Risk factors for the development of systemic lupus erythematosus (sle) in asians: a research case-control

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Abstract. The study aimed to assess the nature of injuries and determine the risk factors for accumulated injuries in a group of patients with SLE. Materials and methods. A retrospective review of the map and medical history in the therapeutic department of the SamMI clinic was conducted on a group of 75 patients with SLE. The collected data included (1) age at the time of diagnosis, (2) gender, (3) heredity, (4) manifestations of the disease at diagnosis, (5) laboratory data, including a general blood test, complement levels (C3, C4). Results. 225 people were included in this study: 75 in the main group (patients with asthma) and 150 in the control group (healthy). Of the participants in the study, 44% were women and 56% were men; both groups were the same gender. The damage from the disease was significantly associated with a younger age at the time of diagnosis ($P = 0.03$), the presence of neuropsychiatric manifestations at any stage of the disease ($P <0.01$), a large number of lesions of the main organs ($P <0.01$), a large number of lesions. outbreaks of lupus ($P <0.01$) and a greater number of episodes of serious infection ($P = 0.02$). Conclusions. This study presents a picture of accumulated damage in a group of 59 Asian patients with SLE. This shows that the presence of neuropsychiatric manifestations is a significant risk factor for damage. Other likely risk factors for the disease include younger age at the time of diagnosis, a greater number of lesions of the main organs, a greater number of exacerbations and serious infections.

1 Introduction

Accumulated damage is an important prognostic factor of systemic lupus erythematosus. However, the nature of the disease lesion and its risk factors have not been sufficiently studied in systemic red in Asia. Systemic lupus erythematosus (SLE) is a multi-organ autoimmune disease that has a wide range of manifestations. SLE with childhood-onset is notorious for occurring with a faster onset and subsequently proceeds with a more severe and aggressive course of the disease compared to SLE with the onset in adults [1]. The overall survival rate of children with SLE has improved significantly over the past decades. Recently, it was reported that the 10-year survival rate is about 80-90%, which is a significant

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improvement compared to the 10-year survival rate of 40%, which was previously reported 50-60 years ago [2-3].

Despite the improved survival rate, a significant part of patients still suffers from the disease due to irreversible organ damage [4, 6-8]. Accumulated damage occurs as a result of the painful process of active inflammation, side effects of therapy, as well as concomitant diseases. The importance of assessing the damage from the disease as a standard assessment in the management of such patients is twofold. First, accumulated damage is one of the important indicators used in describing the prognosis for SLE [10]. Secondly, it was found that damage from diseases is largely associated with a lower quality of life associated with health [11]. It is known that ethnic differences explain the variability of susceptibility to diseases and the severity of SLE [22].

The purpose of this study is to assess the nature of the damage and determine the risk factors for accumulated damage in our group of SLE with the onset in childhood. Treatment strategies aimed at reducing irreversible organ damage can improve the quality of life of these patients and improve the prognosis.

2 Materials and methods

A retrospective review of the map and medical history in the therapeutic department of the Samarkand Medical Institute clinic was conducted on a group of 59 patients with SLE. Patient demographics and clinical variables were collected at diagnosis. Clinical variables that were considered risk factors for damage were also collected. Based on their indicators of the Slick damage index (IPS, SDI), the patients were divided into two groups: the group with the presence of damage from the disease (IPS ≥1) and the group without damage from the disease (IPS score = 0). Clinical variables, ethnic aspects, including age, gender, heredity, duration of the disease, laboratory parameters and activity of the disease at diagnosis. The activity of lupus, serious infection and the intensity of taking immunosuppressive drugs were compared between the two groups. Growth impairment and estimated glomerular filtration rate (GFR) were also analyzed as secondary outcomes.

All patients met the diagnostic criteria for SLE following the criteria for the classification of SLE in 2012, established by International collaborating clinics for systemic lupus [19]. All patients were over the age of 16 years at the time of the onset of SLE with a minimum duration of the disease of 1 year. Patients who were 15 years old or less at the time of diagnosis.

75 patients were included in the study. Patient records were viewed from the moment of diagnosis until the patient's last visit to the therapeutic department.

The collected data included (1) age at the time of diagnosis, (2) gender, (3) heredity, (4) manifestations of the disease at diagnosis, (5) laboratory data, including general blood analysis, complement levels (C3, C4), serum albumin, serum creatinine, urine analysis, daily urine protein and the presence of antinuclear and antiphospholipid antibodies.

The activity of the disease is defined as reversible manifestations of the main inflammatory process. The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is a tool for assessing the activity of the disease in SLE. The SLEDAI consists of 24 points, and the score of each item is evaluated according to the organ system to which it belongs. The total score reflects the activity of the patient's disease at this stage [20]. In this study, SLEDAI was calculated when making a diagnosis.

Medications used to treat SLE at any stage of the course of the disease, including methylprednisolone (MP) intravenously, cyclophosphamide, azathioprine, cyclosporine (CS).

When studying the course of SLE, the damage of internal organs was studied, this included serositis, hematological, renal and neurological disorders. The normality of the data

was evaluated using the Shapiro-Wilk test. Qualitative variables were expressed as absolute frequencies and proportions. The Fisher exact test was used to compare proportional data, whereas the Mann-Whitney U-test was used to compare distributions between nonparametric variables. P-values less than 0.05 were statistically significant. To search for statistically significant factors, one-dimensional analysis of independent variables was carried out. Factors with P-values <0.05, as well as risk factors considered clinically important based on previous studies, were included in a multivariate analysis using logistic regression. Mutually exclusive factors were not selected for multivariate analysis.

3 Results

The average age at the time of diagnosis in this group was 35 years (26-48), and the ratio of women to men was 7.2:1. Uzbeks (82.7%) dominated the ethnic composition, and the average duration of follow–up was 8.1 years (3.2-13.4). Renal (72%) and hematological (64%) were most often affected by the main organs during the disease. The demographic and clinical characteristics of these patients, as well as the various treatment methods used, are presented in Table 1.

Table 1. Demographic data of the study participants

№	Demographic data	Average value [%]
.	Age at the time of diagnosis (year)	35 [26–48]
.	The ratio of women and men	5,6: 1
.	The duration of the disease in years	7,8 [5,5–10,1]
Manifestations of the disease		
.	The presence of neuropsychiatric manifestations	9 (15,3%)
.	The presence of a hematological lesion	40 (67,8%)
.	The presence of kidney damage	47 (79,7%)
.	Lupus nephritis of the II class according to WHO	2 (3,3%)
.	Lupus nephritis of the III class according to WHO	10 (16,9%)
.	Lupus nephritis of the IV class according to WHO	30 (50,8%)
0.	Lupus nephritis of the V class according to WHO	8 (13,6%)
1.	The presence of serositis	10 (16,9%)
Drug therapy		
2.	Have you ever used methylprednisolone intravenously	28 (31,9%)
3.	Have you ever used cyclophosphamide	35 (59,3%)
4.	Have you ever used azathioprine	49 (83,1%)
5.	Have you ever used cyclosporine	13 (22%)
6.	Have you ever used intravenous immunoglobulin	7 (11,9%)

At the end of the study period, 45 patients (60%) had no injuries (IPS=0). 20 patients (33.9%) had acquired pathological changes (IPS ≥ 1). The average IPS score for this group was 0 (range 0-8). One-time evaluation of IPS injuries was as follows: 12 patients had a score of 1,

five patients had a score of 2, one patient had a score of 3, one patient had a score of 5 and one patient had a score of 8. The disease was most often observed in the eye area (15.3%), followed by neuropsychiatric (11.9%) and musculoskeletal (11.9%) areas. The most common forms of the lesion were cataracts (11.9%) and avascular necrosis (unilateral and bilateral combined 10.2%). Detailed information about the frequencies of damage to various objects and organs is presented in

Table 2. The frequency of damage in 12 organ systems and elements of the SLICC/ACR damage index

№	The defeat of the disease of the system/organ at the last observation	Frequency (%)
1.	Ocular	9 (15,3%)
2.	Cataract	7 (11,9%)
3.	Retinal change or optic nerve atrophy	2 (3,4%)
	Psychoneurological	7 (11,9%)
4.	Cognitive impairment or severe psychosis	3 (5,1%)
5.	Seizures requiring therapy for 6 months	3 (5,1%)
6.	Cranial or peripheral neuropathy	1 (1,7%)
	Renal	2 (3,4%)
7.	End-stage renal failure	2 (3,4%)
	Cardiovascular diseases	2 (3,4%)
8.	Cardiomyopathy (ventricular dysfunction)	2 (3,4%)
	Peripheral vessels	1 (1,7%)
9.	Venous thrombosis with edema, ulceration or venous congestion	1 (1,7%)
	Musculoskeletal	7 (11,9%)
10.	Muscle atrophy or weakness	1 (1,7%)
11.	Avascular necrosis (unilateral)	3 (5,1%)
12.	Bilateral avascular necrosis	3 (5,1%)
13.	Skin	3 (5,1%)
14.	Extensive scarring or pancreatic layer, except for the space of the skull and pulp	1 (1,7%)
15.	Skin ulcers> 6 months	2 (3,4%)

The clinical variables between the two groups of patients, "absence of disease damage" (IPS = 0) and "presence of disease damage" (IPS ≥ 1), were first compared using a one-dimensional analysis. The damage from the disease was significantly associated with a younger age at the time of diagnosis (P = 0.03), the presence of neuropsychiatric manifestations at any stage of the disease (P <0.01), a large number of lesions of the main organs (P <0.01), outbreaks of lupus (P <0.01) and a greater number of episodes of serious infection (P = 0.02).

Differences in gender, ethnicity, duration of the disease, laboratory data at diagnosis, the presence of lesions of other major organs (hematological, renal and serositis), SLEDAI at

diagnosis and the last visit, the use of cyclophosphamide and pulse steroids between the two groups were not statistically detected. significant. The number of lesions of the main organs was excluded from the multidimensional analysis since it included the presence of neuropsychiatric manifestations.

Table 3. One-dimensional analysis of risk factors associated with damage from the disease

Risk factors	No damage (n = 50)	The presence of damage from the disease (n = 25)	Odds ratio (95% CI)	p-value
Age at the time of diagnosis	23 [12–15]	22 [10–14,8]	0,77 (0,62–0,97)	0,03*
Male	15 (12,8%)	14 (20%)	1,7 (0,45–7,30)	0,37
Ethnicity (Uzbek)	37 (94,9%)	19 (95%)	1,04 (0,3–11,1)	0,68
Duration of the disease (years)	7,6 [4.6–11.1]	9,45 [6,4–11,3]	1,08 (0,83–2,46)	0,22
Laboratory data for diagnostics Hemoglobin (g/dl)	10,6 [9,5–11,8]	10,6 [6,8–11,8]	0,90 (0,72–1,23)	0,42
Number of white blood cells (× 109 / l)	5 [3,5–7,0]	3,95 [3,6–5,7]	0,87 (0,65–2,01)	0,23
Platelets (× 109/l)	161 [85,5–264,0]	211,5 [96,8–257,5]	1 (0.98–1.21)	0,32
Serum albumin (g/l)	36 [30,0–40,0]	34 [31,0–36,8]	0,98 (0,92–1,05)	0,52
Serum creatinine (mmol / L)	55 [50,0–68,0]	54 [47,0–69,0]	1 (0,87–1,32)	0,61
C3 (g/l)	0,52 [0,3–0,8]	0,41 [0,2–0,5]	0,13 (0,33–1,41)	0,16
C4 (g/l)	0,08 [0,05–0,1]	0,08 [0,04–0,1]	0,03 (0–131,44)	0,32
Anti-dsDNA titer (IU / ml)	210 [83,5–300,0]	300 [213,3–300,0]	1 (0,99–1,00)	0,12
Evaluation of SLEDAI at diagnosis	12 [7,5–14,3]	11,5 [7,3–18,8]	1,05 (0,7–1,27)	0,35
Manifestations of the outbreak during the disease				
Psychoneurological manifestations	1 (2,6%)	8 (40%)	22,4 (2,87-77,62)	<0,01*
Hematological lesion	24 (61,5%)	16 (80%)	2,9 (0,70–8,92)	0,36
Kidney damage	29 (74,4%)	18 (90%)	4,10 (0,71–15,81)	0,27
Serositis	5 (12,8%)	5 (25%)	2,47 (0,57–9,01)	0,35
The number of lesions of the main organs	1 [1–2]	2 [1.3–3]	2,91 (1,34–4,69)	<0,01*
The positivity of antiphospholipid antibodies	9 (27,3%)	6 (42,9%)	3 (0,54–7,39)	0,17
Factors related to treatment				
Cumulative dose of CA (mg/kg)	70 [0–140]	7,5 [0–115,8])	1 (0,99–1,01)	0,83

Have you ever used a CA	20 (51,3%)	15 (75%)	2,85 (0,87–9,38)	0,09
Have you ever used intravenous MP	17 (43,6%)	11 (55%)	1,58 (0,54–4,68)	0,41
Events during the illness Number of clinical exacerbations	1 [0–4]	5 [0,5–8,8]	1,25 (1,06–1,46)	<0,01*
Episodes of serious infection	0 [0–1]	1 [1–3,8]	1,77 (1,11–2,78)	0,02*

Neuropsychiatric manifestations were observed in 9 patients (15.3%). In this group of patients, the age was 12 years (range 7-15) with a ratio of women: men 2: 1. Neuropsychiatric manifestations were observed at diagnosis in six patients. Among nine patients, neuropsychiatric manifestations included seizures (66.7%), acute confusion (22.2%), acute psychosis (11.1%), mood disorder (11.1%), cerebrovascular diseases (11.1%) and severe headache (11.1%). These nine patients had neuropsychiatric (44.4%), ocular (33.3%), musculoskeletal (22.2%), renal (11.1%) and skin injuries (11.1%). No significant correlation was found between the presence of a neurological disorder and the positivity of antiphospholipid antibodies (P = 0.94).

The estimated glomerular filtration rate at the last observation. Two patients had GFR <15 ml/min / 1.73 m^2. These two patients also had the highest rates of IPS in the group: one had 5 points, and the other - 8. The time from diagnosis to end-stage renal failure was 9.8 years and 6.7 years, respectively, and renal replacement therapy was prescribed. In three patients, the GFR was 80-89 ml/min / 1.73 m2, while in the rest (91.5%) in the study group, the normal GFR was ≥90 ml/min / 1.73 m2 during the last follow-up.

4 Discussion

This study presents a picture of accumulated injuries in a group of 59 Asian patients with SLE. It shows that the presence of neuropsychiatric manifestations is a significant risk factor for damage. Other likely risk factors for the disease include younger age at the time of diagnosis, a greater number of lesions of the main organs, exacerbations and serious infections.

Damage refers to irreversible changes that may be associated with previous active inflammation, medication intake, or concomitant diseases such as hypertension and atherosclerosis. The SLICC/ACR Damage Index for SLE is a tool designed to assess accumulated damage over time. In a clinical setting, it is a simple tool that allows clinicians to comprehensively and systematically monitor patients, monitoring the development of injuries from pediatric age to adulthood. Higher damage index values at an early stage of the disease are associated with a poor prognosis and increased mortality.

The present study showed that patients had a low rate of damage accumulation (33.9%) compared to other studies, despite the relatively long average duration of the disease. In particular, despite the high level of kidney damage (79.7%), the level of kidney damage (3.4%) was one of the lowest compared to other groups. The presence of neuropsychiatric manifestations was determined as the most significant risk factor for the disease in this group of patients with SLE.

5 Conclusion

The results of this study highlight the need for larger prospective studies on these patients. The proposed systematic collection of data with special attention to the use of steroids, the severity of exacerbations of the disease, the activity of the disease over time will help to clarify the relationship between SLE that occurred in childhood and the damage caused by it.

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