ORIGINAL ARTICLE

Clinical manifestations of patients with Systemic Lupus Erythematosus (SLE) in Khyber Pakhtunkhwa

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Abstract

Objective: To determine major symptoms and signs in patients of systemic lupus erythematosus.

Methods: This cross-sectional study was conducted at the Lady Reading Hospital, Khyber Teaching Hospital and Hayatabad Medical Complex, Peshawar, Pakistan, from January 15, 2014, to August 15, 2016, and comprised patients of systemic lupus erythematosus. Data was collected through an interview-based questionnaire containing questions about different symptoms. SPSS 20 was used for data analysis.

Results: Of the 663 patients, 606(91.4%) were females and 57(8.6%) males. The overall mean age of patients was 33.09 ± 12.40 years and the mean age of diagnosis was 31.85 ± 12.40 years. The most common general symptom in our study was fatigue which was present in 524(79.03%) patients. Other constitutional symptoms were fever 334(50.04%), body aches 443(66.08%) and weakness 411(62%). The most common clinical manifestation in our study was arthritis 518(78.1%). Malar rash was found in 487(73.5%) patients. Dry eye was in 227(34.2%) patients, followed by conjunctivitis 156(23.5%). Anaemia was present in 444(66.96%) patients, followed by leukopenia 166(25.03%) and thrombocytopenia 42(6.33%).

Conclusion: Significant regional differences existed in the clinical manifestations of systemic lupus erythematosus in Khyber Pakhtunkhwa compared to other regions.

Keywords: Systemic lupus erythematosus, Autoimmune disease, Lupus antibodies. (JPMA 67: 1180; 2017)

Introduction

Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune inflammatory disease that can affect any part of the body. The prominent feature of this disease is immunological abnormalities, mainly the production of a number of antinuclear antibodies. The aetiology of SLE is unknown with a variety of presenting features and manifestations. It affects women more frequently compared to men; more than 90% of new patients presenting with SLE are women in the childbearing years. Symptoms vary in different people who may come and go, depending on the part of the body involved and can be mild, moderate or severe.[1]

The most common pattern is a mixture of constitutional complaints with skin, musculoskeletal, mild haematologic, and serologic involvement, but some patients predominately have haematologic, renal, or central nervous system manifestations. The dominating pattern during the initial years of illness tends to prevail throughout the disease course.[2] About 10% of the people with lupus confined to the skin will develop the systemic form of lupus (SLE).[3]

Since there is significant environmental variability in different countries, the manifestations of SLE will be different depending on the region. For example, as different countries vary in the levels of sunlight they receive and exposure to ultraviolet (UV) rays affects dermatological symptoms of SLE. Some studies hypothesise there is a genetic connection between race and lupus which affects disease prevalence. If this is proved to be true, the racial make-up of countries affects disease, and will cause the incidence in a country to change as the racial make-up changes.[4]

SLE is reportedly more common and more severe in people of African and Asian descent residing in industrialised countries. Renal disease is fairly common in SLE patients in the developing world and is a common cause of morbidity and mortality. Discoid lupus and lymphopenia are frequent clinical features of SLE in patients of African descent. Thrombotic events and associated anti-phospholipid antibodies seldom occur in the Chinese and Black African SLE patients as compared to Caucasian patients. Infections, including tuberculosis, are among the major causes of comorbidity and mortality in SLE across all regions of the developing world.[5]

A study conducted in Asia revealed that common manifestations included mucocutaneous lesions (seen in 52-98% of patients) and arthritis/musculoskeletal complaints (36-95%). The study also revealed that antinuclear antibodies were generally positive in 89-100% of patients. Renal

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involvement of the disease ranged from 18% to 100% with most of the articles reporting this in greater than 50% of their patients. Discoid lesions, serositis and neurologic features were the least frequently seen symptoms.[6]

Keeping in view the onset, progression and severity of the disease, the current study was conducted to determine the most common presenting complaints and clinical features of patients of SLE in a tertiary hospital along with classifying the main presentation and clinical features of the disease according to the American College of Rheumatology (ACR) criteria for proper management.

Patients and Methods

This cross-sectional study was conducted at the Lady Reading Hospital, Khyber Teaching Hospital and Hayatabad Medical Complex, Peshawar, Pakistan, from January 15, 2014, to August 15, 2016, and comprised SLE patients. The patients of SLE visiting the tertiary hospitals residing in Peshawar as well as in the nearby villages and areas of Peshawar were approached to participate in the study and to answer questions of an interview-based survey. The questionnaire was translated into the local language by the interviewer to remove any communication barrier. Data was collected from January 20, 2014, to May 10, 2016, via convenient sampling. Verbal consent was taken from the patients and they were informed of the professional secrecy maintained in this voluntary study.

The questionnaire developed was pretested in a pilot sample of 10 patients after which no major changes were made to the questionnaire. Questions were asked regarding the different symptoms patients had initially at the start of the disease and the symptoms with which they presented at the hospital later on along with the signs observed in the areas of the body affected by SLE with any other peculiar signs noted as well. Most of the major systems were included in the questionnaire. The questionnaire also included laboratory tests for different antibodies present in the serum done by the patients as suggested by the doctors in the hospital.

SPSS 20 was used for data analysis. Continuous data was presented in the form of mean ± standard deviation (SD), whereas categorical and nominal data was presented as frequencies and percentages.

The committee for ethical reviews of Rehman Medical College, Peshawar, approved the study.

Results

Of the 663 participants, 606(91.4%) were females and

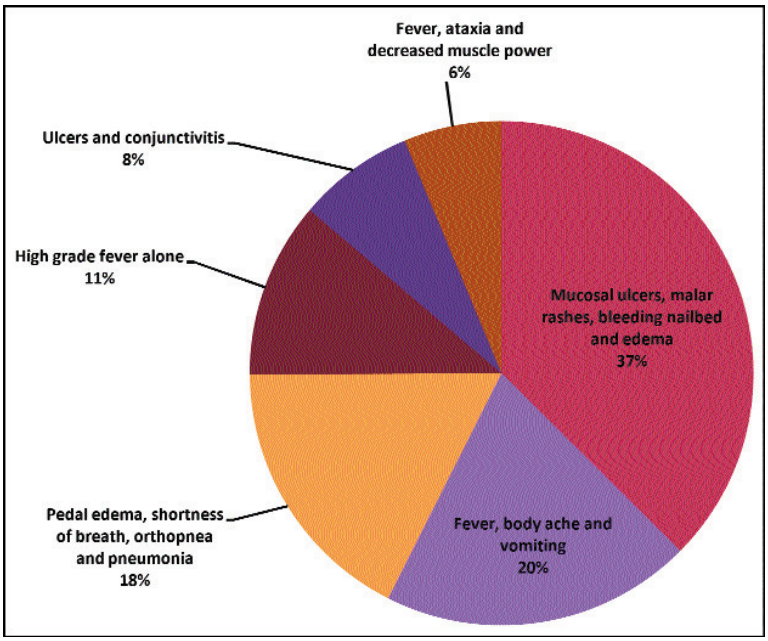
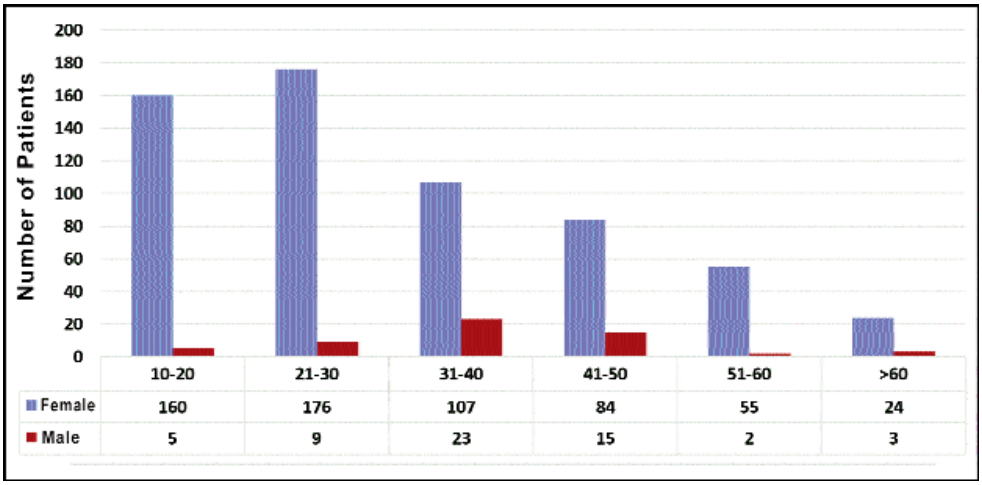


Figure-2: Showing initial symptoms.



SLE: Systemic lupus erythematosus.

Figure-1: Showing age distribution of patients with SLE.

Table-1: Demographic data of patients with SLE.

Characteristics	No. (%)
Total number of patients.	663
Gender	
Female	606 (91.40%)
Male	57 (8.59%)
Gender ratio (Female: Male)	10.63:1
Mean age (years)	33.09±13.34 (15-63)
Mean age of SLE diagnosis (years)	31.85±12.40
Marital status	
Unmarried	133 (20.06%)
Married	530 (79.93%)
Family History	60(9.04%)

SLE: Systemic lupus erythematosus.

57(8.6%) males. Female-to-male ratio (F: M) was 10.63: 1. The overall mean age was 33.09±12.40 years (range: 15-63 years) and mean age of diagnosis was 31.85±12.40 years. About 530(79.93%) patients were married while 133(20.06%) were unmarried. Moreover, 60(9.04%) patients had a positive family history of SLE (Table-1).

Also, 176(29.04%) female patients were in the age group of 21-30 years while 23(40.35%) males were in the age group of 31-40 years. It was followed by 10-20 years in 160(26.40%) females and 41-50 in 15(26.31%) males (Figure-1).

Initial symptoms most commonly included: mucosal ulcers, malar rashes, bleeding nailbed and oedema in 247(37.3%) patients; fever, body ache and vomiting in 138(20.8%) patients; pedal oedema, shortness of breath, orthopnoea and pneumonia in 114(17.2%) patients; high-grade fever alone in 74(11.2%) patients; ulcers and conjunctivitis in 49(7.4%) patients; and fever, ataxia and decreased muscle power in 41(6.2%) patients (Figure-2).

Clinical manifestation showed that 524(79.03%) had fatigue, 334(50.4%) had fever, 383(57.8%) oedema, 156(23.5%) had conjunctivitis and 236(35.6%) had hypertension (Table-2).

Anaemia which was seen in 444(66.96%) patients was the most common haematological clinical manifestation, followed by leukopenia found in 166(25.03%) and thrombocytopenia in 42(6.33%) patients. In addition, 82(12.36%) patients had elevated serum creatinine levels, 270(40.72%) had proteinuria while haematuria was found in 153(23.07%) patients.

Table-2: Showing Clinical manifestation of SLE patients in our study.

Characteristics	Female (n=606) %	Male (n=57) %	Total (n=663) %
Fatigue	484 (79.86%)	40 (70.17%)	524 (79.03%)
Arthritis	469 (77.39%)	49 (85.96%)	518 (78.1%)
Fever	304 (50.16%)	30 (52.63%)	334 (50.4%)
Itching	280 (46.20%)	17 (29.82%)	297 (44.8%)
Weakness	384 (63.36%)	27 (47.36%)	411 (62.0%)
Body aches	399 (65.84%)	44 (77.19%)	443 (66.8%)
Oedema	352(58.08%)	31 (54.38%)	383 (57.8%)
Ocular			
Retinal exudates	48 (7.9%)	2 (3.5%)	50 (7.5%)
Blindness	41 (6.7%)	9 (15.78%)	50 (7.5%)
Dry eye	201 (33.16%)	26 (45.61%)	227 (34.2%)
Conjunctivitis	145 (23.92%)	11 (19.29%)	156 (23.5%)
Mucocutaneous			
Photosensitivity	380 (62.70%)	36 (63.15%)	416 (62.7%)
Malar rash	438 (72.27%)	49 (85.96%)	487 (73.5%)
Alopecia	389 (64.19%)	17 (29.82%)	406 (61.2%)
Mucosal ulcer	391 (64.52%)	41 (71.92%)	432 (65.2%)
Raynaud phenomenon	265 (43.72%)	33 (57.89%)	298 (44.9%)
Pulmonary			
Pleuritis	79 (13.03%)	13 (22.80%)	92 (13.9%)
Cardiovascular			
Hypertension	211 (34.81%)	25 (43.85%)	236 (35.6%)
Pericarditis	57 (9.40%)	11 (19.29%)	68 (10.3%)
Endocarditis	62 (10.23)	6 (10.52%)	68 (10.3%)
Gastrointestinal			
Splenomegaly	110 (18.15%)	4 (7.01%)	114 (17.19%)
Haepatomegaly	80 (13.20%)	6 (10.52%)	86 (12.97%)
Nausea/vomiting	296 (48.84%)	21 (36.84%)	317 (47.8%)
Diarrhoea	177 (29.20%)	16 (28.07)	193 (29.1%)
Melena	16 (2.64%)	0	16 (2.4%)
Neuro Psychiatric			
Neuropathies	177 (29.20%)	25 (43.85%)	202 (30.5%)
Mood swing	325 (53.63%)	28 (49.12%)	353 (53.2%)
Seizures	40 (6.60%)	5 (8.77%)	45 (6.8%)
Psychiatric illness	63 (10.39%)	12 (21.05%)	75 (11.31%)
Paralysis	16 (2.64%)	1 (1.75%)	17 (2.6%)
Gynaecological			
Menorrhagia	171 (28.21%)	-	171 (25.8%)
Amenorrhea	163 ((26.89%)	-	163 (24.6%)
Decreased libido	24 (3.96%)	5 (8.77%)	29 (4.4%)

SLE: Systemic lupus erythematosus.

Furthermore, 42(6.33%) patients had positive serum rheumatoid arthritis (RA) factor in our study. Antinuclear antibody (ANA) was positive in 607(91.55%) patients while 575(86.72%) had positive anti-double stranded deoxyribonucleic acid (anti-ds DNA) antibodies in serum. Besides, 8(1.20%) patients were anti-DNA positive and ANA-negative for antibodies (Table-3).

Table-3: Laboratory investigation in patients with SLE in our study.

Characteristics	Female(n=606) %	Male (n=57) %	Total (n=663) %
Anaemia	404 (66.66%)	40 (70.17%)	444 (66.96%)
Leukopenia	150 (24.75%)	16 (28.07%)	166 (25.03%)
Thrombocytopenia	40 (6.60%)	2 (3.50%)	42 (6.33%)
Elevated serum creatinine	75(12.37%)	7(12.28%)	82(12.36%)
Proteinuria	247 (40.75%)	23 (40.35%)	270 (40.72%)
Haematuria	143 (23.59%)	10 (17.54%)	153 (23.07%)
RA	40(6.60%)	2(3.50%)	42(6.33%)
ANA +ve	557 (91.91%)	50 (87.71%)	607 (91.55%)
Anti-ds DNA	525 (86.63%)	50 (87.71%)	575 (86.72%)
ANA -ve anti DNA +ve	8 (1.32%)	0	8 (1.20%)

Anti-ds: Anti-double stranded
DNA: Deoxyribonucleic acid
ANA: Antinuclear antibody.

of SLE. Systemic lupus erythematosus commonly affects young females of reproductive age, and the mean age of SLE onset ranges between 25.7-34.5 years in the Asian-Pacific region. A complex interplay of genetic, hormonal, environmental and socio-economic factors likely contributes to the incidence and prevalence.[12]

In our study almost 30% of the females were in the age group of 21-30 years while a majority of males (40%) were in the age group of 31-40 years. A correlation between age and incidence of SLE mirrors peak age of production of female sex hormones. Onset of SLE is usually after puberty, typically in the 20s and 30s, with 20% of all diagnosed cases observed during the first 2 decades of life.[13]

In majority of patients (37%), initial symptoms were malar

Table-4: Clinical manifestation of systemic lupus erythematosus in different ethnicities.

Clinical Manifestations	Our Study	Saudi Arabia	India	China	Oman	UAE	Iran
No of patients	663	624	1366	552	73	110	410
F:M	10.63:1	9.8:1	11:1	8.7:1	23.1	-	6.6:1
Arthritis	78.1	90.8	68	62	47.8	86.2	65.5
Photo sensitivity	62.7	26	48	26	-	-	54.5
Malar rash	73.5	56	58.5	51	-	62	60
Pleuritis	13.9	15.8	36	-	23.9	-	26
Pericarditis	10.3	20.7	15	-	7.5	-	12
Neuropsychiatric	30.5	25.3	28	19	33.8	-	31.5
Hepatomegaly	12.97	-	-	19	-	-	-
Leukopenia	25.03	30.1	14	29	23	51	64.5
Thrombocytopenia	6.33	10.9	9	25	10.4	17.4	44.5
ANA	91.55	99.7	97	99.8	97	98.2	93
Anti-Ds DNA	86.72	80.1	68	81.3	92	85.3	83

Anti-ds: Anti-double stranded
DNA: Deoxyribonucleic acid
UAE: United Arab Emirates
F:M: Female-to-male ratio.

Discussion

This was the first study done comprising the people of Khyber Pakhtunkhwa (KPK) which described the epidemiological, clinical and laboratory characteristics. In our study, 663 patients were included from different tertiary care hospitals in the Khyber Pakhtunkhwa province in which F:M ratio was 10.63:1. The findings of our study were close to similar studies done in Saudi Arabia (9.8:1)[7] and America (9.6:1).[8] Our data was a little higher than in India (11.1)[9] and Oman (23.1).[10] The F:M ratio peaks at 11:1 during the childbearing years.[11]

In our study, the mean age of diagnosis of SLE was 31.85±12.40 years. Almost 80% of the patients were married and 9.04% patients had a positive family history

rash, mucosal ulceration, nail bleed and oedema. It was followed by fever and body aches 20% as initial symptoms.

The most common general symptom in our study was fatigue (79.03%). Other constitutional symptoms were fever (50.04%), body aches (66.08%) and weakness (62%).

The most common clinical manifestation in our study was arthritis (78.1%), which was in agreement with previous studies.[12,14] Arthritis and arthralgias have been noted in up to 95% of patients with SLE. These clinical manifestations may be mistaken for another type of inflammatory arthritis and can mislead the diagnosis of SLE by many months or years.[15]

Ocular manifestations were also observed in our study. Dry eye was the most common (34.2%), followed by conjunctivitis (23.5%). A study done by Klejnberg T. et al. showed that dry eye is the most common clinical ocular manifestation of SLE which was 31% in his study.[16] In a study by Jensen et al., 60% of 20 patients with SLE reported at least one symptom of dry eye.[17] In general, dry eye symptoms associated with lupus are mild; however, severe pain and vision loss can occur. Typical findings on ophthalmic examination include corneal epitheliopathy, abnormal tear film and decreased tear production. More significant manifestations such as filamentary keratitis, corneal scarring or ulcerations can occur.

In cutaneous manifestation, malar rash was found in 73.5% of the patients. Malar rash was found in 60.5% patients in a study conducted in Iran,[18] 63% in Tunisia[7] and 62% patients in the United Arab Emirates (UAE)[14] (Table-4). The difference is due to the environmental factors and different geographical areas and the number of patients in each study. Photosensitivity was reported high in our study (62%) compared to other studies done. This difference may be partly due to varying levels of sunshine and the varying amounts of sunlight exposure.

Pleuritis was found in (13.9%) of patients as pulmonary manifestation. In Saudi Arabia it was found in 15.8% of patients with SLE.[8]

Hypertension was found in 35.6% of patients with SLE in our study. Pericarditis was in 10% of patients. Pericarditis is the most common cardiac finding of SLE. Evidence of pericarditis has been found at autopsy in over 62% of lupus patients, but only 25% of cases clinically manifest pericarditis.[19] In the United States, pericarditis is found in 14% of patients,[9] 7.5% in Oman[11] and 12% in Iran.[14] Other studies done in Pakistan showed pericarditis in 9% of the patients (Table-4).

Psychiatric illness was found in 11% patients while seizures were observed in 6.8% patients. About one-third of SLE patients from Iran presented with neurological involvement.[14] Mok et al.[20] described the prevalence of neuropsychiatric (NP) events to be 19% in Chinese SLE patients. The difference in methodologies may explain this discrepancy.

Anaemia was found in 66.9% patients which was almost similar to patients in the UAE,[15] but less than patients in Saudi Arabia[8] and Tunisia.[7] Leukopenia was found in 25.03% of patients and thrombocytopenia found in 6.33% patients. In China,[21] leukopenia was found in 29% patients and in 23.5% patients in Oman[11] which was similar to our study, but it was higher in Iran[19] where it was found in 64.5% patients while in the UAE[20] it was found in 51% of the patients (Table-4).

Our study had ANA prevalence of 91.55% and dsDNA prevalence of 86.72%. This is similar to that in the UAE[20] and Iran[19] and higher than that in Indians[10] and Tunisians[7] (Table-4).

In summary, we have performed a retrospective study on the clinical and immunological characteristics of SLE patients in Khyber Pakhtunkhwa populations. The results of this study have outlined the main characteristics of lupus in KPK populations and revealed several differences between ethnicities worldwide.

The current study had its potential limitations. As it was a descriptive study, it cannot provide statistical associations. Further studies, preferably multicentre studies, should be performed to describe the pattern of SLE in Pakistani populations.

Conclusion

Significant regional differences existed in the clinical manifestations of SLE in KPK compared to other regions. Therefore, measures should be taken to treat and manage the SLE cases based on data of this region rather than following standard therapy procedures which may differ in different regions.

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References

1. Cojocaru M, Cojocaru IM, Silosi I, Vrabie CD. Manifestations of Systemic Lupus Erythematosus. Maedica (Buchar) 2011; 6: 330-6
2. Gladman DD. Overview of the clinical manifestations of systemic lupus erythematosus in adults. [Online] 2017 [cited 2017 Jan 28]. Available from: URL: http://www.uptodate.com/contents/overview-of-the-clinical-manifestations-of systemic-lupus-erythematosus-in-adults
3. William C, Shiel Jr F. Lupus Causes, Treatment, Diagnosis, Pictures & Symptoms [Online] 2017 [cited 2017 January 28]. Available from: URL: http://www.medicinenet.com/systemic_lupus/article.htm
4. Danchenko N, Satia JA, Anthony MS. Epidemiology of systemic lupus erythematosus: a comparison of worldwide disease burden. Lupus 2006; 15: 308-18.
5. Tikly M, Navarra SV. Lupus in the developing world -is it any different? Best Pract Res Clin Rheumatol 2008; 22: 643-55.
6. Osio-Salido E, Manapat-Reyes H. Epidemiology of systemic lupus erythematosus in Asia. Lupus 2010; 19: 1365-73.
7. AlArfaj AS, Khalil N. Clinical and immunological manifestations in

624 SLE patients in Saudi Arabia. Lupus 2009; 18: 465-73.
8. Cooper GS, Parks CG, Treadwell EL, St Clair EW, Gilkeson GS, Cohen PL, et al. Differences by race, sex and age in the clinical and immunologic features of recently diagnosed systemic lupus erythematosus patients in the southeastern United States. Lupus 2002; 11: 161-7.
9. Malaviya AN, Chandrasekaran AN, Kumar A, Shamar PN. Systemic lupus erythematosus in India. Lupus 1997; 6: 690-700.
10. Al-Maini MH, El-Ageb EM, Al-Wahaibi SS, Al-Farsi Y, Richens ER. Demographic, autoimmune, and clinical profiles of patients with systemic lupus erythematosus in Oman. Rheumatol Int 2003; 23: 186-91.
11. Manzi S. Epidemiology of systemic lupus erythematosus. Am J Manag Care 2001; 7 (16Suppl): S474-9.
12. Jakes RW, Bae SC, Louthrenoo W, Mok CC, Navarra SV, Kwon N. Systematic review of the epidemiology of systemic lupus erythematosus in the Asia-Pacific region: prevalence, incidence, clinical features, and mortality. Arthritis Care Res (Hoboken) 2012; 64: 159-68.
13. Klein-Gitelman M, Reiff A, Silverman ED. Systemic lupus erythematosus in childhood. Rheum Dis Clin North Am 2002; 28: 561-77.
14. AlSaleh J, Jassim V, ElSayed M, Saleh N, Harb D. Clinical and immunological manifestationsin 151 SLE patients living in Dubai. Lupus 2008; 17: 62-6.
15. Grossman JM. Lupusarthritis. Best Pract Res Clin Rheumatol 2009; 23: 495-506
16. Klejnberg T, Moraes Junior HV. Ophthalmological alterations in outpatients with systemic lupus erythematosus. Arq Bras Oftalmol 2006; 69: 233-7.
17. Jensen JL1, Bergem HO, Gilboe IM, Husby G, Axéll T. Oral and ocularsicca symptoms and findings are prevalent in systemic lupus erythematosus. J Oral Pathol Med 1999; 28: 317-22.
18. Nazarinia MA, Ghaffarpasand F, Shamsdin A, Karimi AA, Abbasi N, Amiri A. Systemic lupus erythematosus in the Fars Province of Iran. Lupus 2008; 17: 221-7.
19. Doherty NE, Siegel RJ. Cardiovascular manifestations of systemic lupus erythematosus. Am Heart J 1985; 110: 1257-65.
20. Mok CC, Lau CS, Wong RW. Neuropsychiatric manifestations and their clinical associations in southern Chinese patients with systemic lupus erythematosus. J Rheumatol 2001; 28: 766-71.
21. Li WG, Ye ZZ, Yin ZH, Zhang K. Clinical and immunological characteristics in 552 systemic lupus erythematosus patients in a southern province of China. Int J Rheum Dis 2017; 20: 68-75.