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Are Tattoos Safe in Patients with Systemic Lupus Erythematosus? Results From a Single-Center Study

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ABSTRACT

Introduction: Systemic Lupus Erythematosus is a pleiotropic autoimmune disease with common skin involvement. To date, only one study has investigated tattoos safety in SLE patients.

Objective: We performed a single-center study to evaluate the development of local and systemic complications after tattooing in a cohort of systemic lupus erythematosus (SLE) patients. Furthermore, we tried to identify SLE patients who had expressed the will to get a tattoo and why they decided not to.

Methods: Consecutive SLE patients were asked to complete a questionnaire about tattoos, including their number, features, and side effects. Open questions were proposed to non-tattooed patients to describe why they did not have tattoos.

Results: One hundred ninety-two SLE patients were enrolled [M/F 21/171; median age 41 years (IQR 18)]. Almost 50% of them had at least one tattoo. Seven patients (7.4%) referred adverse reactions to tattoos; interestingly, only one patient experienced a systemic reaction, specifically the occurrence of self-limiting lymphadenopathy. The main reason for not getting a tattoo was the diagnosis of SLE.

Conclusions: Our results suggest the safety of tattoos in SLE patients, as demonstrated by a low prevalence of mild adverse events.

Introduction

Tattoos are defined as the introduction of exogenous pigments into the dermis to produce a permanent design for a medical or aesthetic purpose. In the last few years, it has become a widespread cultural phenomenon with an estimated prevalence in Europe and US at 12% and 24%, respectively. This prevalence may be doubled in young adults [1]. Even if generally safe, tattooing may be associated with potential complications, ranging from mild, such as pruritus and swelling, to severe reactions such as infections and allergies [2].

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by frequent skin involvement, potentially occurring in up to 75% of patients [3]. The clinical phenotype of this manifestation is extremely heterogeneous, varying from acute to chronic phenotype, with influence on patients' quality of life [3].

Considering SLE patients' age and the spread of tattoos as a cultural phenomenon, we can assume that more patients may be interested in having a tattoo and may ask their physician about its safety and possible complications. Nowadays, it is impossible to answer this question completely due to a lack of scientific literature on clinical studies designed for SLE patients.

To our knowledge, only one study has been conducted on the safety of tattoos in SLE patients, suggesting no specific contraindication [4]. Furthermore, some data may be extrapolated from other diseases with skin involvement such as psoriasis. A large multicenter study published in 2020 reported a relatively low incidence of adverse effects in patients with psoriatic arthritis, most of which were classified as local complications and including oedema, pruritus, and Koebner phenomenon [5]. The latter is the most common complication described in recent case series and reviews focusing on tattoos in psoriasis patients [6,7]. Thus, considering these data, the authors concluded there were no major risks or contraindications for this procedure.

Thus, in the present study, we aimed to investigate the development of local and systemic complications after tattooing in a cohort of SLE patients. Furthermore, we tried to identify why SLE patients who had expressed the will to get a tattoo had decided not to do it.

Patients and Methods

Consecutive SLE patients classified according to the 2019 ACR/EULAR [8] criteria were enrolled in the present analysis. The clinical and laboratory data for each SLE patient were collected in a standardized computerized electronic form, including demographics, past medical history with the date of diagnosis, clinical and laboratory disease-related manifestations, comorbidities, and treatments. At the time of the visit to our outpatient clinic, each patient was asked to complete a self-administered printed questionnaire that included the following questions about tattoos: the presence of tattoos (Yes/No); if Yes, number of tattoos, age at tattooing, features of tattoos (position and colors of each tattoo), adverse reactions after each tattoo, and any allergies to food or drugs. Furthermore, we asked the patients about the possible association between SLE development and disease flare after tattooing. For patients without tattoos, we asked the reason why they had never had a tattoo.

Statistical Analysis

Data are presented as mean (± standard deviation, SD), median (with interquartile range, IQR) or as a percentage (%). Differences between continuous variables were tested for significance using the Mann–Whitney test. Categorical data were analyzed with a two-tailed Fisher's exact test. A value of $P<0.05$ was defined as statistically significant. Data were analyzed using GraphPad Prism software 9.0 for Mac (GraphPad Software, San Diego, CA, USA).

The study was conducted according to the Declaration of Helsinki statements and was approved by the Ethics Committee of Policlinico Umberto I, Sapienza University of Rome. Informed consent was obtained from all the patients.

Results

One hundred ninety-two SLE patients agreed to participate in the present study [M/F 21/171; median age 41 years (IQR 18)]. Ninety-five patients (49.5%) had at least one tattoo [M/F 5/90, median age 39 years (IQR 15)]. The main demographic, clinical, and laboratory features of SLE patients with and without tattoos are summarized in Table 1.

As expected, patients with tattoos were younger compared to patients without (39 years (15) versus 44 years (20); $P<0.0001$). We did not observe any significant differences between the two groups with regard to clinical and laboratory disease-related features.

Focusing on SLE patients with tattoos, we observed a median of two tattoos per person (IQR 3). Table 2 summarizes the tattoo-related features.

As reported in the table, only seven patients (7.4%) reported adverse reactions to tattoos. In detail, six patients referred a local reaction as described below: three patients referred mild infection in the tattoo site requiring topical empiric antibiotic treatment, one patient developed a hematoma, one occurrence of "halo sign," one localized myalgia, and one erythema. Only one patient reported systemic symptoms: cervical and axillary lymphadenopathy near the tattoo site. Among the 58 patients (61.0%) with at least one tattoo after SLE diagnosis, none reported disease flare after tattooing. Fifty-one patients (54%) had their

Table 1. Clinical and Demographic Features of Tattooed and Non-tattooed patients.

	With tattoo (N=95)	Without Tattoo (N=97)	*p*
Demographic Features			
Males/Females	8/87	13/84	0.42
Age, years [median (IQR)]	39 (15)	44 (20)	*P*< 0.0001
Disease Duration, months [median (IQR)]	120 (132)	144 (171)	*P*=0.1
Clinical features (%)			
Mucocutaneous involvement	63.6	74.7	0.14
Musculoskeletal involvement	51.1	48.3	0.76
Serositis	9.1	15.3	0.25
Kidney involvement	18.2	28.5	0.11
Hematological manifestation	32.9	39.5	0.42
Neurological involvement	6.8	12.1	0.65
Thrombotic events	9.1	9.9	0.30
Laboratory features (%)			
Hypocomplementemia	53.4	49.5	0.99
Anti-dsDNA	41	43.9	0.99
Anti-SSA	20.5	27.4	0.29
Anti-SSB	4.5	9.9	0.25
Anti-Sm	7.9	12.0	0.45
Anti-RNP	7.9	12.0	0.45
Anti-PL	32.9	39.5	0.56

Abbreviations: IQR: interquartile range; anti-PL: antiphospholipid antibodies.

first tattoo before SLE diagnosis. Among these, the median time between the first tattoo and SLE onset was 102 months (IQR 141).

Thirty SLE patients with no tattoos reported the willingness to have one. We therefore investigated the reason why they decided not to get tattooed with the following open question: "Why did you not get a tattoo?" The summary of responses is reported in Figure 1A.

Finally, the remaining 67 SLE patients stated that they were not interested in getting a tattoo; the major reasons are reported in Figure 1B.

Discussion

The present single-center analysis provided information about the safety of tattooing in a disease such as SLE, characterized by frequent skin involvement. In agreement with those observed for psoriasis, our results revealed a low frequency of complications in SLE patients undergoing tattoos. We found a low prevalence of local complications (6.3%) and a very low prevalence of systemic ones (1.1%), with one patient referring lymphadenopathy, which spontaneously resolved after a few weeks. Moreover, no patient reported allergic reactions to tattoos despite the high prevalence of colored tattoos.

Generally, tattoos were well-tolerated in our cohort. However, it should be underlined that tattoos are a source of potentially dangerous substances. By its nature, tattoo ink is a mix of compounds including pigments, diluents, and adjuvants/binders [9]. Among them, heavy metals (chromium, cobalt, lead, antimony, arsenic, beryllium, nickel, mercury) are commonly found as impurities, together with amines and phthalates. Whether it would be useful to precisely know the composition of each ink, the contents in terms of impurities and heavy metals composition are extremely variable [10-11], and it is thus impossible to trace every compound in each ink. With the aim of minimizing side effects and regulating the exact ink composition, the use of heavy metals is prohibited in Europe [12], and as of 2022, new inks should be free of these components. However, our study included patients who were tattooed before 2022; the composition of tattoo ink was not regulated at that time.

In addition to the well-known biological effects on the general population, all of these prohibited elements have been identified as possible stimuli for autoimmune diseases. Among the heavy metals, chromium and mercury

Table 2. Tattoo Features.

Numbers of tattoos per patient	N (%)
1	35 (36.8)
2-5	44 (45.2)
6-10	11 (11.5)
>10	5 (5.2)
Median tattoos per person	2 (IQR 3)
Total tattoos recorded	241
Number of colors	**N (%)**
1	55 (57.9)
2	16 (16.8)
3	9 (9.5)
4	7 (7.4)
5	6 (6.3)
Tattoo colors	**N (%)**
Black	77 (81)
Red/Pink	31 (32.6)
Yellow	14 (14.7)
Blue/Purple	19 (20)
White	4 (4.2)
Green	16 (16.8)
Site of tattoos	**N (%)**
Head and neck	11 (4.6)
Chest and abdomen	39 (16.2)
Back	51 (21.1)
Upper limbs and hands	93 (38.6)
Lower limbs and feet	47 (19.5)
Tattoo Adverse Events	7 (7.4)
Local	6 (6.3)
Systemic	1 (1.1)
Previous allergic reaction to drug	**N pts (%)**
Yes	30 (31.6)
No	65 (68.4)

have shown stronger evidence; they may worsen SLE symptoms [13], while mercury [14] has also displayed a possible pathogenic role as a trigger for SLE development [15]. It thus seems clear that heavy metals may act on the immune system directly or indirectly through various mechanisms. In particular, some studies have tried to unveil the precise pathogenic mechanisms. Recently, in an in vitro mechanistic experiment, immune cells were stimulated with different commercial tattoo inks and heavy metals (cadmium, chromium, mercury, and lead) contained within them, recording the production of IL-18 as a marker of cell activation [16]; with no significant differences between them, the inks were able to stimulate the activation of these cells. In other studies, cadmium, one of the more common heavy metal tattoo inks, was demonstrated to directly induce apoptosis in epidermal cells in mice [17]. Apoptosis is a central mechanism in SLE pathogenesis and is characteristic of the cutaneous sun exposure-induced skin reaction [18]. Moreover, mercury, the most common inorganic compound in red tattoos ink, can induce the production of IL-1 and IL-18, worsening autoimmune disease in mice [19].

Besides heavy metals, inks are a mixture of an incredible number of compounds, including organic elements, and it is almost impossible to analyze the effect of every single component. For instance, benzo(ghi)perylene (BgP), a common component of black ink, can induce reactive oxygen species (ROS), DNA damage, and thus apoptosis, especially after sensitization with UVA irradiation [20]. Photosensitization seems to be responsible for most skin reactions. As recently explained [21], pigments and other elements including heavy metals may have a photosensitizing role. However, in SLE patients, sun exposure is strongly discouraged, and sunscreen is widely applied. This evidence, together with the new rules prohibiting heavy metals in inks, significantly reduces the risk of photosensitivity reactions. On the other hand, heavy metals may also be responsible for classic type IV hypersensitivity reactions [22].

In conclusion, a growing body of evidence suggests a possible role of some tattoo ink compounds as triggers for the immune system, and the lack of extensive studies on different autoimmune diseases does not allow physicians to advise patients with consistent data. It is not surprising that in our cohort, among patients without tattoos, a relevant proportion of them would have liked to get one but avoided doing so because of the disease, sometimes under the advice of their doctor.

The main limitation of our study is the retrospective design with possible memory bias, especially for patients with long disease history and tattoos performed many years ago; this may in some way have underestimated the prevalence of adverse reactions related to tattoos. Furthermore, we lack precise information about disease activity and immunosuppressant therapy at the time of tattooing since most information was referred by the patients, suggesting the need for a prospective study to evaluate the possible effects of disease activity and medication on tattoo outcome. Moreover, the wide heterogeneity in terms of ink type and observation time did not allow us to hypothesize which compound could be responsible for the side effects, and more mechanistic studies are needed.

Despite these limitations, our analysis provides data about the safety of tattoos in SLE patients by demonstrating a very low rate of systemic complications. This finding can certainly help the rheumatologist to answer patients' questions. While general recommendations cannot be given because of the limited amount of available data and considering the high

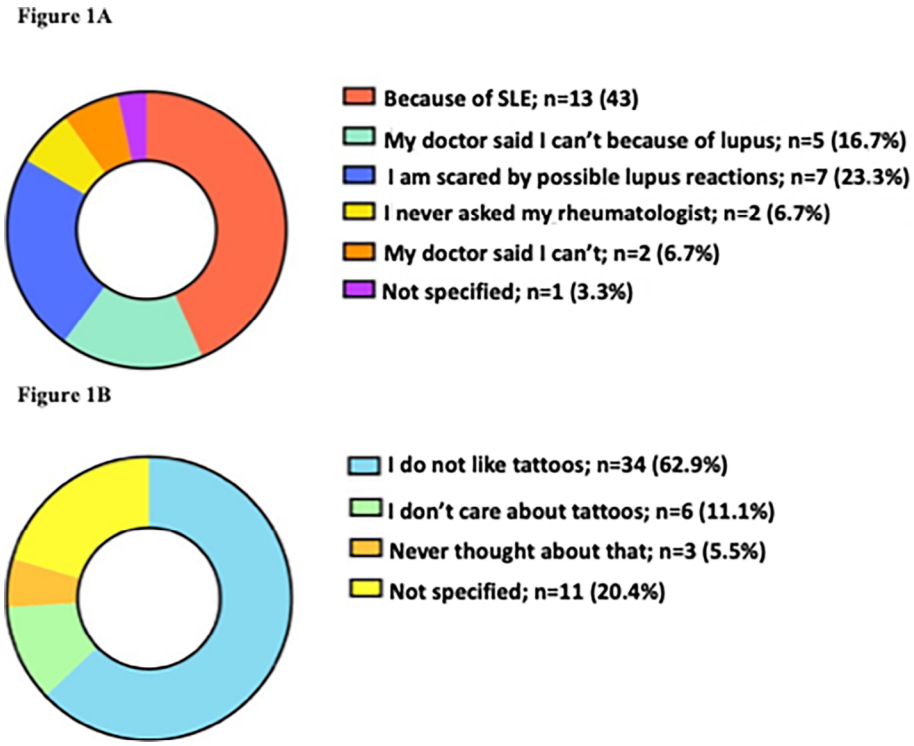

Figure 1. Images show the absolute number and percentage of answers of non-tattooed patients given to the open questions: Why did you not get a tattoo? A) Patients who would have liked to get a tattoo; B) Patients who would not have liked to get a tattoo.

percentage of tattooed patients, we can reassure patients of the low general prevalence of adverse events and that they can be tattooed without risks. At the same time, as a precaution, tattooing should be avoided during disease flare and by patients with extensive cutaneous disease. The decision to get tattooed and the choice of timing should be shared with the rheumatologist after a single-subject evaluation.

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References

1. Piccinini P, Pakalin S, Contor L, Bianchi I, Senaldi C. Safety of tattoos and permanent make-up: Final report. EUR 27947. Luxembourg (Luxembourg): Publications Office of the European Union; 2016. JRC101601.
2. Kluger N. Cutaneous and systemic complications associated with tattooing. *Presse Med*. 2016 Jun;45(6 Pt 1):567-76. DOI: 10.1016/j.lpm.2016.02.016. Epub 2016 May 6. PMID: 27160631.
3. Obermoser G, Sontheimer RD, Zelger B. Overview of common, rare and atypical manifestations of cutaneous lupus erythematosus and histopathological correlates. *Lupus*. 2010 Aug;19(9):1050-70. DOI: 10.1177/0961203310370048. PMID: 20693199.
4. Sabio JM, Betolaza S, Vargas-Hitos JA. Characteristics and safety of tattoos in patients with systemic lupus erythematosus. *Lupus*. 2019 Sep;28(10):1250-1254. DOI: 10.1177/0961203319867395. Epub 2019 Aug 5. PMID: 31382852.
5. Grodner C, Beauchet A, Fougerousse Ac, et al. Tattoo complications in treated and non-treated psoriatic patients. *J Eur Acad Dermatol Venereol*. 2020 Apr;34(4):888-896. DOI: 10.1111 /jdv.15975. Epub 2019 Oct 24. PMID: 31568596.
6. Kluger N, Estève E, Fouéré S, Dupuis-Fourdan F, Jegou MH, Lévy-Rameau C. Tattooing and psoriasis: a case series and review of the literature. *Int J Dermatol*. 2017 Aug;56(8):822-827. DOI: 10.1111/ijd.13646. Epub 2017 May 11. PMID: 28497495.
7. Kluger N. Tattooing and piercing: an underestimated issue for immunocompromised patients? *Presse Med*. 2013 May;42(5): 791-4. DOI: 10.1016/j.lpm.2013.01.001. Epub 2013 Feb 27. PMID: 23453496.
8. Aringer M, Costenbader K, Daikh D, et al 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. *Arthritis Rheumatol*. 2019 Sep;71(9):1400-1412. DOI: 10.1002/art.40930. Epub 2019 Aug 6. PMID: 31385462; PMCID: PMC6827566.
9. Bäumler W. Chemical hazard of tattoo colorants. *Presse Med*. 2020 Dec;49(4):104046. DOI: 10.1016/j.lpm.2020.104046. Epub 2020 Aug 5. PMID: 32768614.
10. Battistini B, Petrucci F, De Angelis I, Failla CM, Bocca B. Quantitative analysis of metals and metal-based nano- and submicron-particles in tattoo inks. *Chemosphere*. 2020 Apr;245:125667. DOI: 10.1016/j.chemosphere.2019.125667. Epub 2019 Dec 16. PMID: 31877461.
11. Forte G, Petrucci F, Cristaudo A, Bocca B. Market survey on toxic metals contained in tattoo inks. *Sci Total Environ*. 2009 Nov 15;

407(23):5997-6002. DOI: 10.1016/j.scitotenv.2009.08.034. Epub 2009 Sep 19. PMID: 19766292.
12. Regulation (EU) No. 2081/2020 amends Annex XVII of Regulation (EC) No 1907/2006 (REACH).
13. Kilburn KH, Warshaw RH. Prevalence of symptoms of systemic lupus erythematosus (SLE) and of fluorescent antinuclear antibodies associated with chronic exposure to trichloroethylene and other chemicals in well water. *Environ Res*. 1992 Feb;57(1):1-9. DOI: 10.1016/s0013-9351(05)80014-3. PMID: 1740091.
14. Crowe W, Allsopp PJ, Watson GE, et al. Mercury as an environmental stimulus in the development of autoimmunity - A systematic review. *Autoimmun Rev*. 2017 Jan;16(1):72-80. DOI: 10.1016/j.autrev.2016.09.020. Epub 2016 Sep 23. PMID: 27666813.
15. Dahlgren J, Takhar H, Anderson-Mahoney P, Kotlerman J, Tarr J, Warshaw R. Cluster of systemic lupus erythematosus (SLE) associated with an oil field waste site: a cross sectional study. *Environ Health*. 2007 Feb 22;6:8. DOI: 10.1186/1476-069X-6-8. Erratum in: Environ Health. 2007 May 17;6:15. PMID: 17316448; PMCID: PMC1821321.
16. Sozer Karadagli S, Kaftan G, Cansever I, Armagan G, Sogut O. Tattoo inks: evaluation of cellular responses and analysis of some trace metals. *Biometals*. 2024 Apr;37(2):495-505. DOI: 10.1007/s10534-023-00564-z. Epub 2023 Dec 1. PMID: 38038794.
17. Son YO, Lee JC, Hitron JA, Pan J, Zhang Z, Shi X. Cadmium induces intracellular Ca2+- and H2O2-dependent apoptosis through JNK- and p53-mediated pathways in skin epidermal cell line. *Toxicol Sci*. 2010 Jan;113(1):127-37. DOI: 10.1093/toxsci/kfp259. Epub 2009 Nov 3. PMID: 19887573; PMCID: PMC2794337.
18. Kuhn A, Wenzel J, Weyd H. Photosensitivity, apoptosis, and cytokines in the pathogenesis of lupus erythematosus: a critical review. *Clin Rev Allergy Immunol*. 2014 Oct;47(2):148-62. DOI: 10.1007/s12016-013-8403-x. PMID: 24420508.
19. Alphonse MP, Duong TT, Tam S, Yeung RSM. Mercury increases IL-1β and IL-18 secretion and intensifies coronary arteritis in an animal model of Kawasaki disease. *Front Immunol*. 2023 Apr 14;14:1126154. DOI: 10.3389/fimmu.2023.1126154. PMID: 37122704; PMCID: PMC10140582.
20. Negi S, Shukla S, Patel SK, et al. Benzo(ghi)perylene (BgP) a black tattoo ingredient induced skin toxicity via direct and indirect mode of DNA damage under UVA irradiation. *Chem Biol Interact*. 2023 Jul 1;379:110508. DOI: 10.1016/j.cbi.2023.110508. Epub 2023 May 5. PMID: 37150498.
21. Kluger N, Andraud M, Lartigau-Roussin C, Sultan-Bichat N. The Koebner phenomenon on tattoos and piercings in a patient with cutaneous lupus: a case report and review of the literature. *Acta Dermatovenerol Alp Pannonica Adriat*. 2021 Mar;30(1):43-46. PMID: 33765758.
22. Lukacs A, Karpati S, Temesvari E. Nickel-induced Koebner phenomenon in chronic cutaneous lupus erythematosus. *J Dtsch Dermatol Ges*. 2011 Jun;9(6):475-6. English, German. DOI: 10.1111/j.1610-0387.2010.07589.x. Epub 2010 Dec 30. PMID: 21199366.