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Photosensitizing Medications Use in Lupus Patients and Relation to Flare and Outcome

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease marked by a broad range of clinical manifestations with photosensitivity being a common and clinically significant feature. Drug-induced photosensitivity is a possibly preventable cause of disease flare and morbidity in SLE patients.

Aim: This study aimed to evaluate the association between the use of photosensitizing medications and disease flare, onset and clinical outcomes in patients diagnosed with SLE.

Subjects and methods: This retrospective cohort study included 120 patients diagnosed with SLE at Menoufia University Hospital, Egypt, between through the period from April 2023 to April 2024. Detailed drug histories, including the use of known photosensitizing agents, were collected. Clinical outcomes such as flare incidence, timing, and skin reactions were recorded and analyzed leveraging descriptive statistical methods.

Results: Most participants were females (84.2%) with a mean age of 41.3 years. Diuretics (53.3%), NSAIDs (46.7%), and antibiotics (45%) were the most commonly used photosensitizing medications. About 24.2% of patients experienced disease flares temporally associated with sun exposure and medication use. Only 25.8% reported using sun protection. Drug-induced photosensitive reactions included lichenoid eruptions, erythema multiforme and discoid lupus lesions. Most patients (70%) started these medications after their SLE diagnosis.

Conclusion: Photosensitizing medications significantly contribute to disease flare and adverse outcomes in SLE patients. Increased awareness, careful drug selection, and consistent sun protection measures are critical for optimizing patient care and reducing preventable complications.

Keywords: Autoimmune disease, Drug-induced, Flare, Photosensitivity.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disorder characterized by periods of remission and exacerbation. It predominantly affects women in their reproductive years, with a striking female-to-male ratio of nearly 9:1, underscoring the potential influence of hormonal and genetic factors in its pathogenesis [1]. The disease manifests with multisystem involvement including cutaneous, renal, hematologic and neuropsychiatric symptoms. Among the cutaneous features, photosensitivity is a hallmark and often serves as both a diagnostic criterion and a trigger for disease activity [2].

Photosensitivity encompasses a spectrum of symptoms and dermatological conditions, collectively known as photodermatosis, that are either induced or aggravated by exposure to ultraviolet (UV) or visible light from sunlight [3]. Photosensitivity in SLE can result from intrinsic disease mechanisms or external factors such as ultraviolet (UV) light exposure and photosensitizing medications.

Drug-induced photosensitivity may manifest as phototoxic or photoallergic reactions, which can overlap with or exacerbate SLE-related cutaneous lesions. More than 80 medications have been implicated in lupus-related photosensitivity, including common drugs such as thiazide diuretics, NSAIDs, antibiotics, and antifungals [4].

Patients with systemic lupus erythematosus (SLE) who receive photosensitizing medications—such as thiazide diuretics, neuroleptics, or tetracyclines—may develop phototoxic reactions that typically manifest as increased susceptibility to sunburn. In rare instances, photosensitivity can present with skin fragility and blistering, particularly among patients with concurrent SLE and porphyria cutanea tarda. Additionally, other photosensitive conditions, including solar urticaria and erythropoietic protoporphyria (EPP), have been documented in association with SLE, however these occurrences are generally considered coincidental rather than causally related [5]. Photosensitivity encompasses a spectrum of symptoms and dermatological conditions, collectively known as photodermatosis, that are either induced or aggravated by exposure to ultraviolet (UV) or visible light from sunlight [6].

Although the phototoxic properties of numerous medications are well recognized, their precise influence on systemic lupus erythematosus (SLE) flare frequency and overall disease progression remains insufficiently investigated, especially among Middle Eastern populations. Therefore, the present study aimed to

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evaluate the relationship between the use of photosensitizing drugs and key disease outcomes—including flare frequency, temporal patterns and cutaneous manifestations—in a cohort of Egyptian patients diagnosed with SLE.

PATIENTS AND METHODS

Study design and setting: This retrospective cohort study was conducted at Menoufia University Hospital, Egypt, through the period between April 2023 and April 2024.

Study population: A total of 120 patients diagnosed with systemic lupus erythematosus (SLE) based on the 2019 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria that were enrolled in the study.

The inclusion criteria: Adult patients aged 18 years or older with a confirmed diagnosis of SLE who had been receiving at least one recognized photosensitizing medication during the study period.

Exclusion criteria: Patients with a history of malignancy. Pregnant or lactating women. Patients with comorbid primary photosensitive conditions (e.g., porphyria, pseudoporphyria, solar urticaria, erythropoietic protoporphyria). Patients on phototherapy or with known light-induced dermatoses independent of drug use.

Data collection

All patients underwent a comprehensive clinical evaluation, including:

- **Demographic data:** Age, gender, occupation and residence.
- **Medical history:** Disease duration, comorbidities, current and previous treatments and family history of autoimmune or photosensitive diseases.
- **Drug history:** Detailed timeline of all medications taken with emphasis on photosensitizing agents (e.g., diuretics, NSAIDs, antibiotics, antifungals & statins). Drug use was categorized as pre-diagnosis, during diagnosis or post-diagnosis of SLE.
- **Photosensitivity assessment:** patients were asked about skin changes following sun exposure, while on the medications, including type of reaction, timing, and whether symptoms improved after drug cessation.

Clinical evaluation

Cutaneous and systemic manifestations of systemic lupus erythematosus (SLE) were documented in accordance with the 2019 EULAR/ACR classification criteria. Disease activity was evaluated using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). A flare was defined by:

1. An increase in the SLEDAI score by ≥ 4 points compared to the previous assessment.
2. Emergence of new clinical features not previously documented.
3. Requirement for treatment escalation (e.g., corticosteroids or immunosuppressants).

Complete remission was defined as a **Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K)** score of Zero in patients who were free from corticosteroid as well as immunosuppressive therapy, while the continued use of antimalarial agents was permitted [7].

Assessment of drug reaction

Suspected drug-related photosensitive reactions were categorized clinically as:

- Phototoxic (e.g., sunburn-like erythema).
- Photoallergic (e.g., lichenoid eruption, chronic cutaneous lupus & erythema multiform).

Timing of rash appearance after sun exposure was recorded in intervals: < 1 week, 1–2 weeks, 2–4 weeks, and 4–8 weeks.

Patients were also asked about sunscreen use, seasonal variation in symptoms and whether sun exposure worsened symptoms or triggered flares.

Ethical approval: Prior to the initiation of the study, every participant executed a written consent form, which had been formally authorized by the Local Ethical Research Committee of the Menoufia Faculty of Medicine. Furthermore, official Institutional Review Board (IRB No. 9/2023INTM16) approval was successfully obtained. The entire research project was conducted in strict adherence to contemporary ethical standards, including compliance with the provisions of the Declaration of Helsinki and its subsequent amendments. Crucially, written informed consents were meticulously collected from all participants before their formal inclusion into the study cohort.

Statistical analysis

Data analysis was conducted leveraging IBM SPSS software, version 22. Categorical variables were summarized using frequencies and percentages. Continuous variables were presented as means and standard deviation (SD). Although the primary analytical approach was descriptive due to limitations concerning the sample size, the Chi-square test of independence was initially planned to statistically assess the potential association between the various medication types and the observed flare incidence. P value ≤ 0.05 was deemed significant.

RESULTS

A total of 120 patients with SLE were included, with a predominance of females (n=101, 84.2%). The mean age was 41.34 ± 8.52 years, and the average disease duration was 7.34 ± 8.52 years. The most common occupations were housewives (43.3%), followed by workers (33.3%).

Table (1): Demographic data of the studied patients (N=120)

Studied variables			No.	%
Sex	Males		19	15.83
	Females		101	84.16
Age /years	Mean ± SD		41.34±8.52	
	Median		41.00	
	Range		20 – 60	
Duration of the disease/ years				
	Mean ± SD		7.34±8.52	
	Median		5.00	
	Range		6 months – 40.0	
Occupation	Retired		9	7.5
	Worker		40	33.33
	House wife		52	43.33
	Student		19	15.83
Residence	Rural		36	30.0
	Urban		84	70.0
Diabetes mellitus			11(9.16)	
Hypertension			34 (28.33)	
Renal disease		**CKD**	30 (25)	
		ATI	5 (4.11)	
		Renal failure	9 (7.5)	
Liver disease		**HCC**	5 (4.11)	
		Liver cirrhosis	20 (16.6)	
		NAFLD	16 (13.33)	
Thyroid disease		**Hypothyroid**	5 (4.11)	
		Hyperthyroid	18(15)	
Stress and anxiety			16 (13.33)	
Dermatological disease			54 (45.0)	
None			15 (12.5)	

Regarding cutaneous manifestations, 38.3% of patients had oral ulcers, 28.3% experienced non-scarring alopecia, and 21.7% showed discoid or subacute cutaneous lupus lesions. Systemic features included arthritis in 53.3%, fever in 32.5% and neuropsychiatric symptoms (delirium, seizures & psychosis) in 10%. Hematologic abnormalities were observed in 43.3% (including thrombocytopenia and leukopenia) and 24.2% of patients presented with renal involvement.

Table (2): SLE diagnostic criteria in the studied cases

	Studied variables	No.	%
Cutaneous	Oral ulcers	46	38.33
	Non scaring alopecia	34	28.33
	ACL	25	20.83
	SACL or discoid le	26	21.66
Constitutional (fever)	Yes	39	32.5
	No	81	67.5
Arthritis (Synovitis or tenderness in at least 2 joints)	Yes	64	53.3
	No	56	46.7
Neurogenic	Delirium	7	5.83
	Seizures	3	2.5
	Psychosis	2	1.66
Serositis	Pleural or pericardial effusion	29	24.16
	Acute pericarditis	11	9.16
hematologic	Leukopenia	16	13.33
	Thrombocytopenia	24	20
	Autoimmune haemolysis	12	10
Renal	Proteinuria>0.5g/24h	29	24.16

Photosensitizing drug exposure was reported in all patients, with diuretics (53.3%), NSAIDs (46.7%), and antibiotics (45%) being the most frequently used. The mean duration of drug use was 6.74 ± 2.21 months.

Reactions attributed to photosensitizing agents included photo distributed erythema multiforme (7.5%), chronic cutaneous lupus (5%), lichenoid eruptions (4.2%) and hyperpigmentation (4.2%).

Table (3): Photosensitizing drugs in the studied cases

Studied variables	No.	%
Antibiotics (ciprofloxacin, cefotax, levofloxacin, sulphonamide…)	54	45.0
NSAIDs (ketoprufen, ibuprofen…)	56	46.7
Diuretics (Spironolactone, Amiloride...)	64	53.3
Hypoglycemics (Sulfonylureas, Thiazolidinediones)	19	15.83
Statins (atorvastatin, simvastatin…)	39	32.5
Antifungals (itraconazole, griseofulvin…)	29	24.16
Others (oral contraceptives, quinidine, amiodarone...)	16	13.33
Route of administration		
Topical	19	15.83
Injection	11	9.16
Oral	90	75
Duration of drug use/days-weeks	6.74 ± 2.21	
Lichenoid reaction	5	4.16
Photo-distributed erythema multiform	9	7.5
Subacute or chronic cutaneous lupus erythematosus	6	5
Hyperpigmentation and dyschromia	5	4.16
Pellagra like reaction	4	3.33

Diuretics were the most common drug used (64 of the cases), followed by NSAIDS (56 case), antibiotics (54 cases), statins (39 case), antifungal (29 case) and hypoglycemic (19 case). Approximately 24.2% of patients experienced SLE flares temporally associated with sun exposure during medication use.

Only 25.8% reported using sunscreens. Notably, 14.2% of patients had used the drug prior to diagnosis, 15.8% during diagnosis, and 70% post-diagnosis. Among those, 24.2% reported a direct correlation between sun exposure and the onset of symptoms.

Table (5): Effect of photosensitive drugs in the studied cases

Studied variables	No.	%
Seasonal variations	10	8.33
Effect of the drug on SLE		
FLARE	29	24.16
remission	91	75.83
Use of sun block or sun screen	31	25.83
Use of the drug		
Before DX	17	14.16
during DX	19	15.83
after DX	84	70
Relation between sun exposure and side effects	29	24.16

The time from sun exposure to clinical manifestation varied: 25.8% developed lesions within one week, 15.8% within 1–2 weeks, and 14.2% within 2–4 weeks, while 36.7% reported no reaction reported.

Table (6): Time between sun exposure and clinical appearance of skin lesions in the studied patients (N=120)

Items	(n=120) No (%)
No reaction	44(36.66)
< 1 week	31(25.83)
1–2 weeks	19 (15.83)
2–4 weeks	17 (14.16)
4–8 weeks	9 (7.5)

DISCUSSION

This study underscored a significant association between the use of photosensitizing medications and the occurrence of disease flares among patients with systemic lupus erythematosus (SLE), suggesting that drug-induced photosensitivity may act as a potential trigger for disease exacerbation, supporting the hypothesis that certain medications may exacerbate photosensitivity and induce cutaneous and systemic manifestations. The predominance of female patients aligns with well-established epidemiological data on SLE incidence [8].

The finding that diuretics and NSAIDs were the most common photosensitizing agents is consistent with previous literature. For instance, **Keyes *et al.*** [9] identified thiazides, NSAIDs and antibiotics as primary culprits in drug-induced cutaneous lupus. However, our study uniquely links these medications with increased flare rates in an Egyptian cohort—a demographic underrepresented in prior studies.

Interestingly, only 25.8% of patients reported using sun protection, suggesting a significant gap in patient education and preventive strategies. In contrast, studies conducted on Western populations report sunscreen use in over 60% of lupus patients [10]. This gap may reflect differences in climate awareness,

healthcare access or physician counseling. While 24.2% of patients experienced flare-ups associated with medication and sun exposure, the majority (75.8%) did not report such events. This suggests that additional factors such as genetic predisposition, skin phototype, UV index or cumulative sun exposure—may mediate individual sensitivity. Future studies using phototesting or controlled UV exposure protocols may help stratify risk more precisely [11].

In our study regarding side effects of photosensitizing drugs, there were 5 (4.16%) had lichenoid reaction, 9 (7.5%) cases had photo-distributed erythema multiforme, 6 (5%) had subacute or chronic cutaneous lupus erythematosus, 5 (4.16%) had hyperpigmentation and dyschromia and 4 (3.33%) had Pellagra like reaction. Reported rates of photosensitivity vary considerably across the clinical subtypes of cutaneous lupus erythematosus (CLE), ranging from 27% to 100% in subacute cutaneous lupus erythematosus (SCLE), 25% to 90% in discoid lupus erythematosus (DLE) and 43% to 71% in lupus erythematosus tumidus (LET) indicating a strong association between CLE and photosensitivity [10]. **Millard *et al.*** [6] further reported that patients with lupus erythematosus (LE) who are prescribed photosensitizing medications—such as thiazide diuretics, neuroleptics, or tetracyclines—may experience phototoxic reactions, typically manifesting as increased susceptibility to sunburn. In rare cases, photosensitivity may present as skin fragility and blistering, particularly in individuals with concurrent LE and porphyria cutanea tarda. Additionally, other photosensitive conditions, including solar urticaria and erythropoietic protoporphyria (EPP), have been observed in association with LE. However, these are generally considered coincidental rather than Pathophysiologically-linked.

Furthermore, most patients (70%) initiated the photosensitizing medications after SLE diagnosis, raising concerns about prescribing patterns and physician awareness of phototoxic potential. This finding underscores the importance of interdisciplinary management between rheumatologists, dermatologists and primary care physicians.

LIMITATIONS

The retrospective design introduced potential recall bias. No control group (SLE patients without photosensitizing drug use) limits the ability to infer causality. The study relied on clinical history rather than objective phototesting or immunological markers of photosensitivity.

Clinical implications:

The study emphasizes the need to:

- Screen all medications in SLE patients for phototoxic potential.
- Educate patients on rigorous sun protection.
- Reconsider first-line drug choices when safer alternatives are available.

CONCLUSION

Photosensitizing medications use in lupus patients causes very high impact on quality of life of the SLE patients. Photosensitizing medications used in lupus patients had a significant relation to triggering SLE, disease flare and bad outcome. Further research with extended follow-up periods is required to substantiate and validate the aforementioned findings and conclusions, thereby providing more definitive evidence regarding the patterns, mechanisms and clinical implications of photosensitivity in lupus erythematosus.

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REFERENCES

1. **McKeon K, Jiang S (2020):** Treatment of systemic lupus erythematosus. Australian prescriber, 43 (3): 85.
2. **Blake S, Daniel B (2019):** Cutaneous lupus erythematosus: A review of the literature. International Journal of Women's Dermatology, 5 (5): 320-329.
3. **Diffey B, Kochevar I (2007):** Basic principles of photobiology. In: Photodermatology CRC Press, Pp: 15-28.
4. **Kim W, Shelley A, Novice K *et al.* (2018):** Drug-induced phototoxicity: a systematic review. Journal of the American Academy of Dermatology, 79 (6): 1069-1075.
5. **Alrashidi A, Rhodes L, Sharif J *et al.* (2020):** Systemic drug photosensitivity—Culprits, impact and investigation in 122 patients. Photodermatology, Photoimmunology & Photomedicine, 36 (6): 441-51.
6. **Millard T, Hawk J, McGregor J (2009):** Photosensitivity in lupus. Lupus, 9 (1): 3-10.
7. **Zen M, Iaccarino L, Gatto M *et al.* (2015):** Prolonged remission in Caucasian patients with SLE: prevalence and outcomes. Annals of the rheumatic diseases, 74 (12): 2117-2122.
8. **Corbin D, Christian L, Rapp C *et al.* (2023):** New concepts on abnormal UV reactions in systemic lupus erythematosus and a screening tool for assessment of photosensitivity. Skin research and technology, 29 (3): e13247.
9. **Keyes E, Grinnell M, Vazquez T *et al.* (2021):** Drug-induced subacute cutaneous lupus erythematosus in previously diagnosed systemic lupus erythematosus patients: a case series. JAAD Case Reports, 12: 18-21.
10. **Kuhn A, Gensch K, Haust M *et al.* (2011).** Photoprotective effects of a broad-spectrum sunscreen in ultraviolet-induced cutaneous lupus erythematosus: a randomized, vehicle-controlled, double-blind study. Journal of the American Academy of Dermatology, 64 (1): 37-48.
11. **Sanders C, Van Weelden H, Kazzaz G *et al.* (2003).** Photosensitivity in patients with lupus erythematosus: a clinical and photobiological study of 100 patients using a prolonged phototest protocol. British Journal of Dermatology, 149 (1): 131-137.