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Study of the Association of Some Blood and Urine Markers in Diagnosing in Pediatric Systemic Lupus Erythematous

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Abstract: Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder that may present in pediatric cohorts, frequently resulting in considerable morbidity. Identifying dependable biomarkers for diagnosis is essential for efficient management. The objective of this study was to examine the link of some laboratory parameters in the diagnosis of juvenile SLE. The study encompassed children aged 5 to 18 years diagnosed with SLE based on the Systemic Lupus International Collaborating Clinics (SLICC) criteria, as well as healthy controls matched for age and sex. Clinical assessments and demographic information were gathered, and a blood and urinary parameters were analyzed. No statistically significant variations were seen in sex distribution ($p = 0.346$) or age ($p = 0.867$) between SLE patients and controls. The average age of SLE patients was 14.4 years, with a majority of females (78.7%). Clinical manifestations comprised fever and malar rash (61.7%), bone discomfort (55.3%), and alopecia (40.4%). Hematological study indicated reduced hemoglobin and leukocyte counts (both $p < 0.001$), although platelet counts exhibited no significant variation ($p = 0.773$). Urinalysis revealed elevated amounts of erythrocytes, leukocytes, and proteinuria in patients with SLE, with 34% demonstrating differing degrees of proteinuria ($p < 0.001$). The findings emphasize the significance of particular blood and urine markers in diagnosing juvenile SLE, indicating the necessity for continued study to enhance diagnostic criteria and optimize patient outcomes.

keywords: Systemic lupus erythematosus (SLE), Pediatric autoimmune disease, Blood proteins, Hematological analysis, Urinary markers, Autoimmune disorders.

1. Introduction

Systemic lupus erythematosus (SLE) is a quintessential chronic autoimmune disease distinguished by its complex characteristics [1]. It mostly impacts women and children, with a significant incidence in adult females at a ratio of 9:1, with onset generally occurring during adolescence [2]. Juvenile SLE, affecting children under 16 years of age, accounts for 15 to 20% of SLE cases and exhibits a reduced female preponderance (3–5:1) relative to adult female SLE patients [3]. The disease is notably prevalent in African populations [4]. In Egypt, childhood SLE has an overall prevalence of 1 per 100,000 population, with 7.4% presenting in the pre-pubertal stage (≤7 years), 73.3% in the peri-pubertal stage, and 19.3% in early adolescence [5].

The characteristics of SLE in Egyptian patients display certain similarities to those in other Middle Eastern nations, albeit with a lower female-to-male ratio [6]. The development of the disease before to the age of 5 is exceedingly uncommon (4.35%), frequently exhibiting hematological signs [7]. SLE is a multifaceted disorder characterized by the immune system's assault on the body's healthy cells and tissues, resulting in many clinical symptoms that may vary from minor fatigue, rashes, and joint discomfort to severe, life-threatening organ damage [8].

Notwithstanding progress in diagnostics and therapies, SLE persists in causing considerable morbidity and premature mortality [9].

The clinical characteristics and test results in juvenile and adult SLE are predominantly analogous. Children with SLE exhibit a greater death rate than adults, and the condition can result in significant morbidity and a reduced quality of life [10]. In contrast to adults, juvenile SLE (J-SLE) patients typically demonstrate more severe organ involvement and a less favorable prognosis [11]. The exact etiology of SLE is ambiguous, and its intricate character has led to the proposal of multiple processes contributing to the disease's development [1]. Despite the identification of numerous biomarkers in SLE, a major difficulty in SLE cases is the absence of a single biomarker that correlates with fluctuations in disease activity [12]. The etiology of SLE remains incompletely elucidated, however it is believed to result from an interplay of genetic, environmental, and immunological variables [13]. The many signs of SLE, regarding both pathogenesis and clinical symptoms, present problems for its identification and treatment [14]. The current study to investigate the association of some laboratory blood and urinary markers in diagnosing in pediatric SLE and to explore their interrelationship.

2. Subjects and methods

2.1. Study Population

The study population consisted of children admitted to Mansoura University Children's Hospital (MUCH) diagnosed with systemic lupus erythematosus (SLE) according to the Systemic Lupus International Collaborating Clinics (SLICC) criteria. Participants aged 5 to 18 years were included. Healthy children of equivalent age and sex were recruited from the General Outpatient Clinic of MUCH. The inclusion criteria encompassed children diagnosed with SLE of both genders, but the exclusion criteria comprised the presence of other autoimmune illnesses, chronic inflammatory conditions, active infections, and malignancies.

2.2. Study Methods

All participants received a sequence of procedures, commencing with a clinical evaluation and management by the physician. Demographic data were gathered, encompassing age, sex, consanguinity, and clinical data from medical records. A 5 ml blood sample was collected from each participant once, with 2 ml of blood in a plain or gel tube for serum analysis. In addition to urine samples and 24 hour urine collection.

2.3. Ethical Considerations

The study protocol was submitted for clearance to the Institutional Review Board (IRB) and the Pediatric Department Board at Mansoura University/Faculty of Medicine (Cod IRB Number……..), from which the study subjects were sourced. Informed written agreement was acquired from the parents of each participant before their involvement in the study. Confidentiality and personal privacy were upheld throughout the study, and the obtained data were not utilized for any other purpose.

2.4. Statistical Analysis

The collected data were analyzed utilizing the SPSS software (Version 25) for Windows (IBM Corp. Released 2017). The t-test or Mann-Whitney U test was employed to assess the differences between SLE patients and healthy controls, chi square was applied for categorical comparisons, with p-values below 0.05 deemed statistically significant.

3. Results

3.1. Demographics

The table demonstrates no statistically significant differences in sex distribution ($p = 0.346$) or age ($p = 0.867$) between the SLE and control groups, indicating demographic matching. Mean age of SLE patients was 14.4 years, ranged from 8.5 to 18 years. They were 78.7% females and 21.3% males. The control group showed matched age and sex. In the group of SLE patients, 12.8% had a history of consanguinity. While the majority (87.2%) did not exhibit consanguinity.

3.2. Clinical data

The clinical symptomatology in the SLE group are presented in the table, with fever and malar rash being the most common (both at 61.7%), followed by bone pain (55.3%), hair loss (40.4%), arthritis (34%), thrombocytopenia

(29.8%), oral ulcers (27.7%), swelling (21.3%), fatigue (19.1%), weight loss (17%), headache (12.8%), bleeding (12.8%), photosensitivity (8.5%) and renal pain (8.4%).

Table 1.: Comparison between SLE and the control group regarding demographic data.

	SLE n = 47		**Control n = 50**		p
	№	**%**	**№**	**%**	
Sex					
Male	10	21.3	7	14.0	0.346
Female	37	78.7	43	86.0	
Age (years)					
Mean ± SD.	14.44 ± 2.32		14.46 ± 2.53		0.867
Median	15.0		15.0		
Min. – Max.	8.50 – 18.0		8.50 – 18.0		
Consanguinity					
No	41	87.2	46	92	0.440
Yes	6	12.8	4	8	

№, number; SD. Standard deviation, Min.: Minimum, Max.: Maximum, U: Mann–Whitney test, χ^2: Chi-Square test, p: Comparing SLE and control.

Table 2: Symptoms among SLE patients.

Symptoms	**SLEn = 47**	
	№	**%**
Fever	29	61.7
Malar rash	29	61.7
Bones pain	26	55.3
Hair loss	19	40.4
Arthritis	16	34.0
Thrombocytopenia	14	29.8
Oral ulcer	13	27.7
Swelling	10	21.3
Fatigue	9	19.1
Weight loss	8	17.0
Headache	6	12.8
Bleeding	6	12.8
Photosensitivity	4	8.5
Renal pain	3	6.4

№, number.

3.3. Laboratory data

Significant hematological differences were seen between the SLE and control groups. Patients with SLE demonstrated reduced hemoglobin levels and leukocyte counts (both $p < 0.001$). While, platelet counts exhibited no significant difference ($p = 0.773$). The urinary analysis showed that the SLE group had much higher levels of red blood cells, pus cells, and proteinuria than the controls. About 34% of SLE patients had different levels of proteinuria (+ to +++), and the amount of protein in their urine over 24 hours was much higher ($p < 0.001$). However, there was no significant difference in urinary creatinine levels ($p = 0.438$).

Table 3.: Comparison between SLE and the control group regarding laboratory parameters.

	SLE n = 47	**Control n = 50**	**p**
Hb (g/dL)			
Mean ± SD.	12.25 ± 1.56	13.27 ± 0.84	<0.001*
Median	12.50	13.30	
Min. – Max.	8.80 – 15.0	11.90 – 15.10	
Platelet ($x10^3/\mu L$)			
Mean ± SD.	289.3 ± 103.0	290.9 ± 90.58	0.773
Median	271.0	284.5	
Min. – Max.	88.0 – 713.0	150.0 – 450.0	
WBCs ($x10^3/\mu L$)			
Mean ± SD.	6.76 ± 2.13	8.74 ± 1.67	<0.001*
Median	6.70	9.10	
Min. – Max.	2.50 – 12.10	5.10 – 10.90	
RBCs (Cell/HPF)			
Mean ± SD.	7.85 ± 20.17	1.68 ± 1.45	0.002*
Median	3.0	2.0	
Min. – Max.	0.0 – 100.0	0.0 – 5.0	
Pus (Cell/HPF)			
Mean ± SD.	9.57 ± 19.94	1.64 ± 1.51	<0.001*
Median	4.0	1.0	
Min. – Max.	0.0 – 100.0	0.0 – 5.0	
Urinary protein (mg/dL)	**№ (%)**	**№ (%)**	
NIL	31(66.0%)	50(100.0%)	MC <0.001*
+	8(17.0%)	0(0.0%)	
++	6(12.8%)	0(0.0%)	
+++	2(4.3%)	0(0.0%)	
24 h protein in urine (g/dL)			
Mean ± SD.	1.57 ± 6.51	0.05 ± 0.04	<0.001*
Median	0.09	0.05	
Min. – Max.	0.01 – 42.0	0.01 – 0.10	
Urinary creatinine (mg/dL)			
Mean ± SD.	6.02 ± 4.53	6.24 ± 3.55	0.438
Median	5.0	5.0	
Min. – Max.	0.50 – 17.0	2.0 – 16.0	

SD. Standard deviation, Min.: Minimum, Max.: Maximum, U: Mann–Whitney test, t: Student t test, p: Comparing SLE and control. *: Significant when p value <0.05.

4. Discussion

The demographic analysis of the study population indicated no statistically significant variations in sex distribution or age between the

systemic lupus erythematosus (SLE) patients and the control group, demonstrating adequate demographic matching. The average age of SLE patients was 14.4 years, ranging from 8.5 to 18 years, with a significant female predominance (78.7%) over males (21.3%). This gender gap aligns with current data, indicating that SLE primarily impacts females, especially during their reproductive years, owing to hormonal factors and genetic predispositions [15].

The discovery that 12.8% of SLE patients had a history of consanguinity is noteworthy, given consanguinity is associated with a raised risk of autoimmune diseases, including SLE. Genetic research indicates that consanguinity may increase the probability of inheriting susceptibility alleles, thereby contributing to the onset of SLE [16]. Nonetheless, the majority of patients (87.2%) did not demonstrate consanguinity, indicating the genetic variety within the examined population and implying that additional environmental or genetic factors may significantly contribute to the pathogenesis of SLE [13].

The demographic similarity between the SLE and control groups supports the study's validity [17], facilitating a more precise evaluation of the link between laboratory markers and SLE susceptibility, free from the confounding influences of age and sex differences.

The clinical symptomatology in the SLE cohort reveals a variety of presentations, with fever and malar rash being the most common symptoms, each recorded in 61.7% of patients. The malar rash, also known as a "butterfly rash," is a characteristic sign of SLE and signifies the autoimmune component of the disease [18]. The occurrence of fever indicates an active inflammatory process, frequently observed in SLE due to immunological dysregulation [19].

Subsequently, 55.3% of patients reported experiencing bone discomfort, potentially attributable to arthritis or myalgia, both prevalent in SLE [20]. Hair loss, impacting 40.4% of the sample, is a common manifestation, either associated with the disease or as a consequence of corticosteroid medication [21]. Arthritis, observed in 34% of patients, has a significant risk since it may result in considerable joint damage if not adequately managed [22]. Additional significant complaints comprised thrombocytopenia (29.8%), mouth ulcers (27.7%), and edema (21.3%). Thrombocytopenia in SLE may arise from immune-mediated platelet destruction or bone marrow suppression [23], whereas mouth ulcers represent a prevalent mucosal presentation of SLE [24]. Fatigue, noted in 19.1% of patients, is a severe symptom that affects quality of life and is frequently undervalued in clinical evaluations [25]. Supplementary symptoms like weight loss (17%), headache (12.8%), and bleeding (12.8%) were also found in the SLE cohort, in line with other studies [26], [27], [28]. Photosensitivity, impacting 8.5% of patients, is a well-established occurrence in SLE, wherein ultraviolet light exposure aggravates cutaneous symptoms [29]. Finally, renal pain, experienced by 8.4% of patients, may signify lupus nephritis, a severe consequence necessitating immediate diagnosis and intervention to avert long-term renal impairment [30]. The symptomatology of SLE in this cohort illustrates the disease's complexity and emphasizes the necessity for thorough clinical evaluation and individualized therapy regimens [19].

The hematological results of this investigation demonstrated notable differences between SLE patients and the control group, especially in hemoglobin levels and leukocyte counts, both of which were markedly diminished in the SLE cohort. Anemia is a prevalent hematological manifestation in SLE, frequently arising from chronic inflammation, autoimmune hemolysis, or renal involvement [31]. A decrease in leukocyte counts may signify leukopenia, commonly seen in SLE due to bone marrow suppression or peripheral loss of white blood cells [32]. Notably, platelet counts exhibited no significant difference ($p = 0.773$), indicating that thrombocytopenia, although frequent in SLE, was not a prominent characteristic in this particular group. Thrombocytopenia may arise from immune-mediated destruction or hypersplenism; nevertheless, its absence in this study could indicate the difference in disease manifestation among SLE patients [23].

Urinalysis further emphasized renal involvement in SLE, with the SLE cohort displaying significantly raised levels of erythrocytes, leukocytes, and proteinuria relative to controls. The detection of red blood cells and pus cells in the urine indicates glomerular inflammation or injury, aligning with lupus nephritis, that may result in significant morbidity [19]. The finding that about 34% of SLE patients exhibited differing degrees of proteinuria indicates a considerable renal impairment burden, and the markedly elevated protein levels in urine over 24 hours further emphasizes renal involvement [33].

The absence of a significant difference in urinary creatinine levels indicates that, despite the presence of proteinuria and hematuria, the overall renal function, as assessed by creatinine levels, remained largely steady in this cohort. This may suggest that whereas certain patients display indications of renal damage, others may not have advanced to substantial renal impairment. In addition, early renal function deterioration may occur in patients with lupus nephritis. Patients with LN exhibiting normal urine protein levels may have hyperfunctioning kidneys [34]. These findings underscore the necessity of routine hematological and urine evaluations in SLE patients to detect potential complications, especially renal involvement, which can profoundly affect patient outcomes.

This study has several limitations, the case-control design restricts the ability to determine causal link between laboratory parameters and SLE activity. Longitudinal studies would be beneficial for evaluating temporal variations and their implications in disease development and progression. Secondly, although the sample size is considered adequate, it may still limit the generalizability of the findings to broader populations. Furthermore, reliance on self-reported symptoms may create bias, as patients may underreport or exaggerate particular presentations. The study did not examine the potential impact of treatment regimens on clinical and laboratory outcomes, which could provide a more comprehensive understanding of the disorder.

Future research should employ a larger, multicenter approach to enhance the generalizability of findings across diverse populations. Longitudinal studies are recommended to track changes in clinical symptoms, hematological and urinary parameters over time, potentially providing insights into disease progression and treatment efficacy. Additionally, incorporating a thorough analysis of treatment procedures and their effects on symptomatology and laboratory outcomes would be beneficial. Investigating the impact of environmental factors and genetic predispositions on the progression of SLE may provide a more thorough comprehension of the disease.

Conclusion

This study highlights the complex clinical symptoms and significant hematological and urinary differences in SLE patients compared to healthy controls. The findings underscore the imperative for thorough clinical assessments and routine laboratory evaluations to identify potential problems, particularly renal involvement, which can significantly influence patient outcomes. These findings augment the understanding of SLE and emphasize the imperative for individualized treatment strategies to optimize patient care and outcomes.

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