Research Article

Study of Clinical Characteristics and Laboratory Biomarkers of Systemic Lupus Erythematous in A Cohort of Egyptian Children

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Abstract:

Background: The chronic autoimmune illness known as systemic lupus erythematosus (SLE) is typified by the generation of autoantibodies, inflammation, and tissue destruction in several organs as a result of the activation of several pre-inflammatory pathways.

SLE diagnosis, disease action prediction, and situation should all benefit considerably from recently labeled possible biomarkers .

Purpose: assessment the clinical characteristics, systemic involvement, and key laboratory biomarkers in a cohort of Egyptian pediatric SLE patients.

Methods: This cross-sectional study was conducted at the Nephrology Unit and Rheumatology Outpatient Clinic of Mansoura University Children's Hospital (MUCH) with 50 Egyptian children with SLE and 50 controls. The patients' markers, biochemistry, and clinical characteristics were assessed. The SLE Disease Activity Index (SLEDAI)-2000 was used to measure the baseline disease activity.

Results: Consanguinity was reported in 30.0% of cases, and 22.0% had a positive family history of autoimmune diseases. The mean age of disease onset was 11.2±2.14 years. Fever (96.0%), mucocutaneous lesions (88.0%), and arthritis (68.0%) were the most common clinical presentations. Lupus nephritis occurred in 78.0% of patients, predominantly presenting as Class IV (41.0%) and Class III (35.9%). Central nervous system (CNS) manifestations were present in 32.0%. Laboratory findings revealed low C3 levels in 94.0%, positive ANA in 98.0%, positive anti-dsDNA in 98.0%, and elevated ESR in 94.0%. Disease relapse was observed in 66.0% of patients.

Conclusion: High rates of renal illness, high disease activity, and frequent relapses are seen in Egyptian pediatric SLE patients. In this population, biomarkers like anti-dsDNA, ANA, low C3, and increased ESR continue to be reliable diagnostic markers.

Keywords: systemic lupus erythematosus, pediatric, clinical, biochemical.

Introduction:

A systemic autoimmune illness that affects several organs, systemic lupus erythematosus (SLE) is characterized by a complex interaction of immune cells, factors, and pathways that produces a range of clinical symptoms. The pathophysiology of SLE includes impaired nucleic acid clearance, elevated type I interferon (IFN) response, dysregulated B cell tolerance leading to increased autoantibody production, immunological complex formation and deposition, and multi-organ damage[(1)]. End-stage disease, severe infection, and cardiovascular problems are the leading reasons of death for SLE patients, and the incidence varies by nation and area. [(2)].

As in Rheumatoid arthritis, a treat to goal approach is immediately favored for SLE [(3)]. To realize this, it is owned by both correctly determine and right identify affliction venture or a spread. For the disease of SLE, anti-basic antibodies (ANA) discovered apiece immunofluorescence assay (IFA), with a awareness of 90–98%, are viewed as a golden-standard screening test; still, allure precision is only 78–83 % [(4)]. Another antibody frequently seen in systemic lupus erythematosus is the anti-double-stranded DNA antibody (anti-dsDNA), which has a 60% sensitivity and a 97% specificity. We can diagnose SLE with greater sensitivity and specificity by combining these two antibodies. [(5)].

For identifying disease activity, specific tools for measuring diseases are available; SLE Disease Activity Index (SLEDAI) is a global score that combines laboratory and clinical data to assess the severity of the illness during the previous 10 days [(6)]. Because it is quick, simple to use, and has shown impressive psychometric qualities during validation, it has been shown to be a great tool for assessing disease activity in p-SLE patients. [(7)].

Malar rash, oral ulcers, hematuria, proteinuria, decreased complement levels (particularly of C3), and an elevated ESR are examples of clinical appearances that have been shown to promote disease action [(8)].

In current age, biomarkers have been widely working in the disease, prophecy, assessment, and administration of SLE. This biomarker concede possibility be specific, smooth to discover, path disease action, beneficial in follow-up, and fairly priced. However, on account of the complicatedness of the disease and the difference of the etiologies, it is consistently troublesome to distinguish SLE from different analogous afflictions. Therefore, screening and labeling trustworthy markers and telling potential devices of operation are crucial for better disease and active situation of SLE [9].

Subjects and Methods:

This a case control study completed activity in Nephrology Unit and Rheumatology Outpatient Clinic at MUCH all the while the age 2021- 2022.at which point 100 teenagers mellowing 5-18 age were detached into two groups; the P-SLE group, diagnosed clinically as SLE based on the American College of Rheumatology's (ACR) tests, 1997 and pathologically in accordance with WHO categorization, 1995. The P-SLE group (n = 50) and the control group of doubled two together age and sexuality (n = 50). The histological judgments of renal medical checkup samples from lupus nephritis (LN) cases were classification utilizing the International Society of Nephrology-Renal Pathology Society classification form (2003). Patients accompanying never-ending comorbidities, additional autoimmune ailments, precariously ill sufferers, or those the one falled to take part in the trial were not contained in the P-SLE group.

Children contemporary and sexuality the one appeared expected healthy were picked from the inexact outpatient hospitals at Mansoura University Children Hospital to form the control group. Their ancestry pressure and burden were usual, and they wanted any syndromes or ancestry of inflexible ailments.

Clinical and laboratory data:

The hospital electronic records of patients with P-SLE were reviewed for the patient's age at the disease onset, duration of illness, clinical manifestations of SLE, histopathology of LN, and Laboratory tests include hemoglobin level, platelet count, total leucocyte count (TLC), erythrocyte sedimentation rate (ESR), spot urine for protein to creatinine ratio, hematuria (> 5 RBCs), pyuria (> 5 WBCs) on high power field, and urine full analysis for proteinuria (by dipstick method); tests specific to SLE, such as anti-nuclear antibody (ANA), anti-double strand DNA (anti-dsDNA), and complement C3 level. These investigations were done by taking 6cm blood, 3cm in edita tube for CBC and PCR, other 3cm blood in a plane tube for ANA, anti-dsDNA (specific for SLE) and Anti- histone Ab by ELIZA technique.

Statistical analysis

IBM-SPSS software was used to enter and analyze the data (IBM Corp. Released 2017). Version 25.0 of IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp. Qualitative data were expressed as N and percentage (%).The Kolmogorov-Smirnov test was initially used to determine whether quantitative data were normal. If the data was regularly distributed, it was expressed as mean ± standard deviation (SD); if not, it was expressed as median and range. Fisher's exact test or the Chi-Square test were utilized for qualitative data. Quantitative information for two groups: Independent-Samples t-Test for parametric data or its non-parametric equivalent; Mann-Whitney U test was used. To identify potential disease-related variables, the OR and 95% confidence interval (95% CI) were obtained. If the p value is less than 0.05 at the 95% confidence interval, it is deemed significant.

Results:

The present study is cross-sectional study included two groups: The demographic comparison between the SLE group and the control group is summarized in Table 1. The median age was 14.0 years (range 11–18) in the SLE group and 13.0 years (range 9–17) in the control group (P = 0.079). Females represented 72.0% of the SLE group and 60.0% of the control group (P = 0.205). The two groups are matched as regard sex and age (P>0.05).

Table (1): General characteristics of studied groups.

Parameter		Control group (n=50)	SLE group (n=50)	P value
SEX*	Male	20 (40.0%)	14 (28.0%)	0.205
	Female	30 (60.0%)	36 (72.0%)	
Age	Median (Min-Max)	13.0 (9-17)	14.0 (11-18)	0.079

Table (2) shows that the family history was detected in 22.0% of SLE children, positive consanguinity was noted in 30.0% of the patients. The sickness lasted between 0.1 and 10.0 years, with an average age of 11.2 years. Abnormal blood pressure was diagnosed in 28.0% of cases. Mucocutaneous lesion was diagnosed in 88.0% of cases in form of malar rash, rash, alopecia, oral ulcers and photosensitivity. CNS manifestation was presented in 32.0% of the patients either with single or combined symptoms as fits in 9 cases, psychosis in 2 cases, headache in 6 cases and vasculitis in 4 cases. Lymphadenopathy, serositis, arthritis, and fever were diagnosed in (28.0%, 20.0%, 68.0%, and 96.0% respectively). SLE children classified into SLE without nephritis (22.0%) and SLE with nephritis (78.0%), most of them class 4 (41.0%). Relapse was detected in 66.0% of cases in form of either with single or combined symptoms as nephrotic (36.0%), systemic flare (44.0%), hepatitis (2.0%) and vasculitis (2.0%). Most cases relapsed once time (60.6%).

Table (2): Clinical characteristics of studied SLE patients.

Parameter		SLE patients
Consanguinity	Negative	35 (70.0%)
	Positive	15 (30.0%)
Family history of other immune disease	Negative	39 (78.0%)
	Positive	11 (22.0%)
Duration of disease (years)	Median (Min-Max)	2.7 (0.1-10.0)
Age of onset (years)	Mean ± SD	11.2 ± 2.14
BMI	Mean ± SD	19.6 ± 3.9
BMI Z score	Median (Min-Max)	-0.26 (-8.0/3.3)
BMI status	Thinner (BMI Z score <-2.0)	1 (2.0%)
	Normal (BMI Z score -2.0/2.0)	48 (96.0%)
	Obese ((BMI Z score >-2.0)	1 (2.0%)
Activity index	1-6	36 (72.0%)
	7-12	14 (28.0%)
Chronicity index	1-3	49 (98.0%)
	3-6	1 (2.0%)
Blood pressure	Normal	36 (72.0%)
	Hypertension	14 (28.0%)
SBP (mmHg)	Median (Min-Max)	110.0 (90-180)
DBP (mmHg)	Median (Min-Max)	80.0 (60-110)
Mucocutaneous lesion	Absent	6 (12.0%)
	Present	44 (88.0%)
Type of Mucocutaneous lesion	Malar rash alone	2 (4.5%)
	Rash alone	2 (4.5%)
	Alopecia alone	2 (4.5%)
	Oral ulcers alone	14 (31.8%)
	Photosensitivity alone	4 (9.1%)
	Oral ulcer + photosensitivity	7 (15.9%)
	Rash + oral ulcer	5 (11.4%)
	Malar rash + oral ulcer + photosensitivity	3 (6.8%)
	Malar rash + photosensitivity	3 (6.8%)
	Malar rash + oral ulcer	2 (4.5%)
CNS manifestation	Absent	34 (68.0%)
	Present	16 (32.0%)
Type of CNS manifestation	Fits	9 (18.0%)
	Psychosis	2 (4.0%)
	Headache	6 (12.0%)

	Vasculitis	4 (8.0%)
Lymphadenopathy	Absent	36 (72.0%)
	Present	14 (28.0%)
Serositis	Absent	40 (80.0%)
	Present	10 (20.0%)
Arthritis	Absent	16 (32.0%)
	Present	34 (68.0%)
Fever	Absent	2 (4.0%)
	Present	48 (96.0%)
SLE groups	Without nephritis (extrarenal)	11 (22.0%)
	With nephritis	39 (78.0%)
Nephritis class	Class 1	6 (15.4%)
	Class 2	3 (7.7%)
	Class 3	14 (35.9%)
	Class 4	16 (41.0%)
Relapse	Absent	17 (34.0%)
	Present	33 (66.0%)
Relapse manifestation	Nephrotic	18 (36.0%)
	Systemic flare	22 (44.0%)
	Hepatitis	1 (2.0%)
	Vasculitis	1 (2.0%)
Relapse frequency	Once	20 (60.6%)
	Twice	8 (24.2%)
	Three times	4 (12.1%)
	Frequent	1 (3.0%)

Table (3): Laboratory data of SLE patients.

Parameter		SLE patients
C3	Normal	3 (6.0%)
	Low	47 (94.0%)
Anti-dsDNA	Negative	1 (2.0%)
	Positive	49 (98.0%)
ANA	Negative	1 (2.0%)
	Positive	49 (98.0%)
CRP	Normal	38 (76.0%)
	High	12 (24.0%)
ESR	Normal	3 (6.0%)
	High	47 (94.0%)
CBC	Normal	2 (4.0%)
	Anemia (AIHA)	20 (40.0%)
	Bicytopenia	18 (36.0%)
	Pancytopenia	10 (20.0%)
Urine analysis	Normal	11 (22.0%)
	Abnormal	39 (78.0%)
Proteinuria	Present	24 (48.0%)
Hematuria	Present	15 (30.0%)
Creatinine	Median (Min-Max)	0.7 (0.4-4.7)

Table (3) shows the Laboratory findings;

Low C3, positive anti-dsDNA, and positive ANA were detected in (94.0%, 98.0%, and 98.0% of cases respectively). In 24.0% and 94.0% of patients, respectively, CRP and ESR were elevated. CBC was abnormal in 48 cases either anemia (40.0%), bicytopenia (36.0%) and pancytopenia (20.0%), also urine analysis was abnormal in 78.0% of cases with

either single or combined finding as proteinuria (48.0%), and hematuria (30.0%). The median serum creatinine level was 0.7 (range 0.4–4.7)

Discussion:

Pediatric intrinsic lupus erythematosus (P-SLE) is a complex ailment accompanying variable dispassionate verbalizations. Variation of dispassionate picture and ultimately pathophysiology betwixt Pediatric and adult onsets of the affliction is raising an demanding need to study the fundamental causes from the Pediatric attack view accompanying point or direct at a goal new biomarkers and specific pathways for early disease and guide situation [10].

In this Egyptian pediatric cohort, the female-to-male ratio (2.57:1) and median age of 14.0 years align with established pediatric literature showing female predominance, particularly in adolescent cohorts.

The reported female to male ratio for SLE is 8–15:1; pre-pubertal and post-menopausal ratios are much lower at 2–6:1 and 3–8:1, respectively, indicating hormonal involvement in its development. [11]. Shamim et al [5] revealed that 91.3% of the population was female. The average age upon diagnosis was 11 years ± 4 years.

Because SLE affects numerous tools and structures, like the skin, bronchi, nervous system, musculoskeletal system, courage, and sort, it is a difficult multisystem illness that comes with a wide range of indifferent presentations. Hematological abnormalities such as anemia (80% of SLE patients), leukopenia (50% of SLE patients), or thrombocytopenia (30 to 50% of SLE patients) are very frequently observed in patients with SLE. This makes it difficult to disclose the right illness right away. Neonatal and pediatric lupus erythematosus (NLE), round lupus erythematosus (DLE), drug-induced lupus (DIL), and basic lupus erythematosus (SLE) are the four primary forms of lupus [12].

P-SLE is a major cause of death and morbidity in young people, despite the fact that allure endurance has improved in recent years because to early disease detection [13], renal involvement is a prevalent aspect among its clinical signs, occurring 37–82% of the time [14]. Afro-Caribbean and Indo-Asians have a higher number of SLE patients with expanded nephritis than gloss over. Proliferative nephritis class IV has been thought to be the most outspoken person and the lowest histopathology found in p-SLE [15]. There have been reports of severe illness activity when p-SLE coexists with lupus nephritis. [16].

In our study the positive rate of consanguinity (30.0%) and family history of autoimmune disorders (22.0%) highlight potential genetic contributions to disease susceptibility in this population.

In the present study, Analysis of clinical and laboratory results in studied SLE patients revealed that abnormal blood pressure was diagnosed in 28.0% of cases. Mucocutaneous lesion was diagnosed in 88.0% of cases in form of malar rash, rash, alopecia, oral ulcers and photosensitivity. CNS manifestation was presented in 32.0% of the patients either with single or combined symptoms as fits in 9 cases, psychosis in 2 cases, headache in 6 cases and vasculitis in 4 cases. Lymphadenopathy, serositis, arthritis, and fever were diagnosed in (28.0%, 20.0%, 68.0%, and 96.0% respectively). SLE children classified into SLE without nephritis (22.0%) and SLE with nephritis (78.0%), most of them class 4 (41.0%). Relapse was detected in 66.0% of cases in form of either with single or combined symptoms as nephrotic (36.0%), systemic flare (44.0%), hepatitis (2.0%) and vasculitis (2.0%). Most cases relapsed once time (60.6%).

In line with our study Emorinken et al [16] in their study, SLE was identified in 52 patients, with a frequency of 4.7%. Of the study participants, 47 (90.4%) were female, resulting in a female-to-male ratio of 9.4:1. The study group's average age was 28.42 years. The illness lasted an average of 4.04 months prior to diagnosis, with a range of 1–15 months. Polyarthritis was the most prevalent organ system manifestation among the patients (86.5%). Mucocutaneous (78.8%), hematological (69.2%), serositis (40.4%), renal (38.5%), and neurological symptoms were among the others. Anti-double-stranded DNA and antinuclear antibody (ANA) assays were positive in 69.2% and 100% of patients, respectively.

The present study revealed low C3, positive anti-dsDNA, and positive ANA were detected in (94.0%, 98.0%, and 98.0% of cases respectively). In 24.0% and 94.0% of patients, respectively, CRP and ESR were elevated. CBC was abnormal in 48 cases either anemia (40.0%), bicytopenia (36.0%) and pancytopenia (20.0%), also urine analysis was abnormal in 78.0% of cases with either single or combined finding as proteinuria (48.0%), and hematuria (30.0%). The median serum creatinine level was 0.7 (range 0.4–4.7).

Lupus nephritis (LN) is individual of ultimate harsh clinical exhibitions of P-SLE, it presents often, performs former and shows more aggressive course distinguished to adult beginning of the ailment. Inefficient or postponed situation of LN exhibits higher bias to progress to leading stages producing severe, chronic or yet end stage renal affliction [17]. In our cohort study Lupus nephritis occurred in 78.0% of cases. Biopsy findings revealed that proliferative forms—Class IV (41.0%) and Class III (35.9%)—comprised the majority of nephritis cases. This extreme burden of proliferative nephritis joins with prior reports signifying a higher risk for harsh renal connection in pediatric populace relative to adult SLE inmates [5].

The gold standard screening test for SLE is anti-nuclear antibodies (ANA) by immunofluorescence method (IFA), which has a sensitivity of 90–98% but a specificity of just 78–83% [18]. Anti-double stranded DNA antibody (Anti-dsDNA), another antibody frequently seen in SLE, with a 97% specificity but a 60% sensitivity. Combining these two antibodies improves the sensitivity and specificity of SLE diagnosis. [5].

The SLE Disease Activity Index (SLEDAI), a global score that evaluates the severity of the disease during the preceding 10 days and includes both clinical and laboratory indicators, is one of the disease measuring methods used to identify disease activity [19]. Because it is brief, simple to use, and has demonstrated exceptional psychometric qualities in validation, it has proven to be a great tool for evaluating the disease activity in p-SLE patients [20].

Conclusions

This study explains a extreme burden of major tool engrossment in Egyptian pediatric SLE patients, from a 78.0% predominance of lupus nephritis (predominantly Class III and IV) and a high frequency of relapses. Serological gravestones (ANA, anti-dsDNA, reduced C3) and instigative indices (ESR) wait strong diagnostic forms in this place cohort. Early hide for renal engrossment and aggressive healing methods are urged to improve complete consequences in pediatric SLE.

Limitations of the study

It includes the small cohort, conducted at a single center, and a tertiary care referral bias.

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