluorescence technique, anti- DNAn and anti-cardiolipin antibodies using immune-enzymatic technique and nuclear antigens extractable by immunodot.

Results: The mean age of symptoms onset was 29.47 ± 11.24 years and the sex ratio of female to male was 9.68 : 1. The frequency of most clinical manifestations was 75.9%, 71.4% and 71.9% for rheumatological, dermatological and haematological disorders respectively. In total, about 25% of the cases had lupus nephropathy. The positivity of antinuclear antibody (ANA) was found in 94.8% of cases, anti-DNAn (66.1%), anti-Sm (32.7%), anti-RNP (21.8%), anti-SSA (38.5%) and anti-SSB (18.4%). A significant correlation was found between these auto-antibodies and clinical manifestations of SLE ($p<0.05$), in particular with anti-DNAn, anti-Sm, anti-RNP and anti-SSA.

Conclusion: Anti-DNAn and anti-Sm antibodies strongly correlate with clinical manifestations and lupus nephropathy. The high frequency of anti-SSA antibodies in the Algerian population gives them a significant predictive value for the diagnosis of SLE.

Key Words: Auto-antibodies, Algeria, Systemic lupus erythematosus

This article may be cited as: **Rania BN, Khalida Z, Khedoudja K, Noria H, Bachaou BM, Tadj HS. Systemic lupus erythematosus; correlation of autoantibodies with clinical manifestations. J Postgrad Med Inst 2020;34(4):259-66.**

INTRODUCTION

Systemic lupus erythematosus (SLE) is a prototype of organ non-specific inflammatory autoimmune diseases. Typified by a female predominance and heterogeneous etiologies, the clinical and serological expression of lupus disease varies from one population to another, it is characterized by a dysfunction of the activity of the immune system and the production of a wide variety of auto-antibodies (AAc) directed mainly against nuclear antigens; some of which have a direct pathogenic role[1]. Auto-antibodies used for diagnosis, correlate with clinical manifestations and provide important information for prognosis[2]. The antinuclear antibodies (ANA) are the most prevalent, occurring in approximately 95% of lupus patients. Some antibodies are useful for diagnostic purposes, like ANA, anti-ds DNA, anti-Sm and anticardiolipin antibodies (aCL). While other antibodies are associated with certain clinical features (anti-ds DNA with nephritis[3,4], anti-Ro antibodies with cutaneous lupus and photosensitivity, aCL antibodies are associated with pregnancy loss and thrombosis and anti-Sm antibodies have shown associations with constitutional symptoms[5], lupus nephritis[3,6] and central nervous system disease[7,8].

Algerian studies on systemic lupus erythematosus epidemiology and more specifically on the prevalence of different auto-antibodies and their clinical significance are scarce. The objective of this study was to present a detailed analysis of 203 Algerians lupus patients and determine the correlation between serological markers

(AAc) and the various clinical manifestations and to look for possible associations of autoimmune disease (AID) in a group of Algerian lupus.

METHODOLOGY

This was a retrospective multicenter study of 203 patients with SLE, carried out over a period of 13 years (January 2006 to December 2019) in two Western Algeria hospitals: the University Hospital of ORAN region (EHUO) and the University Hospital Abdelkader hassani of Sidi Bel Abbes region (CHU-SBA). All patients were Algerian, adults, and met the criteria for the diagnosis as laid by American College of Rheumatology (ACR), 1997[9]. These patients were actively followed in the internal medicine departments. Patients under the age of 16 were excluded because they were followed by a different medical team.

The study was approved by local ethics committee of the University Hospital. A clinical information sheet was established for each patient, recording of the demographic characteristic such as sex, age and clinical findings including managements like laboratory assessment. The immunology department of the Oran University Hospital took a blood sample from each patient. After centrifugation, the serum obtained was divided into several aliquots and stored at -20°C until the day of analysis. The sensitivity and specificity of the different tests used for the detection of auto-antibodies can vary widely from study to study. The search for ANA was done by the indirect immune-fluorescence technique (IFI) on rat liver section. In case of negativity, the analysis was carried out on a more sensitive substrate, Hep-2 cells were used (human epithelial cell line type 2) (Diagnostic Pasteur-Biorad®, France). The ELISA-type immune-enzymatic technique (Binding site®, United Kingdom) was used to assay anti-DNAn antibodies (native) and anticardiolipin antibodies (aCL) of isotype IgG and IgM. The search for anti-nucleosome antibodies as well as for extractable nuclear antantigens (anti-ENA) such as anti-Sm, anti-RNP, anti-SSA and anti-SSB was carried out by the immunoenzymatic technique of the immunodot type (Alphadia Diagnostic®, Belgium). Patients with 24 hours proteinuria >0.5 g, underwent a renal biopsy puncture (RBP). Histological lesions were classified according to the WHO classification[10].

In statistical analysis SPSS v. 22 was used, patients' characteristics of numerical variables were presented as means and standard deviation and as frequencies and percentages for categorical variables. To cross study, the categorical variables were tested using Pearson's Chi- Square test ($\chi 2$) with Fisher correction as and where needed. Significance was retained for values of $p \leq 0.05$.

RESULTS

Out of total, 184 were women (90.6%) and 19 men (9.4%). The mean age of attack was 29.47 ± 11.24 years (range 11 - 89) and the mean age of diagnosis was 42.34 ± 13.89 years (range: 19 - 99). Table 1 summarizes the main clinical manifestations observed in our patients. The most common manifestations were articular, dermatological and haematological. Lupus nephropathy was found in 25.1% of cases but end-stage renal disease in 05 cases only. Neuropsychiatric manifestations were noted in 25 cases (12.3%).

Majority of the patients suffered from other associated autoimmune diseases; 12.3% type 1 and 2 diabetes and 7.4% rheumatoid arthritis. Antiphospholipid syndrome (aPL) was noted in only female sex, Gougerot-Sjogren syndrome (SGS) was found in ten cases (4.9%). Other autoimmune diseases were found in 35% of cases such as: Hashimoto's thyroiditis, dermatopolymiositis (DPM), and psoriasis etc. The main immunological abnormalities and the frequency of the different autoantibodies assayed during this study are summarized in Table 2.

ANA testing was performed for only 174 patients, as the other patients were unavailable for blood collection. Most of the patients had 94.8% positive ANA with an appearance most often speckled (59%) or homogeneous (35%). Anti-native DNA, anti-SSA and anti-Sm antibodies were most frequently observed in 66.1%, 38.5% and 32.7% of cases, respectively. Anti-RNP wasnoted in 21.8% of cases and anti-SSB in 18.4%. Anti Histone, anti nucleosome, anti Ribosome and anti centromere antibodies were less frequent. Twenty-five patients (12.3%) had antiphospholipid antibodies. We found a significant correlation of anti-native DNA antibodies with several clinical manifestations as shown in table 3. A significant correlation has been established between the anti-DNAn Ab and neuropsychiatric damage ($p = 0.058$).

A significant correlation was also established between anti-Sm antibody and fever, cutaneous manifestations, anemia and raynaud's syndrome ($p = 0.018$, $p= 0.023$, $p = 0.016$; $p = 0.001$) respectively (Table 3). In addition, significant correlations was observed between anti-RNP, and cutaneous manifestations, malar rash ($p = 0.022$, $p =0.055$), anemia ($p =0.009$) and with Raynaud's syndrome ($p =0.003$). The later also presented significant correlation with anti-SSA Ab ($p = 0.006$). Another antibody has been found in association with clinical-biological manifestations, anti-SSB which significantly correlated with pericarditis ($p= 0.052$), hypocomplementemia ($p =0.059$) and with primary Gougerot-Sjogren syndrome ($p= 0.038$).

DISCUSSION

Most of these clinical correlates are consistent with numerous studies[12-14]. SLE is a predominantly female autoimmune disease, with a female to male ratio of 9.68

in our study while this is 6 in Tunisia[15], 6.1 in Lebanon[16] and 10 in Europe[17]. The mean age of attack in our study was 29.47 years which is in agreement with other literature[15,17-20]. A younger average age was found in Saudi Arabia (24.4 years)[21], India (24.5 years)[22] and 25.8 years in Egypt[23].

Our study confirms the clinical polymorphism of SLE in Algeria and its great similarity with other series around the world. The main manifestations studied at the time of diagnosis were cutaneous, articular, renal, hematological and neuropsychiatric. A higher frequency was found in the Moroccan population (67.4%)[25], but lower in Saudi Arabia (37%)[21]. Lupus nephropathy,was noted in 25.1% of cases in our series. which is significantly higher in other populations, varying from 37 to 73%[15, 17, 20, 22, 24,26].

A low frequency of neuropsychiatric manifestations was found in our series (12.3%) and in the Tunisian population (14.3%)[15]. However, in other studies the frequency was greater, varying between 20 to 52%[17, 20, 21, 22, 24]. In our series 63.1% of cases had anemia and 9.4% had autoimmune haemolytic anemia. This later was noted at 8% in Europe[17], 7% in India[22] and slightly higher in North America (18%)[24].

Some antibodies are useful for diagnostic purposes, for example, ANA, anti-DNA, anti-Sm and anticardiolipin (aCL) antibodies. Anti-ds DNA levels can be used to monitor overall disease activity in patients who are clinically and serologically consistent[4,27]. It was positive

Table 1: Clinicat manifestations. (n=203)

	Number of patients	%
General signs :		
Fever	21	10.3
Asthenia	83	40.9
Weight loss	38	18.7
Anorexia	19	9.4
Articular manifestation	154	75.9
Dermatological disorders	145	71.4
Malar rash	111	54.7
Photosensitivity	83	40.9
Mucosal ulcer	34	16.7
Alopecia	41	20.2
Raynaud's syndrome	52	25.6
Lupus nephropathy	51	25.1
Cardiacinvolvement	18	8.9
Pericarditis	13	6.4
Pleuritis	68	33.5
Neuropsychiatric	25	12.3
APLS	21	10.3
Ocular damage	6	3.0
Gastrointestinal	5	2.5
Haematological disorder	146	71.9
Anemia	128	63.1
AIHA	19	9.4
Leucopenia	44	21.7
Lymphopenia	65	32.0
Thrombopenia	47	23.2
Neutropenia	10	4.9
Hypocomplementemia (C3/C4)	68/97	70.1

APLS : anti-phospholipid syndrome ; AIHA : autoimmunehemolyticanemia.

Table 2: Biological and immunological abnormalities in 174 lupus patients)

	N	%
ANA	165	94.8
Anti-DNAn	115	66.1
Anti-Sm	57	32.7
Anti-RNP	38	21.8
Anti-SSA	67	38.5
Anti-SSB	32	18.4
Anti histone	16	9.2
Anti Ribosome	06	3.4
Anti centromere	4	2.3
Anti nucleosome	11	6.3
APL	25/203	12.3
Anticardiolipin antibody	20/25	80
aCLIgG	11/20	55
aCLIgM	9/20	45
Hypocomplementemia (C3/ C4)	68/97	70.1
Cryoglobulinemia	30/ 54	55.5

ANA: antinuclear antibodies, Anti-DNAn: anti-native DNA antibody, APL : anti-phospholipid, aCL: anticardiolipin, IgG: immunoglobulin type G, IgM: immunoglobulin type M.

in 66.1% of cases in our series, and ranged from 47% to 78% in Tunisia, Europe, Kuwait, India, North America and Brazil series[15,17,20,22,24,26]. The correlations that we have established with the some clinical manifestations are found in numerous studies[12,28,29,30]. Zonana-Nacach et al.[31], found that a significantly higher proportion of patients with damage had antibodies against ds DNA than those without damag. In our study, no correlation between anti ds DNA and nephritic lupus (NP) was found. Alba et al.[3], ireported that ANA were positive in 99% of cases with or without nephritis, of which 68% of nephritic lupus cases were positive for anti ds DNA. Generally anti ds DNA has not been associated with NP disease activity[7]. A correlation between anti-ds DNA and neuropsychiatric damage was found in our study. More recently, De Giorgio et al., showed that some anti-DNA antibodies recognized the NR2A and 2B polypeptide chains, which together with the NR1 chain, form the glutamate receptor NMDA of nerve cells. In vitro, on cultured fetal brain cells and in vivo in mice, De Giorgio et al. demonstrated that these antibodies induced apoptosis of nerve cells and could induce cognitive disorders[28,32]. In addition, we found a significant correlation between each of anemia and hypocomplementemia respectively.

The positivity of anti-ENA varies during lupus disease, notably anti-Sm antibodies, twhich are detected in 10 to 30% of patients with lupus and present a high specificity for lupus[4, 27]. A frequency equal to 32.7% was found in our series, comparable to that of North America (31%)[24], Tunisia (36.9%)[15] and higher than that noted in the European and Indian population[17,22]. Isenberg et al.[33], showed that this incidence can vary according to the ethnic origin of the patients or the sensitivity of anti-Sm equal to 50% in black subjects compared to other populations where the anti-Sm Ab were found in less than 25%[17].

Another study showed that this incidence also vary depending on the technique used for their detection. Sensitivity of anti-Sm from 3 to 7% in the European population and 30% in the African-American populations by the Ouchterlony technique respectively becomes[19] and 52% by the ELISA technique[34,35]. In Tunisia, Louzir et al.[19], noted that 57% of cases had positive anti-Sm Ab in a series of 295 lupus patients. The detection of anti-Sm antibodies was carried out by counter-immunoelectrophoresis. While Haddouk et al.[15] used an immunodot technique and the positivity of anti-Sm Abs was at 36.9%.

Anti-RNP was found in 21.8% of our patients while a lower frequency has been noted in the European and Kuwaiti population (13%)[17,20]. It varied between 32.1% and 49% in the Tunisian population[15,18]. A significant correlation has been observed between this auto-ab and skin damage[36,37]. Interestingly, anti-RNP antibodies did not correlate with presence of an overt overlap syndrome or mixed connective tissue disease (MCTD), i.e., features of SLE and inflammatory myositis. There was, however, an association with Raynaud's phenomenon

Table 3: Frequency of clinical manifestations as a function of the positivity or otherwise of auto-antibodies

Clinical manifestations	Anti-DNAn Positive (n=115)	Anti-DNAn negative (n=59)	P value (χ^2Pearson)	Anti-Sm positive (n=57)	Anti-Sm negative (n=117)	P value (χ^2Pearson)	Anti-RNP positive (n=38)	Anti-RNP negative (n=136)	P value (χ^2Pearson)	Anti-SSB Positive (n=67)	Anti-SSB Negative (n=107)	P value (χ^2Pearson)
Cutaneous damage	85	46	0.557	49	82	0.023	34	97	0.022	26	105	0.387
Photosensitivity	48	32	0.117	28	52	0.561	18	62	0.846	14	66	0.780
Malar rash	64	36	0.498	37	63	0.166	27	73	0.055	23	77	0.068
Fever	14	6	0.710	12	8	0.018	8	12	0.101	4	16	0.878
Articular manifestation	95	48	0.838	49	94	0.363	34	109	0.184	27	116	0.720
Lupus Nephropathy	36	11	0.075	20	37	0.094	13	34	0.258	8	39	0.777
Pericarditis	11	2	0.142	5	8	0.649	2	11	0.558	5	8	0.052
Neuropsychiatric	14	2	0.058	6	10	0.672	4	12	0.748	2	14	0.523
Haematological disorders	91	42	0.341	47	86	0.371	33	100	0.222	27	106	0.479
Anemia	84	32	0.013	45	71	0.016	32	84	0.009	24	92	0.268
AIHA	9	8	0.228	6	11	0.815	3	14	0.660	1	16	0.161
Leucopenia	29	13	0.642	15	27	0.639	10	32	0.723	7	35	0.741
Lymphopenia	43	20	0.650	21	42	0.903	14	49	0.927	12	51	0.866
Thrombopenia	30	14	0.735	14	30	0.878	11	33	0.557	5	39	0.164
Raynaud's syndrome	34	15	0.565	25	24	0.001	18	31	0.003	12	37	0.194
SGS	5	4	0.493	1	8	0.155	1	8	0.424	4	5	0.038
APLS	16	4	0.163	7	13	0.820	5	15	0.716	3	17	0.677
Hypocomplementemia	54	14	0.009	29	39	0.077	20	48	0.066	18	50	0.059

SGS: Gougerot-Sjogren syndrome

(p= 0.003), which is a common but less specific feature of MCTD.

The frequency of anti-SSA was noted in 38.5% of cases, it varied during SLE from 20 to 65% depending on the different series of the literature[15-20]. These antibodies have a strong predictive value for the diagnosis of lupus disease, particularly for patients with positive ANA but without anti ds DNA or anti-Sm[38]. We found a significant correlation between anti-SSA antibodies and Raynaud's syndrome. The possible association of the anti-SSA antibody with photosensitivity in SLE patients has been a matter of controversy. Dillon et al.[39], Synkowski et al.[40] and our study found no relation between anti-SSA and photosensitive erythema. Scopelitis et al[41] in a study included 88 patients, reported no relation between anti-SSA and photosensitivity and no difference in the manifestations of SLE between lupus patients with or without anti-SSA. In contrast, Mond CB et al[42], in a study of 131 SLE patients; demonstrated a significant association between anti-Ro and rash photosensitivity.

Anti-SSBs are particularly frequent in primary Gougerot-Sjogren syndrome (SGS). They were found in 10% of patients with SLE[42], at 18.4% in our patients, at 33.6% and 14.3% in the Tunisia[15,18] and at 19% in the European and Kuwaiti population[17,20]. Moreover, six patients of our series had positive anti-SSB and SGS associated with the lupus with a significant correlation. In addition, anti-SSB was significantly correlated with pericarditis (p =0.052) in our study. Oshiro AC et al.[14] in a study of cardiac manifestations in children with SLE, demonstrated an association between cardiac manifestations of SLE and anti-La/SS-B antibodies (p=0.03) . This finding represents the first association of anti-La antibodies with cardiac manifestations of SLE in both children and adults.

CONCLUSION

The study concludes that the auto-antibodies identified for diagnosis correlate with clinical manifestations and provide important prognostic information. Our work also highlights the high frequency of auto-antibodies in Algerians patients with SLE at the time of diagnosis. Prospective multicentre approach involving more patients is required to estimate the prevalence of auto-antibodies and to define more accurately prognostic factors associated with the disease.

ACKNOWLEDGEMENTS

We would like to thank the patients for their participation and the staff at the Internal Medicine department of the University Hospital of ORAN (EHUO) and the University Hospital of Sidi-bel-Abbes (CHU-SBA) for their invaluable support, guidance, and educational insight.

REFERENCES

1. Tan EM. Antinuclear antibodies: diagnostic markers for autoimmune diseases and probes for cell biology. Adv Immunol 1989; 44:93-151.
2. Merkel PA. Systemic lupus erythematosus. In: Andreoli TE, Carpenter CCJ, Griggs RC, Loscalzo J Cecil essentials of medicine. 6th Ed. Philadelphia (PA): WB Saunders; 2004:745-9.
3. Alba P, Bento L, Cuadrado MJ, Karim Y, Tungekar MF, Abbs I et al. Anti-ds DNA, anti-Sm antibodies, and the lupus anticoagulant: significant factors associated with lupus nephritis. Ann Rheum Dis 2003; 62:556 60.
4. Ter Borg EJ, Horst G, Hummel EJ, Limburg PC, Kallenberg CG. Measurement of increases in anti-double-stranded DNA antibody levels as a predictor of disease exacerbation in systemic lupus erythematosus. A long-term, prospective study. Arthritis Rheum 1990; 33:634 43.
5. Janwityanuchit S, Verasertniyom O, Vanichapuntu M, Vatanasuk M. Anti-Sm: Its predictive value in systemic lupus erythematosus. Clin Rheumatol 1993; 12:350 3.
6. Ravirajan CT, Rowse L, MacGowan JR, Isenberg DA. An analysis of clinical disease activity and nephritis-associated serum autoantibody profiles in patients with systemic lupus erythematosus: a cross-sectional study. Rheumatology 2001; 40:1405 12.
7. Winfield JB, Brunner CM, Koffler D. Serologic studies in patients with systemic lupus erythematosus and central nervous system dysfunction. Arthritis Rheum 1978; 21:289 94.
8. Riboldi P, Gerosa M, Moroni G, Radice A, Allegri F, Sinico A et al. Anti-DNA antibodies: a diagnostic and prognostic tool for systemic lupus erythematosus? Autoimmunity 2005; 38:39 45.
9. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997; 40:1725.
10. Churg J, Bernstein J, Glassock RJ. Lupus nephritis. In: Renal disease : classification and atlas of glomerular diseases. 2nd Ed. New York, USA: Igaku-Shoin; 1995.
11. Meyer O. Lupus et syndrome des anticorps antiphospholipides. Critères de diagnostic et de suivi. Rev du Rhum Monograph 2010; 77:82 8.
12. Parker MD. Ribonucleoprotein antibodies: frequency and clinical significance in systemic lupus erythematosus, scleroderma, and mixed connective tissue disease. J Lab Clin Med 1973; 82:769-75.
13. Tikly M, Burgin S, Mohanlal P, Bellingan A, George J. Autoantibodies in black South Africans with systemic lupus erythematosus: Spectrum and clinical associations. Clin Rheumatol 1996; 15:143 7.

14. Oshiro AC, Derbes SJ, Stopa AR, Gedalia A. Anti-Ro/SS-A and anti-La/SS-B antibodies associated with cardiac involvement in childhood systemic lupus erythematosus. Ann Rheum Dis 1997; 56:272 4.

15. Haddouk S, Ben Ayed M, Baklouti S, Hachicha J, Bahloul Z, Masmoudi H. Autoantibodies in systemic lupus erythematosus: Spectrum and clinical associations.. Pathol Biol 2005; 53:311-7.

16. Uthman I, Nasr F, Kassak K, Masri AB. Systemic lupus erythematosus in Lebanon. Lupus 1999; 8:713–5.

17. Cervera R, Khamashta MA, Font J, Sebastiani GD, Gil A, Lavilla P et al. Systemic lupus erythematosus: clinical and immunological patterns of disease expression in a cohort of 1000 patients. The European Working Party on systemic lupus erythematosus. Medicine 1993; 72:113–24.

18. Ghedira I, Sakly W, Jeddi M. Clinical and serological features of systemic lupus erythematosus: 128 cases. Pathol Biol 2002; 50:18-24.

19. Louzir B, Othmani S, Ben Abdelhafidh N. Systemic lupus erythematosus in Tunisia. A multicentric study. About 295 cases. Rev Méd Interne 2003; 24:768-74.

20. Al-Mekaimi A, Malaviya AN, Serebour F, Umamaheswaran I, Kumar R, Al-Saeid K et al. Serological characteristics of systemic lupus erythematosus from a hospital-based rheumatology clinic in Kuwait. Lupus 1997; 6:668 74.

21. Alballa SR. Systemic lupus erythematosus in Saudi patients. Clin Rheumatol 1995; 14:342 6.

22. Malaviya AN, Chandrasekaren AN, Kumar A, Shamar PN. Systemic lupus erythematosus in India. Lupus 1997; 6:690–700.

23. El Hadidi KT, Medhat BM, Abdel Baki NM, Abdel Kafy H, Abdelrahaman W, Yousri AY et al. Characteristics of systemic lupus erythematosus in a sample of the Egyptian population: a retrospective cohort of 1109 patients from a single center. Lupus 2018; 27:1030 8.

24. Tan EM, Cohen AS, Fries JF, Masi AT, Mcshane DJ, Rothfield NF et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982; 25:1271 7.

25. Bouras M, Hali F, Khadir K, Benchikhi H. Systemic lupus erythematosus: mortality and poor prognostic factors in a Moroccan series of 129 cases. Ann Dermatol Venereol 2014; 141:141-3.

26. Chahade WH, Sato EI, Moura Jr JE, Costallat LT, Andrade LE. Systemic lupus erythematosus in Sao Paulo/Brazil: a clinical and laboratory overview. Lupus 1995; 4:100–3.

27. Swaak AJ, Groenwold J, Bronsveld W. Predictive value of complement profiles and anti-ds DNA in systemic lupus erythematosus. Ann Rheum Dis 1986; 45:359 66.

28. DeGiorgio LA, Konstantinov KN, Lee SC, Hardin JA, Volpe BT, Diamond B. A subset of lupus anti-DNA antibodies cross-reacts with the NR2 glutamate receptor in systemic lupus erythematosus. Nat Med 2001; 7:1189 93.

29. Winn DM, Wolfe JF, Lindberg DA, Fristoe FH, Kingsland L, Sharp GC. Identification of a clinical subset of systemic lupus erythematosus by antibodies to the sm antigen. Arthritis Rheum 1979; 22:1334 7.

30. Koffler D, Schur PH, Kunkel HG. Immunological studies concerning the nephritis of systemic lupus erythematosus. J Exp Med 1967; 126:607 24.

31. Zonana-Nacach A, Barr SG, Magder LS, Petri M. Damage in systemic lupus erythematosus and its association with corticosteroids. Arthritis Rheum 2000; 43: 1801–8.

32. Kowal C, DeGiorgio LA, Nakaoka T, Hetherington H, Huerta PT, Diamond B et al. Cognition and immunity; antibody impairs memory. Immunity 2004; 21:179–88.

33. Isenberg DA, Garton M, Reichlin MW, Reichlin M. Long-term follow-up of autoantibody profiles in black female lupus patients and clinical comparison with Caucasian and Asian patients. Br J Rheumatol 1997; 36:229 33.

34. Meyer O. Acute Disseminated lupus erythematosus. Diagnostic, course, principles of treatment. Rev Prat 1997; 47:1821–31.

35. Meyer O. Biologie du lupus érythémateux systémique. Rev Rhum 1999; 66:75s–80.

36. Al-Jarallah K, Al-Awadi A, Siddiqui H, Al-Salim I, Shehab D, Umamaheswaran I et al. Systemic lupus erythematosus in Kuwait—hospital based study. Lupus 1998; 7:434 8.

37. Reichlin M, Van Venrooij WJ. Autoantibodies to the URNP particles: relationship to clinical diagnosis and nephritis. Clin Exp Immunol 2008; 83:286 90.

38. Sánchez-Guerrero J, Lew RA, Fossel AH, Schur PH. Utility of anti-Sm, anti-RNP, anti–Ro/SS-A, and anti–La/SS-B (extractable nuclear antigens) detected by enzyme-linked immunosorbent assay for the diagnosis of systemic lupus erythematosus. Arthritis Rheum 1996; 39:1055 61.

39. Dillon CF, Jones JV, Reichlin M. Antibody to Ro in a population of patients with Systemic Lupus Erythematosus: distribution, clinical and serological associations. J Rheumatol 1983; 10:380-6.

40. Synkowski DR, Reichlin M, Provost TT. Serum autoantibodies in systemic lupus erythematosus and correlation with cutaneous features. J Rheumatol 1982; 9:380-5.

41. Scopelitis E, Biundo JJ, Alspaugh MA. Anti-SS-A antibody and other antinuclear antibodies in systemic lupus erythematosus. Arthritis Rheum 1980; 23:287 93.

42. Alexander EL, Hirsch TJ, Arnett FC, Provost TT, Stevens MB. Ro (SSA) and La (SSB) antibodies in the clinical spectrum of Sjogren's syndrome. J Rheumatol 1982; 9:239-46.

CONTRIBUTORS

BNM conceived the idea, wrote initial manuscript, collected and interpreted data and finalized the draft. ZK and KK helped correction of the proposal, literature search, data collection, interpretation and overall supervision of the project. HN, BBM and HST provided technical support, helped in data interpretation and provided expert guidance where needed. All authors contributed significantly to the submitted manuscript.