Gender impact in systemic lupus erythematosus

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Abstract

Objective

Systemic Lupus Erythematousus (SLE), an autoimmune disease of unknown etiology manifesting as a pleomorphic systemic disease, affects mostly females, (female:male ratio 9:1). Clinical differences between genders, including a higher death rate in males, has been reported. Here we compared clinical manifestations and the 5-year survival probability in Mexican male and female crossbred cases living under similar socioeconomic conditions. A systematic review of published literature was also carried out.

Material and Methods

SLE patients treated at the Instituto Nacional de Cardiología "Ignacio Chávez" México City who fulfilled at least four classification criteria (ACR) were included. The frequency of clinical variables with emphasis on cardiovascular findings before and after the diagnosis were described, disease activity based on a validated scale (SLEDAI) was determined, and the 5-year survival rate was estimated.

Results

There were 33 men and 158 women, average age of 31 in both groups ranging from 7 to 65 and from 10 to 75 year in male and female patients respectively; both groups were followed for 3.8 years (median), average activity was of 12 points with a range of 5 to 23 in men, and 11 with a range of 2 to 24 in women. Main clinical characteristics in men were: discoid lupus, psychosis, pericarditis, lymphopenia, thrombocytopenia and SLE kidney disease. Immunological tests showed gender-linked differences in regard auto-antibodies (U1-nRNP, Sm, anticardiolipine and false VDRL) and hypocomplementemia. Cardiovascular features and survival rate were not different between gender.

Conclusion

Male Mexican SLE patients share clinical findings with other male SLE cases reported everywhere as can be deducted from systematic literature review covering 25-year.

Key words

Systemic Lupus Erythematosus (SLE), gender difference, male disease, ethnicity, survival rate and systematic literature review.

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Introduction

Systemic Lupus Erythematosus (SLE) an autoimmune disorder of unknown etiology, involves genetic, immune, environmental and hormonal factors; it has an immune-mediated pathogenesis through immune complex formation and deposition as well as immune and inflammatory cell participation in widespread tissue damage (1,2). Lupus is over-represented in women of childbearing age; in pediatric and elderly patients SLE did not show any gender preference. Young adults are affected in a sex ratio 9:1 favoring women. Previous studies on male SLE have suggested a higher mortality due to kidney and hematological disease and a race preference for colored people (3, 4). Criticism of these studies have focused on problems of population heterogeneity and incomplete criteria used to describe and follow-up the disease. In order to gain information in a relatively homogeneous population, we reviewed male SLE in a population that shared race, genetic, social and environmental characteristics, compared the clinical manifestations, and estimated 5-year survival rate between female and male patients and conducted a systematic review of published work on male SLE in the last 25 years.

Material and methods

Patients

Clinical charts from female and male patients who fulfilled at least 4 classification criteria (ACR) for SLE, seen between 1 January 1982 and 31 December 2002 were reviewed. The diagnosis was independently established by qualified rheumatologists at the Instituto Nacional de Cardiología I. Chávez, which is a national referral center serving people without social security, mostly low income people of Mexican Mestizo ancestry. In this study period a standard clinical approach was utilized and an equivalent diagnostic protocol was followed without major differences in laboratory procedures or standards. The immunologic studies included the presence of antinuclear antibodies by indirect immunofluorescence (IIF); antidouble-stranded DNA by IIF against Crithidia luciliae; anti-Smith, anti-small nuclear RNP, anti-Ro/SSA and anti-La/SSB by double immunodiffusion and ELISA; and anti-phospholipid (cardiolipin) IgG isotype antibodies by enzyme-linked immunosorbent assay.

Clinimetrics

For analysis purposes we accepted, arbitrarily, disease onset as being the same as the time when the definitive diagnosis was made at the hospital. Clinical characteristics evaluated were those accepted in the ACR classification and its simple frequencies were measured. To assess disease activity we used an adapted and validated Mexican version of the SLEDAI (5). A search for heart disease, either valvular or ischaemic, before the SLE diagnosis or afterwards, was also performed (37). Kidney disease was defined by abnormal urine sediment containing blood cells, cellular and hyaline casts, proteinuria higher than 500 mg/day and reduced creatinine clearance (< 60 ml/min). Percutaneous kidney biopsy findings were classified according to published WHO criteria.

Literature review

A MEDLINE search from 1978 up to 28 February 2003 for female and male SLE was done. Key words used were "gender differences AND lupus" according to the MESH system in English. Search was limited to human studies, any gender and without age restriction. Papers were selected according to the following criteria: (a) comparative studies between male and female SLE patients, (b) studies about male SLE patients, if diagnosis was established with at least 4 ACR classification criteria, and (c) a minimum 5-year follow up. Every paper was critically reviewed to verify the validity and relevance, and was classified according methodological design as case studies, case series, cross-sectional, case and controls and cohort/longitudinal studies.

Final review included only those papers that described comparative clinical studies between male and female SLE independent of its design, when outcomes were described as clinical manifestations, prevalence and clinical laboratory features.

Statistical analysis

An Excel format data-base was built with patient's clinical data from medical charts. Due to the fact that variables were categorical, $\chi 2$ or exact Fisher's test were used, as convenient. Five year survival was estimated by the Log Rank/Kaplan-Maier's technique. To compare published data with ours, a qualitative analysis of proportions was carried out. Statistical significance was accepted at α 0.05.

Results

Patients and clinimetrics

The frequency of the clinical manifestations among our female and male patients are shown in Table I. Differences between these groups were found in very few of them. In relation to skin and mucosal membrane manifestations, alopecia and malar erythema were found to be 4 and 2 times more frequently developed by female patients ($p < 0.05$ in both cases), on the other hand, discoid lupus was a male predominant manifestation ($p < 0.05$). Serositis is a common finding in this disease, since we were studying patients at a cardiovascular referal center, a major component of thoracic serositis could be expected. Only pericarditis was two times more common among male patients ($p < 0.05$).

With regard to central nervous system involvement, gender difference were found in relation to psychosis. It was observed that this manifestation occurred in 14% of male patients, while only

Table I. Clinical features in female/male SLE Mexican mestizo patients.

Manifestations	Female n = 151	Male n = 36	P
Bone and joint disorders			
Arthralgia	95 (63)	24 (67)	NS
Arthritis	114 (75)	25 (69)	NS
Skin and mucous membranes			
Alopecia	56 (37)	3 (8)	0.001
Butterfly erythema	80 (53)	12 (33)	0.05
Discoid lesions	8 (5)	9 (25)	0.001
Photosensitivity	61 (40)	11 (31)	NS
Oral ulcers	61 (40)	13 (36)	NS
Serositis			
Pleuritis	45 (30)	11 (31)	NS
Pericarditis	28 (19)	15 (42)	0.005
Peritonitis	17 (11)	7 (19)	NS
Neurological			
Convulsive disorders (Grand mal)	18 (12)	4 (11)	NS
Psychosis	6 (4)	5 (14)	0.05
Cardiovascular disorders			
High blood pressure	43 (28)	4 (11)	NS
Raynaud phenomenon	52 (34)	5 (14)	0.022
Pulmonary hypertension	22 (15)	3 (8)	NS
Laboratory			
Leukopenia	90 (60)	17 (47)	NS
Lymphopenia	88 (58)	33 (92)	0.000
Thrombocytopenia	47 (31)	19 (53)	0.02
Hemolytic anemia	37 (25)	7 (19)	NS
Urinary casts	36 (24)	20 (56)	0.000
Dyslipidemia	33 (22)	8 (22)	NS
Syndromes			
Vasculitis	32 (21)	7 (19)	NS
Renal failure	59 (48)	21 (70)	0.03
Associated pathology			
SLE + APLS*	21 (14)	9 (25)	NS
SLE + RA**	4 (3)	1 (3)	NS

*Anti-phospholipid syndrome; ** rheumatoid arthritis.

Table II. Kidney biopsy features in SLE Mexican mestizo patients according gender.

Original WHO classification of lupus nephritis[38]	Female no. (%)	Male no. (%)
I Normal glomeruli (by LM, IF, EM)	—	—
II Purely mesangial disease a) Normocelular mesangium by LM, but mesangial deposits by IF and/or EM b) Mesangial hypercellularity with mesangial deposits by IF and/ or EM	7 (12)	4 (25)
III Focal segmental proliferative glomerulonephritis	9 (15)	—
IVDiffuse proliferative glomerulonephritis	34 (58)	12 (75)
V Membranous glomerulonephritis	9 (15)	—
	59 (100)	16 (100)

LM: light microscopic abnormalities; IF: immunofluorescence positivity; EM: electron microscopic location of electron-dense deposits.

4% of females developed this disorder ($p<0.05$).

Vascular manifestations such as Raynaud's phenomenon and high blood pressure shown ($p<0.05$) a female predilection.

When the comparison focused on laboratory findings lymphopenia and thrombocytopenia were common male findings ($p<0.05$). Kidney disease defined on clinical grounds was common in males with marginal statistical significance in comparison to females. Renal biopsies shown heterogeneous results among female patients; most of them had diffuse and generalized glomerulonephritis (58%), but other types of glomerular involvement were also found. In contrast male patients had type IV glomerular changes or minor mesangial features without focal and segmentary membranous or glomerular sclerosis. Statistical analysis confirmed gender differences at a significant level ($p < 0.05$) (Table II).

There was no gender preference for a particular clinical syndrome such as vasculitis or renal failure, nor for an associated pathology like the antiphospholipid syndrome or rheumatoid arthritis-like features, the so-called "Rhupus syndrome" proposed by Panush (6) to designate those patients who had rheumatoid arthritis-like joint involvement as part of a clear multi-systemic disease which fulfilled the SLE classification criteria (Table I).

Sero-immunological tests showed that autoantibodies are common in SLE. We found that 9 out of 10 patients had circulating autoantibodies regardless of gender. However, anti-Sm and anti-U_1RNPn were seen more frequently in male than in female patients ($p<0.05$ in both cases); on the other hand, a false-positive VDRL was instead a female feature in these SLE patients, even though only a marginal p value was reached. Rheumatoid factor, another non-organ-specific autoantibody, was found with equal frequency in male and female SLE patients. As for the complement system analysis, differences between gender were only observed in the CH50% hemolytic test (functional), which was more frequently found in male than in female patients (Table III).

Finally, survival analysis failed to reveal gender-associated differences at five years.

Literature review

The published information is heterogeneous and comparison among studies was not always possible because designs were different, ethnic groups varied and outcomes and/or clinical findings, were not equally measured (Table IV). Studies which allowed to compare major clinical features and laboratory data, are shown in Table V. These data will be discussed below.

Table III. Autoantibody and complement tests in female/male Mexican mestizo patients.

Determination	Female no. (%)	Male no. (%)	p
Autoantibodies	149/151 (94)	32/36 (89)	
Specificity AAN			
Anti-DNA	43/150 (29)	4/20 (20)	NS
Anti-Sm	34/150 (23)	8/18 (44)	0.04
Anti-U_1RNPn	34/150 (29)	9/19 (47)	0.03
Anti-SSA/Ro	30/150 (20)	4/17 (10)	NS
Anti-SSB/La	14/150 (9)	2/18 (11)	NS
False VDRL	110/151 (73)	8/16 (50)	0.05
Anti-CL(IgG)	29/77 (38)	6/21 (29)	NS
R.F.	47/93 (51)	12/18 (67)	NS
Complement			
CH50 ↓	61/131 (47)	18/26 (70)	0.05
C3 ↓	44/117 (38)	14/27 (52)	NS
C4 ↓	54/123 (44)	15/29 (52)	NS

Discussion

Although SLE is predominantly a disease of childbearing women, accounting for 80 to 90% of cases, male SLE represents 4 to 30% of cases in different series (7, 8), reaching 30% in studies considering familial aggregation of SLE (8). Differences in clinical manifestations have been observed and an apparent race-linked variation has raised controversy (9,10). Diverse methodological approaches, sample size and other factors contributed because relatively biased opinions have been reported in the literature (11-14). The present study measured and compared the prevalence of most clinical and seroimmunological manifestations of SLE in a homogenous population of female and male patients and found that, in fact, male SLE has distinctive features.

A detailed comparison of the mean age at diagnosis revealed no difference between male and female SLE as seen by Molina *et al.* (15), Azizah *et al.* (13), Mok *et al.* (14),and Aranow *et al.* (16). Several authors claim that male SLE patients are younger than women patients (3, 17) or viceversa (4), but no explanation is offered and this variation seems irrelevant.

Considering specific clinical features such as skin involvement, kidney disease and hematologic findings, which carry important morbidity and mortality risks, we found discoid lupus, thrombocytopenia and renal involvement to be more frequent among male SLE. This observation compared with published studies in different ethnic groups agrees with most clinical reports. Latin-American (15) and Asian authors (13, 14) observed similar results with statistical difference, male SLE seems to be more aggressive than female disease in regard of progressive kidney disease ending in kidney failure (3, 11, 12, 15).

Skin and mucosal membranes involvement were studied by Asian observers, Azizah *et al.*, Mok *et al.*, Wang *et al.* (18). Independent studies showed a similar simple frequency in their patients, slightly above the observed frequency in Mexican Mestizo patients, discoid skin disease with cicatricial changes was seen in male Asian pa-

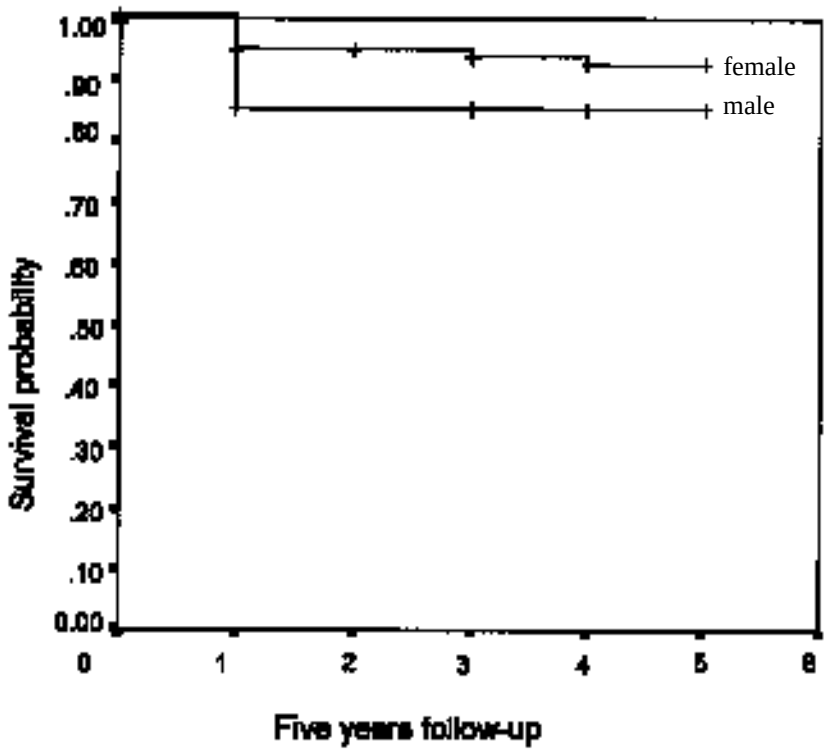

Fig. 1. Five years survival study (Kaplan-Maier-Log rank test) between SLE Mexican mestizo patients according gender.

tients as reported by Mok *et al*. with a similar frequency to our male Mexican Mestizo cases, while Wang *et al*. reported a low incidence of skin manifestations, especially in Indian patients.

Kidney disease and central nervous system involvement was mentioned by three papers, Azizah *et al*., Molina *et al*. and Wang *et al.*; their data agree with ours: there is a major frequency of these severe complications among male SLE patients, even they had higher number of male SLE patients suffering from either kidney or CNS disease in their independent studies. In our experience, in addition, kidney biopsy data showed 75% of male SLE suffering severe lupus glomerulonephritis WHO type IV, which may explain the progression to terminal renal failure in male cases (Table II).

Other studies covering small samples and specific aspects of male SLE confirms thrombocytopenia, neuropsychiatric abnormalities and a worse prognosis as gender-asocciated caracteristics (3, 4, 17, 19, 20).

Laboratory findings are many and complex in patients having a systemic and pleomorphic disease such as SLE. Hematologic abnormalities have been described in SLE for some time, and Koh *et al*. reported a female preference for low peripheral leukocyte quantitation. We found a male dominance only on lymphopenia, maybe this is a finding related to active and severe SLE in our male cases, but no definitive explanation is available with this limited observational study. Thrombocytopenia was also more common in our male SLE patients, as was seen by Mok *et al*. and others (10, 12, 17, 20); however, it was not confirmed by another study (4). Again, there is no explanation and no gender preference was demonstrated. In comparison between Asian patients and our series, hemolytic anemia had a variable frequency between 8 and 24% in Asian cases and a lower prevalence in Latin-American cases, 15 to 19% our cases showed no difference in comparison with Asian observers. Leukopenia is far more common, 30 to 60% of SLE patients showed reduced circulating white blood cells. Our cases are closer to Ward *et al.* (11), they studied patients collected in the US and found and slightly different from Colombian patients described by Molina *et al*. and 61 Chinese male patients seen by Koh *et al*..

Psychosis was a common disorder in Aranow's male SLE patients, this results were similar to our experience, in which higher psychosis prevalence in male patients was found ($p<0.05$), however other papers did not confirm this finding, therefore, functional brain abnormalities showed a tendency toward gender dominance without confirmation (16).

In regard of rheumatic disease such as arthritis we compared our data on male/female patients with those informed in Chinese and Latin-American groups by Mok *et al*. and Molina *et al*., they both found similar results, in contrast, Mexican patients resembles features reported in an ethnically mixed population in the USAby Ward *et al*., arthritis affected mostly female patients (17, 20, 21). However, Azizah *et al*. in an Asian group which includes Hindu, Malaysians and Chinese patients seen in Singapore found an increased frequency of arthritis in male SLE.

Serositis, pleural, pericardial or peritoneal effusion, has been described only in Latin-American patients, this clinical finding either pleural or pericardial effusion is common in male cases.

A large European cohort evaluating clinical manifestations at onset and under follow up of 1000 cases, found that male SLE showed serositis (28%) more common than in women SLE (16%), as well as a low frequency of arthritis, however, such findings become age dependent; when age control was included skin and kidney disease manifestations occur in younger patients, late onset male SLE is, like late onset female SLE, a milder disease with fewer severe manifestations (21).

Lupus serositis is very common, gender differences were not observed in many studies, Cervera *et al*. (21) mentioned gender difference with statistical significance ($p = 0.008$), but this observation was isolated and in relation to peritonitis, without further comments. Azizah *et al.* results coincide with ours, he reported that pericarditis was twice more common in male than in female

Table IV. Systematic literature review on SLE gender-associated features 1978-2002.

Date	Study type (N)	Objective	Main outcomes
1978	A Case series (12)	To determine the role of androgen deficiency for the expression of SLE in men	There were not evidence of hypogonadism nor androgenic dysfunction.[30]
1979	A Case series (10)	To study estrogen metabolism measuring urinary metabolites excretion (glucuronide).	Men with SLE had increased 16-hydroxyestrone. Women had raised 16-hydroxyestrone and estriol. Data suggest that patients with SLE had abnormal patterns of estradiol metabolism leading to increased estrogen activity.[26]
1982	A Case series (8)	To assess the genetic and hormonal status of 16 men with SLE	Hyperestrogenemia and hypoadrogenemia were present in some cases.[22]
1982	A Case series (138)	To compare the frequency of clinical features of SLE and determine survival in younger-onset SLE compared with 25 older-onset SLE patients	Patients with older-onset were mostly female and black. Only serositis and hypocomplementemia showed difference. Both groups had similar survival rate, however, there was a tendency to improve survival in late-onset patients.[9]
1989	A Case series (52)	To present clinical, laboratory and survival trend of 52 male patients and literature review of male SLE .	There were only difference in thrombocitopenia and renal disease. Disease onset occurred as teenagers (79%), generally they had poor prognosis.[10]
1990	A Case series (351)	A search for gender difference in American SLE patients.	After adjusting for differences in age, race and duration of follow-up, men were found to have more frequently seizures and showed a trend to progress to renal failure.[11]
1994	A Case series (147)	To determine if there are gender differences in oriental SLE patients	Arthritis and renal disease, (diffuse proliferative glomerulonephritis) were more common in males, while prevalence of leucopenia, anti-Ro (SSA) and anti-La (SSB) antibodies were higher in females. Arthritis and serositis were uncommon in oriental in contrast to caucasian males. These findings suggest gender difference linked to SLE as well as race factors influencing clinical features.[12]
1996	A Case series (1,316)	To compare the clinical and laboratory features in male and female SLE patients.	Male SLE showed increased prevalence of renal disease, vascular thrombosis and presence of anti-ds DNA antibodies, as well as, higher dose of corticosteroids to control disease when compared with female SLE patients.[15]
2001	A Case series (24)	To determine gender related difference among women and men with SLE	Disease onset: lower incidence of mucocutaneous findings and arthritis, increased incidence of discoid lupus and serositis in male patients. Follow up: lower incidence of arthritis and increased serositis with a tend toward renal involvement in male patients. Serology: both , male/female patients, had similar incidence for auto-antibodies and hypocomplementemia.[13]
1985	B Cross-sectional (150)	To analyze and interrelate clinical, serologic and immunogenetic features of patients with SLE with respect to more specific demographically defined subgroup.	Men were older than women at diagnosis and had peripheral neuropathy. Black patients were significantly younger at diagnosis than whites, and had higher frequency of nephritis, hypertension, acute lupus pneumonitis, discoid lupus, hyperglobulinemia and hypocomplementemia.[19]
1999	B Cross-sectional (252)	To study gender difference in clinical manifestations, disease course and organ damage in SLE	There was no gender difference in the involvement of major organs/systems.[1]

1996	C Case-control (170)	To analyze the bone mineral density status in a population of male patients with SLE.	The study did not show a loss in bone mass in SLE men on corticoesteroid therapy.[34]
2002	C Case-Control (54)	Assess the severity of SLE in men compared to women	Severity of disease index was not different in men vs. women Cerebritis, thromboembolic phenomena and antiphospholipid antibodies were more common in men.[16]
1978	D Logitudinal (33)	Examined the relationship of the immunoglobulin class anti-double standed DNA antibodies to the histological and clinical evidence of glomerulonephritis in patients with SLE.	The class of the anti-DNA antibodies in the serum did not always correspond with the class of immunoglobulin deposited in the glomeruli of renal biopsy specimens.[35]
1981	D Retrospective cohort (609)	To examine the overall survival in a cohort with consistent treatment for 30 years	Patients without nephritis had better survival. Male patients did worse than female patients. Irrespective of gender,younger patients, without nephitis had better prognosis and the most common causes of death were renal disease and sepsis.[3]
1982	D Cohort (1,103)	To study causes of death among SLE patients treated at specific facility.	Lupus related organ-system involvement (mainly active nephritis) and infections were the most frequently primary cause of death. Active nervouse system disease and myocardial infraction were infrequent cause of death . There were no deaths for malignancy.[36]
1983	D Cohort (102)	To examine prognostic utility of certain clinical and pathological features in 87 female vs 15 male patients.	Young men who had high serum creatinine at diagnosis showed worst prognosis. These clinical preduictors plus chronicity index on kidney biopsy enhanced significantly a prognostic model. Immunosuppresive agents provide an slight therapeutic advantage over oral corticosteroides alone.[7]
1993	D Cohort (1,000)	Analyze prevalence and characteristics of the main clinical and immunological disease patterns at onset and during evolution of SLE mostly (97%), white European patients.	Male patients had serositis at disease' onset, and female patients has arthritis over follow up as the only significant differences. Childhood patients often had malar rash, nephopathy and lower prevalence of rheumatoid factor. Older onset patients (> 50 years old) showed decreased prevalence for photosensitive malar rash, arthritis, nephropathy, thrombosis and anti- La(SSB) antibodies but increased prevalence of sicca syndrome.[21]
1997	D Cohort (539)	To examine clinical features, identify differences in disease pattern and survival rates among races and genders	There was a high incidence of renal disease. Indian patients had less incidence of skin manifestation compared to other racial group. No difference in disease expression was detected between the ethnic Chinese and Indians, and between genders. Indians had the poorest survival rate, and Chinese and Malay were similar. These findings are a broad agreement with those previously reported.[18]
2000	D Cohort (172,300)	To identify new cases of SLE within a defined area in Southern Sweden with validated methods of retrieval and to compare 2 cohorts assembled during 1981-86 and 1987-91	Median annual incidence was constant during the 11 years follow-up. Mortality (due to atherosclerosis) was low and only late mortality exceeded age and sex matched control population. Sensibility (94%) and specificity (92.7%) of ACR classification criteria were high in this study.[30]

A: Case series, B: Cross-sectional, C. Case-Control and D: Cohort or Longitudinal.

Table V. Clinical features, female/male SLE according to main published series a comparison.

	Ward[11] (USA, 1990)		Wang (Malaysia, 1997)		Mok[16] (China, 1999)		Azizah[14] (Malaysia, 2001)		Molina[13] (Colombia, 1996)		Present study (Mexico, 2003)	
	Female n = 299	Male n = 62	Female n = 499	Male n = 40	Female n = 201	Male n = 51	Female n = 122	Male n = 12	Female n = 1209	Male n = 107	Female n = 151	Male n = 36
Age at onset	35	45	25	26	32	31	27	31	28	26	30	32
I. Clinical manifestation*												
Arthritis	76	71	37	29	94	86	45	25	88	85	75	69
Butterfly erythema	34	27	——-	——-	67	67	70	67	——-	——-	53	33
Discoid lesions	12	10	3	5	11	18	14	8	——-	——-	5	25
Raynaud´s phenomenon	——-	——-	——-	——-	31	14	4	17	46	28	34	14
Renal disease	——-	——-	50	45	——-	——-	63	75	44	58	48	70
Neurological disease	——-	——-	7	5	——-	——-	20	8	22	26	5	14
Pleuritis	——-	——-	13	10	——-	——-	——-	——-	36	38	30	31
Pericarditis	——-	——-	6	5	——-	——-	——-	——-	13	16	19	42
II. Laboratory findings*												
Hemolytic anemia	27	15	———	———	23	24	22	8	11	16	25	19
Leucopenia	43	42	24	24	28	16			39	37	60	47
Thrombocytopenia	20	21	16	14	23	25	22	25	20	21	31	53
Anti-DNA	60	61	34	29	68	67	67	58	37	54	29	20
Anti-Sm	20	18	———	——-	12	14	16	17	15	19	23	44

*percent/proportions

SLE patients. Our male predominance was very clear, however, we are working in a cardiology referral center and selection bias is a real concern even after a 4:1 female predominance in regard of incoming patients

Vasospasm, as Raynaud phenomenon, was studied by Asian and Latin-American researchers, both, Mok *et al*. and Molina *et al*. and showed similar frequencies which are not different from our observation, female predilection was present in all studies reviewed on our own.

In regard serological data, anti DNA antibodies, a hallmark for SLE, shown similar prevalence among Asian (13, 14, 18) and American studies (11), close to 60% without gender difference. A Latin-American study (15), in contrast, showed lower prevalence with non significant difference between female and male Colombian patients, although a discrete male predominance was informed. In our cases, anti-DNA was slightly more common among female cases but a lower prevalence in the whole group was detected. When other autoantibodies were considered, anti Sm prevalence is similar in all published reports, in our male cases it was more common than in females and this characteristic differentiate our study.

Five-year survival was chosen because it was generally available in our hospital. In this retrospective and descriptive study we did not find a statiscally significant difference between male and female SLE, although it was a clear tendency towards a longer survival period among women SLE. Wallace *et al*. (3) studying a large series with 609 patients also found longer women survival ($p = 0.05$), kidney disease was more common among men and death was attributed to kidney failure and sepsis.

We did not explore hormonal status in our male patients. Several studies suggested increased plasma estrogen (3, 4, 17, 20, 22-25) or raised 16αOH estradiol (26, 27) without evidence of hypogonadism or androgen deficiency (4), as well as, increased testosterone oxidation or hyperprolactinemia (28, 29). The role of these hormonal changes in male SLE pathogenesis is not established yet (26). However, hyperprolactinemia (30) and low monocyte and neutrophil FcRIIγ receptor (31) has been found in male SLE and not in normal male nor female SLE, leaving the pathogenic hypothesis still untested.

The present study offers evidence based consistent with distinct clinical findings in male SLE when compared with similar studies done on different ethnic groups. It was clear that, clinical manifestations, as well as, serological findings in SLE patients are not related to their ethic group, on the other hand, gender differences were common feature when comparing female and male SLE patients. Skin manifestations such as discoid lesions, serositis, severe and progressive kidney disease, thrombosis and thrombocytopenia are relatively common in male patients.

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