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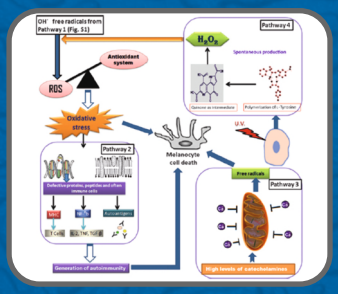


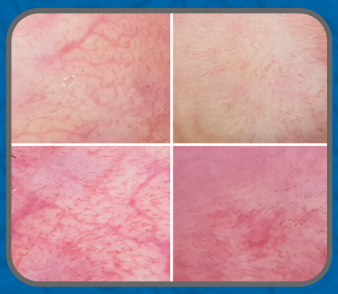

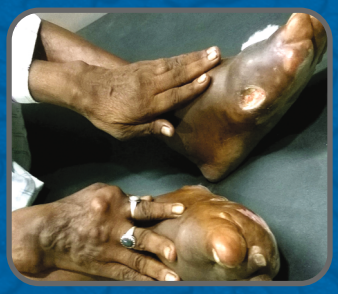

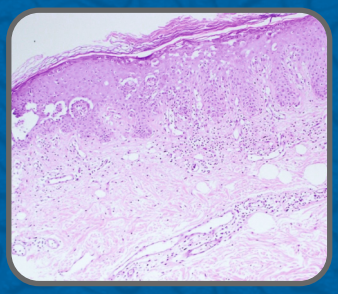

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Review Article

# Statins Role in Vitiligo: A Mini-Review

**Hayder M. Al-Kuraishy, Nawar R. Hussian, Marwa S. Al-Naimi, Ali I. Al-Gareeb**

Department of Pharmacology, Toxicology and Medicine, College of Medicine Al Mustansiriya University, Baghdad, Iraq

## Abstract

Vitiligo is a chronic acquired disease of pigmentation disorder. Melanocytes damage and hypopigmentation relate to the induction of oxidative and autoimmune disorders. Different previous studies illustrated the possible role of statins in the treatment of different types of vitiligo. Therefore, objective of this study was to elucidate the role of statins in the management of vitiligo. In general, an endeavor of this study article was to present a mini-review regarding the potential therapeutic effect of statins in the therapy of vitiligo. Results of the present study illustrated that statins inhibit the production of interferon gamma, expression of major histocompatibily complex, and T-cells activation in patients with active vitiligo. Statins have significant anti-inflammatory and immune-modulating activates in different modalities of vitiligo. Statins, have a potential effect against oxidative stress through the activation of anti-oxidant capacity and reduction of ROS in human melanocytes by upregulation of nuclear erythroid 2-related factor in the melanocytes. Statins improve melanogenesis in melanocytes though increasing tyrosinase mRNA production and augment the stimulatory effect of α-melanocyte-stimulating hormone from the pituitary gland on the melanocytes. Finally, statins therapy may produce significant inhibition of inflammatory reactions through the inhibition of chemokines. In conclusion, this study highlighted the potential role of statins in the treatment of vitiligo either systemic or localized through significant suppressions of oxidative stress, autoimmunity, and inflammatory reactions. Bidirectional effects of statins on oxidative and autoimmunity/inflammatory pathway making it as a novel therapy for vitiligo.

**Keywords:** Autoimmunity, melanocytes, statins, vitiligo

## Introduction

Vitiligo is a chronic acquired disease with genetic susceptibility of pigmentation disorder, due to the destruction of skin melanocytes leading to hypopigmentation. Besides, vitiligo may involve other organs that contain melanocytes such as the inner ear, mucous membrane, and eyes, which could explain the associations between vitiligo with hearing loss and autoimmune diseases.[1] The incidence of vitiligo is 1% worldwide, and it occurs at any age, but 80% more under the age of 30, affect both sex equally.[2] It has been reported that the pathogenesis of vitiligo is linked to the three main theories, which are the followings:

### Biochemical and oxidative stress theory

Melanocytes damage and hypopigmentation relate to the induction of oxidative. The highest concentration of free radical and reduction of body anti-oxidant capacity is associated with melanocytes injury and the incidence of vitiligo. Besides, the level of hydrogen peroxide ($H_2O_2$) is increased in patients with vitiligo due to oxidative stress injury.[3] In addition, Hazneci *et al*., the study found that nitric oxide synthase (NOS) and nicotinamide adenine dinucleotide phosphate oxidase are elevated in vitiligo.[4] Similarly, high catecholamine levels are associated with melanocytes injury due to the upregulation of monoamine oxidase A, sympathetic activation, and activation of hypothalamic-pituitary-adrenal axis.[5] The reduction of melanin production is also caused by high levels of 6-tetrahydrobiopterin (6-BHP) which inhibits phenylalanine hydroxylase, leading to the reduction of L-tyrosine and then melanin biosynthesis.[6]

### Adhesion theory (melanocytorrhagy)

Adhesion defects of melanocytes lead to migration of melanocytes through the epidermal basal layer, causing T-cells

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activation by melanocytes auto-antigens and subsequent melanocytes injury and hypopigmentation.[7] Remarkably, Ricard *et al*. illustrated that discoidin domain receptor-1, which is an adhesion molecule of melanocytes is diminished in vitiligo.[8]

### Autoimmune theory

Vitiligo is associated with different autoimmune disorders, including alopecia, Hashimoto thyroiditis, Addison disease, and polyglandular syndrome.[9] Autoantibodies against melanocytes and tyrosinase enzyme are detected in 10% of vitiligo patients. As well, VIT40, SOX transcription factor, and tyrosinase are regarded as melanocytes target antigens for different autoantibodies.[10] Besides, cytotoxic T-lymphocytes against melanocytes are increased in patients with vitiligo, highlighting the role of cell-mediated immunity in the pathogenesis of vitiligo. Moreover, regulatory T-cells are reduced in the blood that increases the risk of melanocytes damage by the cytotoxic T-lymphocytes.[11] What's more, different cytokines such as tumor necrosis factor (TNF-α), interleukin 10 (IL-10), and IL-17 are elevated and regarded as biomarkers of vitiligo.[12]

### Neural theory

Certain peripheral chemical neurotransmitters such as neuropeptide Y are increased peripherally leading to the destruction of melanocytes. Furthermore, the degeneration of axons and Schwann cell has been reported to be linked with the induction of vitiligo.[13]

### Viral theory

Various types of viral infection may induce the induction of vitiligo, as the DNA of cytomegalovirus has been observed in skin biopsy in patients with vitiligo.[14] As well, hepatitis C virus and the Epstein–Barr virus might be a causative factor in the initiation of the pathogenesis of vitiligo.[15]

Therefore, it seems that the etiopathogenesis of vitiligo is likely of the convergence of several of these pathways; thus, vitiligo is regarded as a syndrome rather than a single pathologic entity.

## Basic Therapy of Vitiligo

Skin repigmentation is the main goal of therapy regardless of its types; however, spontaneous repigmentation is occurring in about 1%–25% of patients.[16] Topical corticosteroids are the first-line therapy and more effective for small vitiligo lesions and should not use more than 4 months due to the risk of skin atrophy.[17] Topical calcineurin inhibitors such as tacrolimus are effective as topical corticosteroids without risk of skin atrophy.[18] Systemic corticosteroids, such as dexamethasone, prednisolone, and methylprednisolone are effective for generalized progressive vitiligo.[19] Besides, oral methotrexate is a useful therapy for vitiligo.[20] On the other hand, physical therapy such as phototherapy with ultraviolet A (UVA), narrow-band UVB with psoralen and monochromatic excimer light, is safe and more effective than other therapeutic modalities.[21] Indeed, different previous studies illustrated the potential role of statins in the treatment of different types of vitiligo.[22] Therefore, the objective of this study was to elucidate the mechanistic role of statins and/or molecular effects of different types of statins in the management of vitiligo.

## Search Strategy

In general, an endeavor of this study article was to present a mini-review regarding the potential therapeutic effect of statins in the therapy of vitiligo. Evidence from experimental, preclinical and clinical studies are evaluated, given the nature of the subject area; it remains clear that this literature search cannot be regarded as systemic review.

A multiplicity of search strategies took on and assumed which included electronic database searches of, Scopus, Web of Science, Medline, and PubMed using MeSH terms, keywords, and title words during the search. The terms used for these searches were as follows: (vitiligo OR pigmentation disorders) AND (statins OR cholesterol-lowering drug OR pleiotropic). (Vitiligo OR statins class OR simvastatin) AND (depigmentation OR type of vitiligo). Reference lists of identified and notorious articles were reviewed. In addition, only English articles were considered, and case reports were not concerned in the review. The key features of recognized applicable search studies were considered and the conclusions summarized in a mini-review.

## Statins

Statins inhibit *de novo* cholesterol biosynthesis through the inhibition of hydroxy-methyl-glutaryl-coenzyme A reductase (HMG-Co A) leading to noteworthy decline in serum levels of cholesterol and low-density lipoprotein with the elevation of high-density lipoprotein.[23] Beyond cholesterol-lowering effect, statins are also effective in the management of different cardio-metabolic disorders through amelioration of endothelial functions, anti-oxidant and anti-inflammatory effects, which collectively referred to as statins pleiotropic effects.[24]

## Role of Statins in the Treatment of Vitiligo

### Autoimmunity and vitiligo: Role of statins

Statins are conventionally used in the treatment of dyslipidemia, mainly hypercholesterolemia, which was previously evaluated in the treatment of vitiligo depending on its antioxidant, anti-inflammatory, and immune-modulating effects.[25] Repigmentation and regression of vitiligo were initially reported in man with vitiligo who was on simvastatin therapy for hypercholesterolemia.[26] The animal model study showed that statins reverse and prevent melanocytes degeneration and depigmentation through inhibiting the proliferation of CD8-T-Cells.[27]

It has been noted that statins inhibit the production of interferon-gamma (INF-γ), expression of major histocompatibility complex (MHC-II) and T-cells activation

in the endothelial cells.[11] The dose-dependent effect of simvastatin leads to significant inhibition of INF-γ-dependent MHC-II expressions with subsequent inhibition of activated T-lymphocytes in patients with active vitiligo.[28] This immune-modulating effect of statins may play an important role in the management of vitiligo. The immune-modulating effect of statins was previously reported since pravastatin prevents and reduces acute transplant rejections in human subjects.[29]

Similarly, pravastatin prevents acute rejection of cardiac transplant due to the inhibition of proinflammatory mediators and expression of adhesion molecules, which are independent of its cholesterol-lowering effect.[30] It has been reported that different types of statins prohibit the expression of inflammatory and proinflammatory adhesion molecules such as lymphocyte function-associated antigen (LFA-1) and intercellular adhesion molecule-1 (ICAM-1) on leukocytes. As well, statins block LFA-1 on the lymphocytes and inhibit its interaction with ICAM-1 on antigen-presenting cells and by this way statins prevent the activation of lymphocytes and antigen presentation.[31] Moreover, Weber *et al*. found that atorvastatin is the selective inhibitor of inducible MHC-II on the macrophages and endothelial cells as it not affect MHC-I and constitutive MCH-II.[32] In addition, statins inhibit chemokine release by endothelial cells, block chemokine receptors on T-cells, inhibition of natural killer cells, and attenuate the proliferation of stimulating leukocytes.[33] Besides, lovastatin inhibits different mediators and cytokines such as inducible NOS, TNF-α, IL-6, and IL-1 β leading to significant anti-inflammatory and immune-modulating activates in different modalities of vitiligo.[34]

The precise anti-inflammatory and immune-modulating mechanisms of statins are as the followings;

- HMG-CoA reductase dependent pathway: inhibition of HMG-CoA reductase leads to the reduction of active inflammatory metabolites known as isoprenoids[11]
- HMG-CoA reductase independent pathway
- Statins block LFA-1 so, prevent lymphocyte activations
- Statins inhibit T-cell function through the inhibition of the second messenger phosphatidylinositol-30-kinase/Akt transduction pathway.[35]

Moreover, IL-17 serum level is increased in patients with vitiligo and statins have been found to be a potent inhibitor of IL-17 through inhibition of T-cells proliferation and induction of immunotolerance.[36]

Therefore, statins may be an effective therapy against various types of autoimmune diseases such as multiple sclerosis and vitiligo. The immune-modulating effect of statins is summarized in Figure 1.

## Oxidative Stress and Vitiligo: Role of Statins

Oxidative stress is regarded as one of the potential pathogenic events in melanocyte loss and the development of vitiligo.

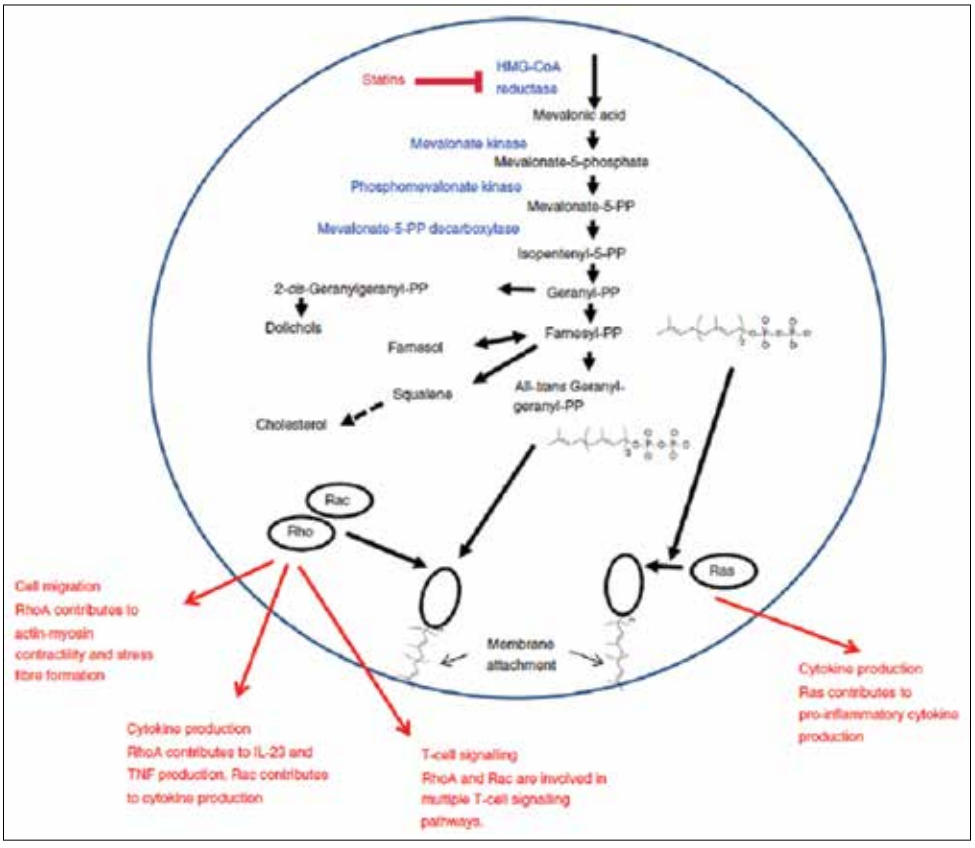


**Figure 1:** Immune-modulating effect of statins

The evidences of oxidative stress in vitiligo are mitochondrial dysfunction due to highly reactive oxygen species (ROS), depletion of endogenous anti-oxidant capacity, and low epidermal tetrahydrobiopterin levels.[37]

The source of oxidative stress in vitiligo may be endogenous or exogenous. Endogenous stresses are due to melanogenesis and mitochondrial dysfunctions. Exogenous stressors are due to environmental exposure to monobenzone, cytotoxic agents, UV irradiation, and phenols as well as other factors such as severe infection, hormones, and vaccinations.[38]

High ROS leads to the inhibition of tyrosinase also; secondary substrates that are generated due to binding of $H_2O_2$ to dihydroxyphenylalanine are also inhibiting tyrosinase.[39] Long-term accumulations of oxidative stress induced-free radicals cause epidermal cellular protein and lipid peroxidations as well as DNA damage. Besides, the inhibition of thioredoxin reductase and high extracellular $Ca^{+2}$ contribute to the induction of epidermal oxidative stress.[40] It has been shown that systemic oxidative stress is associated with induction of vitiligo, as depletion of body anti-oxidant potential, and reduction of pseudocholinestrase are reduced by free radicals and high $H_2O_2$.[41] Furthermore, augmented oxidative stress in the melanocytes leads to the induction of abnormal apoptosis and the emergence of new aberrant proteins which act as auto-antigens leading to autoimmunity.[42] Moreover, ROS upregulates TNF-α and other proinflammatory cytokines such as TGF-β and IL-2 which play a role in the inhibition of melanogenesis and stimulates the expression of anti-apoptotic proteins.[43] Recently, the intrinsic melanocytes defect may be the initial factor in the pathogenesis of vitiligo. Oxidative stress in the melanocytes leads to the induction of local inflammatory reactions and innate immune response which together inducing specific melanocytes immune response and the development of vitiligo in a genetically susceptible subjects, [Figure 2].[44]

On the other hand, statins, mainly simvastatin have a latent effect against oxidative stress through the activation of anti-oxidant capacity and reduction of ROS in human melanocytes. The anti-oxidative stress effect of simvastatin is mediated by upregulation of nuclear erythroid 2-related factor (Nrf2) in the melanocytes.[45] Oxidative stress factors activate Nrf2 which activates cellular anti-oxidant response element gene for the expression and synthesis of anti-oxidant enzymes. Therefore, imperfect Nrf2 activation in melanocytes increases melanocytes intolerance to the effect of oxidative stress and contributes to the melanocyte injury and development of vitiligo.[46] As a result, the direct effect of simvastatin on melanocytes may be of an additional mechanism against vitiligo.

Haendeler *et al*. found a novel anti-oxidant mechanism of statins through S-nitrosylation of thioredoxin and improvement of thioredoxin reductase activity,[47] which might explain the protective effect of statins against low level of thioredoxin reductase in vitiligo. As well, statins inhibit TNF-α and other proinflammatory cytokines, which are implicated

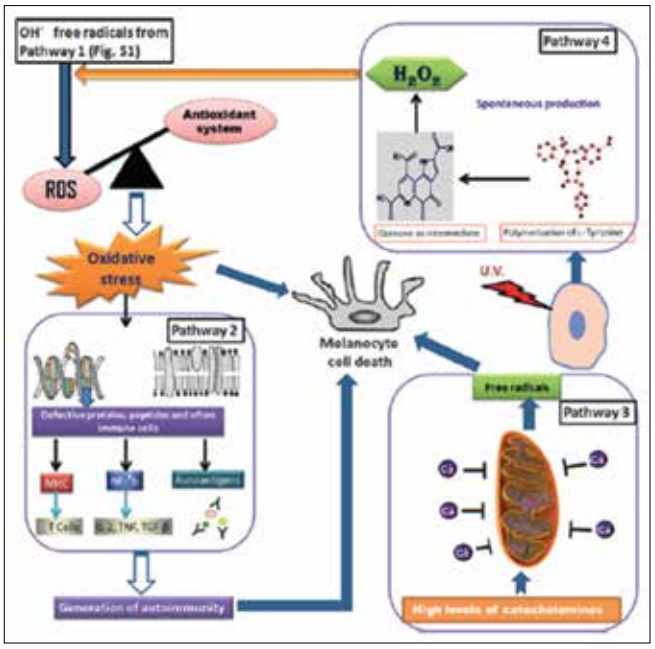


**Figure 2:** Oxidative stress and vitiligo

in the induction of oxidative stress and pathogenesis of vitiligo.[25] Remarkably, fluvastatin improves melanogenesis in melanocytes though increasing tyrosinase mRNA production by modulation of Akt and melanocyte proliferations. Furthermore, fluvastatin augments the stimulatory effect of α-melanocyte-stimulating hormone from the pituitary gland on the melanocytes.[48] Similarly, fluvastatin increases tyrosinase activity that induced by UVB irradiation in B16F10 melanoma cell line.[49] These findings indicate the protective role of statins against UV irradiation.

It has been noticed that the effective dose of simvastatin for repigmentation of vitiligo is 80 mg/day in human, and 40 mg/kg in mice. However, high dose of statins may increase risk of adverse effects such as rhabdomyolysis, myopathy, and type 2 diabetes mellitus, limit the use of high dose of statins in the management of vitiligo.[50] Topical simvastatin may be used at a concentration of 1.0 mmol/L for vitiligo lesions, which is more effective with low adverse effects than systemic statins therapy.[51]

Indeed, Qiao *et al*. illustrated that autophagy plays a protective role in the attenuation of epidermal oxidative stress through the regulation of melanocytes proliferation. Defective autophagy increases the risk of oxidative stress induced-depigmentation and the development of vitiligo.[52] Statins, mainly pitavastatin induces autophagy in human melanoma cell line through modulation of cytochrome c; therefore, statins therapy is effective in the regulation of melanocyte growth and proliferation that prevent melanoma and the development of vitiligo.[53]

## Chemokines in Vitilgo: Role of Statins

Chemokines are small glycoproteins that are activated by INF-γ and act on a wide variety of cell types such as

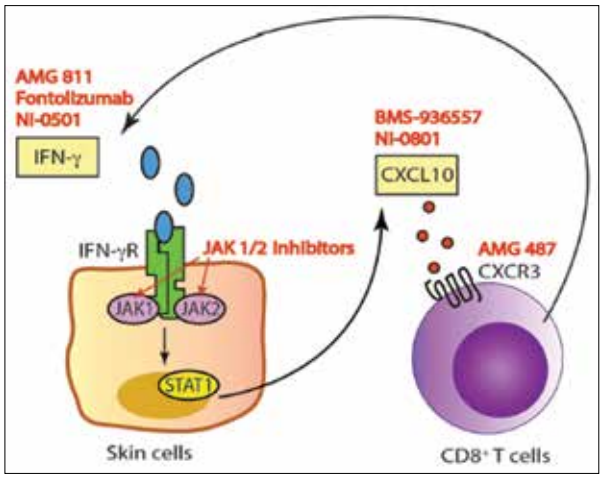


**Figure 3:** Interferon gamma/CXCL10 signaling in vitiligo

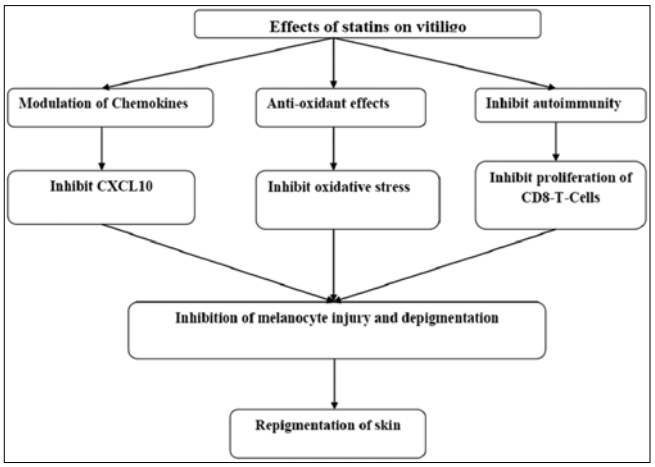


**Figure 4:** Potential effects of statins on vitiligo

lymphocytes, fibroblasts, neutrophils, and endothelial cells. Chemokine receptors (CXCR3) and its ligand (CXCL10) are increased in vitiligo and other autoimmune diseases, leading to the induction of tissue inflammation and damage.[54] High CXCR3 and CXCL10 reflects host immune response of Th1 lymphocytes. INF-γ-specific Th1 immune response provokes CXCL10 release and expression of CXCR3 on melanocyt-specific CD8+ T-cells that lead to melanocytes injury and depigmentation [Figure 1].[55]

Therefore, neutralization of CXCL10 reduces depigmentation and risk of vitiligo with a significant reversal effect on the depigmentation process. Thus, CXCL10 is regarded as a novel target in the treatment of vitiligo, [Figure 3].[54]

Statins therapy may produce significant inhibition of inflammatory reactions through the inhibition of chemokines and Veillard *et al*. illustrated that statins reduce chemokine and chemokine receptors in human macrophages and endothelial cells through suppression of geranyl-geranyl pyrophosphate pathway.[56]

As well, simvastatin interferes with INF-γ-/ACXCL10 pathway which is activated in patients with vitiligo, and hence, simvastatin is regarded as a potential new treatment targeting inflammatory pathways.[57]

Similarly, signal transducer and activator of transcription (STAT) protein family, mainly STAT-1 is required INF-γ-signaling in vitiligo.[58] Simvastatin downregulates JAK/STAT pathway in different inflammatory conditions.[59]

Furthermore, CXCR3 and its ligand CXCL10 induce the accumulation of cytotoxic autoreactive T-cells in the human epidermis leading to melanocyte degenerations and induction of vitiligo. Atorvastatin inhibits epidermal cytotoxic autoreactive T-cells that may explain the potential role of this drug in the management of vitiligo.[60] In addition, CXCR3/CXCL10 is an important pathway in the pathogenesis of vitiligo; serum level of CXCL10 is regarded as a novel biomarker in monitoring vitiligo activity and guiding treatment of progressive vitiligo.[61] Atorvastatin inhibits CXCL10 activity in different types of autoimmune diseases, which may explain the therapeutic potential effect of statins in vitiligo.[62]

## Conclusion

This mini-review study highlighted the potential role of statins in the treatment of vitiligo either systemic or localized through significant suppressions of oxidative stress, autoimmunity, inflammatory reactions, and CXCR3/CXCL10 axis pathway. Bidirectional effects of statins on oxidative and autoimmunity/inflammatory pathway making it as a novel therapy for vitiligo, [Figure 4]. Therefore, statins may be used as adjuvant therapy with other basic therapy against progressive and resistance vitiligo.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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Original Article

# Parents' Knowledge about Sun Exposure and a Comparison of their Personal Practices versus Those Used to Protect their Children against the Sun

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## Abstract

**Objectives:** Overexposure to the sun during childhood is a well-known risk factor for skin cancer. Childhood is a crucial period for establishing and continuing to develop healthy sun protection behaviors. The purpose of our study was to investigate parents' knowledge and compare their personal behaviors in regard to sun protection for themselves and for their children. **Materials and Methods**: We conducted a cross-sectional population-based study. A questionnaire was given to 738 parents, 700 of whom completed the questionnaire and were included in the study. **Results:** Among the 700 parents, 88% ($n$ = 616) were female and 12% ($n$ = 84) were male. The mean age of the parents and children was 35.1 ± 5.6 years and 5.2 ± 3.0 years, respectively. Eighty-three percent ($n$ = 580) of the parents were aware of sun exposure during childhood as a risk factor for skin cancer, but approximately only 15% of the parents reported using sunscreen regularly for themselves and for their children. Fifty-two percent ($n$ = 367) of the parents implied not using any protective clothing for their children. **Conclusion:** Our study showed that parents were aware of the risks of sun exposure and the need for sun protection for themselves and children, but protective practices were low overall. Parents should be included in educational interventions targeting sun protection behaviors toward themselves and their children.

**Keywords:** Child, dermatology, parent, sun protection

## Introduction

It is well known that the most important factor in the etiology of melanoma is ultraviolet (UV) radiation, mainly in childhood.[1] In 2008, more than 20,000 deaths due to melanoma were reported in Europe, and 35.5% of these were from the middle and eastern parts of Europe.[2] Turkey is in the eastern part of Europe, populated by Caucasians, primarily with Fitzpatrick skin types III and IV. In 2017, Baykal *et al*. reported that lentigo maligna melanoma, in which cumulative sun exposure plays a major role in the etiology, was higher in Turkey than in other European countries.[3] The harmful effects of UV rays have relatively increased because of vacation and tanning habits and thinning in the ozone layer. In recent years, tanning seems to have become fashionable and desirable among the people, especially in adolescents.[4]

Previous studies have shown that intermittent or intense sun exposure is a major determinant in the development of melanoma in adult life.[5] Hence, avoidance from sunburn and acquiring healthy habits regarding the sun in childhood is very important, especially in sunny countries such as Turkey. In this context, parental practices in terms of sun protection are of crucial importance for both themselves and their children and also for developing a positive approach regarding these behaviors.[6]

We conducted this study to assess parental beliefs about the harmful effects of UV radiation and compare the sun

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protection behaviors that parents used for themselves and their children.

## Materials and Methods

A cross-sectional population-based study was conducted between February 2017 and September 2018 in two tertiary hospital settings in Istanbul among parents with a child aged under 10 years. Participants were excluded if their questionnaires were incomplete or their children had diseases that could affect outdoor activities or sun protection behaviors (e.g., cerebral palsy, severe heart disease, severe asthma, and photosensitive disorders such as xeroderma pigmentosum). Seven hundred and thirty-eight parents gave consent for participation and 700 completed the survey. The study was approved by the ethics committee (No: 1946). A semi-structured questionnaire was developed by the authors, which included items on demographics, knowledge about sun exposure, skin cancer awareness, and questioned the practices of the parents in terms of protecting children against the sun.

### Demographic characteristics

Demographic characteristics of parents and children were recorded. The children were divided into two groups: lighter (Fitzpatrick phototype [FP] I–III) and darker skinned (FP IV–VI) based on the parents' statements about their children's FP. The FP is a standard scale based on an individual's tanning characteristics and it correlates well with phenotypic skin color, ranging from I (always burns) to VI (never burns).

### Sun protection knowledge

In the second part, questions about sun safety knowledge were answered on a 4-point Likert scale (never, rarely, sometimes, and always) in five categories: sunscreen use, hat use, sunglasses use, wearing long-sleeve clothing, and seeking shade. Furthermore, parents' beliefs were assessed about sun protection (response categories were "yes, no, and do not know") such as tanned skin is healthy, tanned skin does not need sun protection, and individuals who only go into the sun for 1–2 weeks a year are not at risk for skin cancer, and number of nevi and frequency of sunburns during childhood are important for skin cancer development.

### Practices in children's sun protection

In the third part of the questionnaire, a 4-point Likert scale about sun protection behaviors – using sunscreen, wearing a hat, sunglasses, and long-sleeve clothing, and seeking shade – were answered by parents for their children. Furthermore, beliefs about children's sun protection were questioned with true/false/don't know answers such as if the child was in water, was it still necessary to apply sunscreen, and was it acceptable for a child to stay outside when sunscreen had been applied? The total number of times a child had had sunburn during the child's life was also recorded.

### Data analysis

Descriptive statistics are given as number and percentage for categorical variables and average and standard deviation for numeric variables. Comparisons between the two dependent groups were made using the McNemar–Bowker test, and categorical variables were compared using the Chi-square test. The bivariate associations between parental knowledge and practices of sun protection were assessed using the Mantel–Haenszel Chi-square test.

## Results

### Parents and children's sociodemographic factors

The study included 700 parents, of which 88% ($n$ = 616) were female and 12% ($n$ = 84) were male. The mean age of the parents and children was 35.1 ± 5.6 years and 5.2 ± 3.0, respectively. Among the parents, 21% ($n$ = 151) had graduated from primary school, 24% ($n$ = 171) had graduated from high school, and 54% ($n$ = 378) were university graduates. One hundred and twenty-six (18%) children had lighter skin and 574 (82%) had darker skin according to the FP. According to the parents' responses, most of the children (82%, $n$ = 574) had no history of sunburn. Seventy-four (10.6%) children had a history of one sunburn, 24 (3.4%) children had been burned twice, 19 (2.7%) children had been burned three times, and 9 (1.2%) children had a history of more than three sunburns.

### Parental knowledge about sun safety and skin cancer

A high level of knowledge (82.9%) concerning "skin cancer risk-related sunburns during childhood" and "preference of very high-sun protection factor (SPF) sunscreens for their children" (82.3%) was observed. However, 59.3% of the parents believed that individuals who only went into the sun for 1–2 weeks a year were not at risk for skin cancer and almost 40% believed that "tanned skin did not need sun protection" [Table 1]. Among the women, 82% ($n$ = 507) and 68.3% ($n$ = 100) of men were aware of the causal relationship between sunburn during childhood and skin cancer ($P$ = 0.003).

### Comparison of the parents' sun protection behaviors and practices in their children's protection

The sun protection behaviors of the parents and practices for their children's protection are shown in Table 2. Fifteen percent of the parents implied using sunscreen regularly for themselves and for their children. Hats were more frequently worn by children, and sunglasses were more frequently worn by parents. Regular using of long-sleeved clothing on sunny days was very low (~2% in both the groups). In bivariate analyses [Table 3], the association between parental behaviors and practices for their children corroborated that parental behaviors were associated with the sun protection practices for their children. Parents who had lighter-skinned children were more likely to use sunscreen regularly (27%) than parents of darker-skinned children (13%) [Table 4]. Only 1% of the parents who graduated from primary school regularly used sunscreen for their children, whereas 24% of the university graduates regularly applied sunscreen to their children. The number of parents who "always sought shade on sunny days" was similar in all the groups, 23% for primary school graduates, 25% for high school graduates, and 26% for

university graduates. We found that 32% of the parents did not use protective clothing for themselves and 52% of the parents failed to use it for their children [Table 5].

## Discussion

Protection against UV radiation of the sun is a fundamental rule in the primary prevention of melanoma and other skin cancers. The increasing incidence of melanoma worldwide indicates the need for awareness of sun protection behaviors.[7] Evidence suggests that sun protection behavior in Turkey is still inadequate, despite the sunny period in Istanbul averaging 5.55 h daily, more than in most European cities. Cınar *et al*. reported that 47% of people had sunburn at least once[8] and in the past year, and Balcı *et al.* conducted a survey with 1634 individuals and found that the rate of using sunscreen was only 40%.[9] Ilter *et al*. conducted a cross-sectional study with 764 individuals between 2005 and 2006 and reported that 44% of participants did not use sunscreens. Hats and umbrellas (40%) were the most common accessories used for sun protection.[10] Terzi *et al*. reported that 69% of patients had satisfactory knowledge about sun protection.[11] Our results were similar with high percentages of correct answers in knowledge questions; however, 60% of individuals believed that 1–2 weeks' sun exposure per year was not a risk for skin cancer.

Childhood is an especially important period for protection against UV rays.[12] Studies showed that sun exposure during early life was a strong future risk factor for melanoma.[13] Moreover, unlike adults, children spend most of their time in the open air. It has been estimated that approximately half of cumulative UV radiation exposure occurs before the age of 20 years.[14] Young children are unable to adopt sun-protective practices independently, and they are dependent on their parents or caregivers to provide sun protection. Sun protection behaviors in adolescents are more difficult to change due to significant peer influences; tanning is thought to be fashionable among teenagers.[15] Therefore, targeting children regarding modifiable approaches for sun protection may be more achievable, and sun behaviors established during childhood are often seen to endure into adulthood.[16] Baz *et al*.[17] conducted a survey with Turkish parents, and it was reported that 88% of participants tried to protect their children from the sunlight, whereas 11.2% did not. Later, Kaptanoğlu *et al*. revealed that 33% of families reported a lack of application of sun protection measures.[18] In agreement with the results of other studies, we found that 95% of the parents tried to protect their children from the sun.

In the United Kingdom (UK), a study was conducted on 1000 parents with children aged 11 years and under, which revealed that 7% of participants admitted had never applied sunscreen to their children and 40% of children had experienced sunburn in the past 2 years.[19] In Turkey in 2003, Baz *et al*. reported that 65% of children had a history of sunburn according to their parents' statements.[17] We found that 82% of the children had no history of sunburn. This difference may

**Table 1: Parents' knowledge about harmful effects of sun (*n*=700)**

| | Correct answers | |
|---|---|---|
| | ***n* (%)** | **95% CI (minimum-maximum)** |
| Higher number of nevi is a risk factor for skin cancer | 503 (71.9) | 68.42-75.06 |
| Tanned skin is healthy | 565 (80.7) | 77.62-83.46 |
| Tanned skin does not need sun protection | 422 (60.3) | 56.62-63.85 |
| Individuals who only go into the sun for 1-2 weeks a year are not at risk for skin cancer | 285 (40.7) | 37.13-44.39 |
| Frequency of sunburns during childhood increases risk of skin cancer | 580 (82.9) | 79.89-85.47 |
| It is ok if a child stays out in the sun when sunscreen is applied | 451 (64.4) | 60.81-67.89 |
| Very high SPF (>50) sunscreens should be used in children | 576 (82.3) | 79.29-84.94 |
| If the child is in water, it is still necessary to apply sunscreen | 485 (69.3) | 65.78-72.59 |

SPF: Sun protection factor, CI: Confidence interval

**Table 2: Comparison of sun protection practices of parents and those used for their children**

| | **Sunscreen, *n* (%)** | **Hats, *n* (%)** | **Shade, *n* (%)** | **Sunglasses, *n* (%)** | **Clothing, *n* (%)** |
|---|---|---|---|---|---|
| Parents themselves | | | | | |
| Never | 201 (28.7) | 177 (25.3) | 37 (5.3) | 72 (4.5) | 226 (32.2) |
| Rarely | 244 (34.9) | 293 (41.9) | 209 (29.9) | 158 (22.5) | 235 (33.5) |
| Sometimes | 148 (21.1) | 125 (17.9) | 348 (49.7) | 192 (27.4) | 183 (26.1) |
| Always | 107 (15.3) | 105 (15.0) | 106 (15.1) | 278 (39.7) | 16 (2.2) |
| For their children | | | | | |
| Never | 176 (25.1) | 43 (6.1) | 32 (4.6) | 208 (29.7) | 367 (52.4) |
| Rarely | 233 (33.3) | 226 (32.3) | 195 (27.9) | 291 (41.6) | 269 (38.4) |
| Sometimes | 182 (26.0) | 235 (33.6) | 293 (41.9) | 129 (18.4) | 46 (6.6) |
| Always | 109 (15.6) | 196 (28.0) | 180 (25.7) | 72 (10.3) | 18 (2.6) |

**Table 3: The bivariate association of parents' personal behaviors regarding sun protection and practices for their children**

| | Never, *n* (%) | Rarely, *n* (%) | Sometimes, *n* (%) | Always, *n* (%) | *P* |
|---|---|---|---|---|---|
| **Frequency of sunscreen use on sunny days** | | | | | |
| Frequency of sunscreen use on sunny days to their children | | | | | |
| Never | 139 (69.2) | 26 (10.7) | 4 (2.7) | 7 (6.5) | <0.001 |
| Rarely | 48 (23.9) | 157 (64.3) | 19 (12.8) | 9 (8.4) | |
| Sometimes | 10 (5.0) | 50 (20.5) | 86 (58.1) | 36 (33.6) | |
| Always | 4 (2.0) | 11 (4.5) | 39 (26.4) | 55 (51.4) | |
| **Frequency of putting a hat on a child on sunny days** | | | | | |
| Frequency of putting a hat to their children on sunny days | | | | | |
| Never | 33 (9) | 0 (1) | 176 (33) | 9 (0) | <0.001 |
| Rarely | 56 (146) | 15 (9) | 233 (56) | 146 (15) | |
| Sometimes | 58 (87) | 74 (16) | 182 (58) | 87 (74) | |
| Always | 30 (51) | 36 (79) | 109 (30) | 51 (36) | |
| **Frequency of staying in the shade on sunny days** | | | | | |
| Frequency of keeping the child in the shade on sunny days | | | | | |
| Never | 22 (7) | 1 (2) | 22 (7) | 1 (2) | <0.001 |
| Rarely | 11 (122) | 56 (6) | 11 (122) | 56 (6) | |
| Sometimes | 1 (58) | 206 (28) | 1 (58) | 206 (28) | |
| Always | 3 (22) | 85 (70) | 3 (22) | 85 (70) | |

**Table 4: Parental sun protection practices for their children according to Fitzpatrick phototype skin types**

| | Darker skinned (FP I-III), *n* (%) | Lighter skinned (FP IV-VI), *n* (%) | *P* |
|---|---|---|---|
| Sunscreen | | | |
| Never | 142 (24.7) | 34 (27.0) | <0.001 |
| Rarely | 206 (35.9) | 27 (21.4) | |
| Sometimes | 151 (26.3) | 31 (24.6) | |
| Always | 75 (13.1) | 34 (27.0) | |
| Clothing | | | |
| Never | 306 (53.3) | 61 (48.4) | 0.286 |
| Rarely | 220 (38.3) | 49 (38.9) | |
| Sometimes | 36 (6.3) | 10 (7.9) | |
| Always | 12 (2.1) | 6 (4.8) | |
| Hat | | | |
| Never | 34 (5.9) | 9 (7.1) | 0.021 |
| Rarely | 200 (34.8) | 26 (20.6) | |
| Sometimes | 187 (32.6) | 48 (38.1) | |
| Always | 153 (26.7) | 43 (34.1) | |
| Shade | | | |
| Never | 29 (5.1) | 3 (2.4) | 0.479 |
| Rarely | 160 (27.9) | 35 (27.8) | |
| Sometimes | 242 (42.2) | 51 (40.5) | |
| Always | 143 (24.9) | 37 (29.4) | |
| Sunglasses | | | |
| Never | 166 (28.9) | 42 (33.3) | 0.022 |
| Rarely | 253 (44.1) | 38 (30.2) | |
| Sometimes | 102 (17.8) | 27 (21.4) | |
| Always | 53 (9.2) | 19 (15.1) | |

FP: Fitzpatrick phototype

be attributed to the increased awareness of the harmful effects of the sun in childhood. The implementation of public health campaigns about melanoma and sun protection throughout the past 15 years has generated widespread sun protection awareness. Furthermore, we included parents with children aged younger than 10 years because parents have less control over their children in adolescent ages, whereas Baz *et al*. included all age groups. Moreover, in the UK, children are lighter skinned than in Turkey, which could lead to more frequent sunburn.

Baykal Selcuk *et al*. conducted a survey in Turkey among 17,769 participants and found that sunscreen use was the most preferred sun protection method.[20] Similarly, we found that 71% of the parents used sunscreen for themselves and 75% used it for their children to some degree. Furthermore, 28% of the parents always made their children wear hats, but only 15% wore hats themselves. In line with this, a study showed that parents were more likely to practice skin cancer prevention for their children than for themselves.[21] In another study, authors implied that family-based interventions would be a more efficacious strategy to increase sun protection behaviors.[22] In a recent study, authors showed that "parental permission to tan" and "parental behaviors toward tanning" were strong predictors for indoor tanning in adolescents.[23] In our study, there was poor adoption of protective clothing. Wearing long-sleeved clothing was associated with reduced number of nevi; however, the use of sunscreen, although preventing sunburn, may lead to increased overall sun exposure in children.[24] Educational programs should emphasize the importance of the use of sunscreens and wearing protective clothing. McMichael *et al*. claimed that the majority of participants in their study stated that they would consider umbrella use if recommended by a dermatologist.[25]

Tan *et al*. showed that most parents of darker-skinned children expressed a lack of concern regarding the need for routine sun protection for their children.[26] Our study results support these

**Table 5: Education levels of parents and sun protection practices for their children**

| | Primary school, *n* (%) | High school, *n* (%) | University, *n* (%) | *P* |
|---|---|---|---|---|
| Sunscreen | | | | |
| Never | 72 (47.7) | 56 (32.7) | 48 (12.7) | <0.001 |
| Rarely | 65 (43.0) | 71 (41.5) | 97 (25.7) | |
| Sometimes | 12 (7.9) | 30 (17.5) | 140 (37.0) | |
| Always | 2 (1.3) | 14 (8.2) | 93 (24.6) | |
| Clothing | | | | |
| Never | 73 (48.3) | 92 (53.8) | 202 (53.4) | 0.342 |
| Rarely | 68 (45.0) | 64 (37.4) | 137 (36.2) | |
| Sometimes | 5 (3.3) | 11 (6.4) | 30 (7.9) | |
| Always | 5 (3.3) | 4 (2.3) | 9 (2.4) | |
| Hat | | | | |
| Never | 13 (8.6) | 15 (8.8) | 15 (4.0) | <0.001 |
| Rarely | 70 (46.4) | 64 (37.4) | 92 (24.3) | |
| Sometimes | 38 (25.2) | 39 (22.8) | 158 (41.8) | |
| Always | 30 (19.9) | 53 (31.0) | 113 (29.9) | |
| Shade | | | | |
| Never | 17 (11.3) | 9 (5.3) | 6 (1.6) | <0.001 |
| Rarely | 57 (37.7) | 52 (30.4) | 86 (22.8) | |
| Sometimes | 42 (27.8) | 66 (38.6) | 185 (48.9) | |
| Always | 35 (23.2) | 44 (25.7) | 101 (26.7) | |
| Sunglasses | | | | |
| Never | 56 (37.1) | 57 (33.3) | 95 (25.1) | <0.001 |
| Rarely | 71 (47.0) | 69 (40.4) | 151 (39.9) | |
| Sometimes | 14 (9.3) | 19 (11.1) | 96 (25.4) | |
| Always | 10 (6.6) | 26 (15.2) | 36 (9.5) | |

findings. Other sun protection measures except sunscreen use were similar between dark-skinned and light-skinned children, which could indicate that parents may not be aware of other sunscreen methods or their importance. Not surprisingly, we found that university graduates reported more regular use of sunscreens.

Our study limitations were the high educational level of the parents, representative for a narrow geographic distribution. The questionnaire was prepared for this study and has not been assessed for validity or reliability.

## Conclusion

Our study results showed that parents' personal sun protection behaviors were correlated with their sun protection practices to their children. Furthermore, it indicated that even they had sun protection knowledge, parents showed suboptimal sun protection practices. Sun protection behaviors instituted from birth may reduce the risk of future skin cancers and also have an impact as behavioral guidance in the adoption of protective practices against the sun in children.

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### Conflicts of interest

There are no conflicts of interest.

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Original Article

# The Effect of Smoking on Oral Labial Mucosa: A Controlled Dermoscopic Study

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## Abstract

**Background/Aim:** Although the effects of smoking on large blood vessels are known, research on the effects of smoking on microcirculation continues. In this study, we investigated whether the dermoscopic features of the labial mucosa of smokers differed from the healthy control group. **Materials and Methods:** In this study, 164 patients (82 smokers and 82 nonsmokers) aged between 20 and 75 years who were admitted to the dermatology department were included. Dermoscopically obtained data were analyzed. **Results:** Hemorrhagic dot (48.8% vs. 26.8%, *P*: 0.004), matchstick hairpin vessels (37.8% vs. 15.9%, *P*: 0.002), microaneursym (35.4% vs. 18.3%, *P*: 0.014), targetoid brown round areas (37.8% vs. 19.5%, *P*: 0.010), white dot (22% vs. 9.8%, *P*: 0.033), and hyperkeratosis (37.8% vs. 18.3%, *P*: 0.005) were found to be significant in terms of dermoscopic features. **Conclusion:** In this study, we think that structures such as hemorrhagic dot, matchstick hairpin vessels, microaneursym, which are found to be high in smokers, may be caused by microcirculation disorders.

**Keywords:** Dermoscopy, labial mucosa, smoking

## Introduction

Smoking is an important modifiable risk factor for cardiovascular disease, and its effects on large-vessel atherosclerosis and thrombosis are well known.[1] Due to the difficulties in imaging the microcirculation, the effect of smoking on the microvascular structure is less pronounced.[2] At present, efforts are being made to clarify the effects of tobacco smoke on microcirculation. The presence of endothelial dysfunction is considered to be an early marker of vascular injury that is prone to the development of atherosclerotic lesions.[3] However, smoking also releases free radicals and pro-oxidant factors that may result in inflammation and oxidative damage to the vascular endothelium and impair coronary circulation functions.[4]

The information about the vascular structures of the oral mucosa has been presented by studies on capillaroscopy. Labial mucosal visibility is probably the best in the oral region.[5] The chronic smoking habit creates significant morphological changes in the microcirculation of the human labial mucosa and these changes can be easily recorded by videocapillaroscopy.[6] Capillaroscopic examination revealed that the diameter of the capillary loops in the labial mucosa decreased and their number increased and the presence of more pronounced tortuous capillary loops.[6] However, there are no dermoscopic studies showing the effect of smoking, the changes on vascular and nonvascular structures in the labial mucosa. In this study, the dermoscopic examination of the oral labial mucosa of smokers and nonsmokers was performed comparatively.

## Materials and Methods

The study included 82 smokers (at least 2 years) and 82 nonsmokers, who presented to the dermatology department and aged 20–75 years. Patients with diseases that could affect microcirculation such as diabetes, hypertension,

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hyperlipidemia, and heart disease and patients receiving medical treatment were not included in the study.

This study includes three stages including dermatological and dermoscopic examination of the lesions, macroscopic and dermoscopic (Dermatoscope Delta 20; Heine, Herrsching, Germany; Handyscope Fotofinder Systems) photographing, and evaluation of the findings. Macroscopic (at least 2) and dermoscopic (at least 15) pictures of all lesions in the study were taken and the data were recorded. Vascular structures and nonvascular structures were defined as dermoscopically. The pressure on the lesion was relieved to prevent collapse of the vascular structures.

All patient data were uploaded to SPSS 21.0 statistic application software (SPSS Inc., Chicago, IL, USA). The data were analyzed with the Student's *t*-test for independent samples with regard to parametric data and with the Mann–Whitney U-test with regard to nonparametric data. $P < 0.05$ was considered statistically significant.

## Results

The study included 82 smokers (64 men and 18 women; mean ± standard deviation [SD] age 38.15 ± 13.54; patients range 20–73) and 82 nonsmokers (64 men and 18 women; mean ± SD age 36.62 ± 16.99; patients range 20–75). There was no significant difference between the groups in terms of age ($P > 0.05$).

Hemorrhagic dot (48.8% vs. 26.8%, *P*: 0.004), matchstick hairpin vessels (37.8% vs. 15.9%, *P*: 0.002), microaneursym (35.4% vs. 18.3%, *P*: 0.014), targetoid brown round areas (37.8% vs. 19.5%, *P*: 0.010), white dot (22% vs. 9.8%, *P*: 0.033), and hyperkeratosis (37.8% vs. 18.3%, *P*: 0.005) were found to be significant in terms of dermoscopic features.

There was no significant difference between the two groups in terms of deep vascular network (92.7% vs. 96.3%, *P*: 0.304), superficial vascular network (90.2% vs. 96.3%, *P*: 0.191), mixed retinal arrangement (82.9% vs. 74.4%, *P*: 0.182), grouped hairpin vessels (70.7% vs. 62.2%, *P*: 0.247), dot vessels (54.9% vs. 47.6%, *P*: 0.349), chain hairpin vessels (24.4% vs. 17.1%, *P*: 0.248), clear reticular arrangement (17.1% vs. 25.6%, *P*: 0.086), glomerular vessels (2.4% vs. 6.1%, *P*: 0.246), yellow background areas (95.1% vs. 91.5%, *P*: 0.349), yellowish-white streaks (30.5% vs. 26.8%, *P*: 604), purple areas (20.7% vs. 25.6%, *P*: 0.459), microulceration (9.8% vs. 4.9%, *P*: 0.230), and honeycomb appearance (8.5% vs. 3.7%, *P*: 0.192) (smokers and nonsmokers, respectively) [Figures 1-4]. All dermoscopic structures are shown in Table 1.

## Discussion

The properties of the capillary structures in the oral mucosa are probably a mirror of what happens in every organ of the human body.[5] In the studies of microcirculation on retinal vessels, narrow retinal arteriole caliber has been associated with hypertension and may even precede clinical hypertension.[7,8] In contrast, larger retinal venular diameter

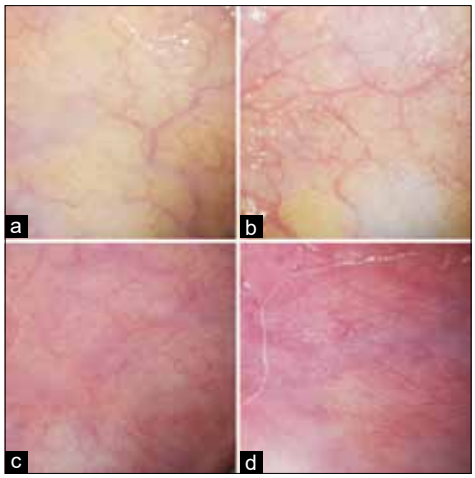


**Figure 1:** Clear reticular arrangement (a and b) and mixed reticular arrangement (c and d)

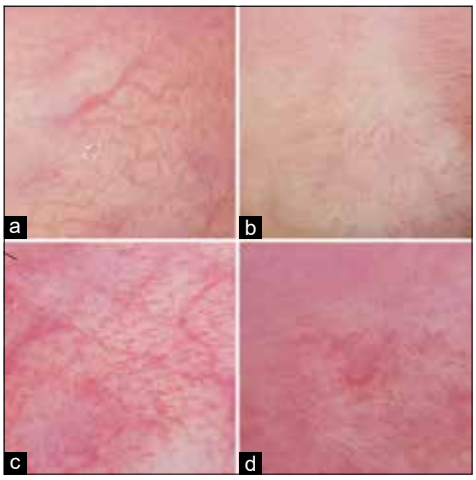


**Figure 2:** Chain-shaped hairpin vessels (a), grouped hairpin vessels (b), matchstick hairpin vessels (c and d)

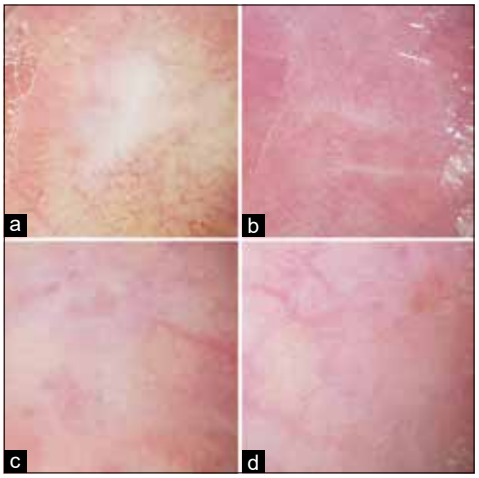


**Figure 3:** Yellowish-white streaks ([a] starburst-shaped, [b] linear), targetoid brown round areas ([c] in the upper left corner), microulceration ([d] in the upper right corner)

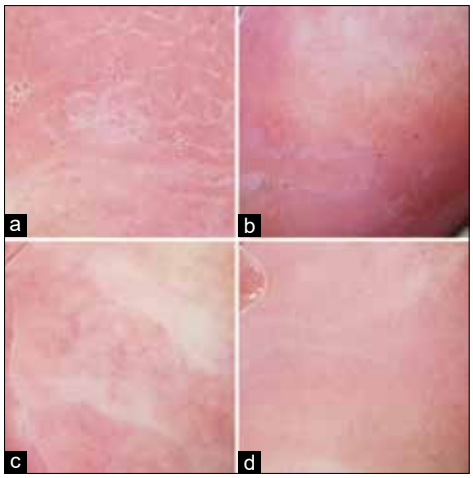


**Figure 4:** Honeycomb appearance (a), hyperkeratosis (a-d), white dot (a and d), grouped hairpin vessels (b and d), chain hairpin vessels, (a), hemorrhagic dot (b)

is associated with markers of systemic inflammation and various components of the metabolic syndrome (obesity, dyslipidemia, and hyperglycemia)[9-11] and can also predict stroke and cardiovascular events.[12-14] Smoking has both acute and chronic effects on microcirculation.[6,15,16] It has been observed that smoking has negative effects on skeletal muscle, retinal, and coronary microcirculation.[15-17] In the study evaluating the effects of smoking on the microcirculation of the oral labial mucosa by video capillaroscopy, smokers had lower diameter capillary loops, more visible capillary loops, lower background optical permeability, and more pronounced tortuous capillary loops.[6] In our dermoscopic study, hemorrhagic dot, matchstick hairpin vessels, and microaneursym were found to be significantly higher in smokers. Matchstick hairpin vessels have been defined as the condition where the loop portion of the hairpin vessels was more swollen, darker, and more pronounced than the branches.[18] With this change, we think that hemorrhagic dot and microaneursym may be caused by tortuous changes detected in capillaroscopic studies.

Other vascular structures such as deep vascular network, superficial vascular network, mixed reticular arrangement, clear reticular arrangement, chain hairpin vessels, grouped hairpin vessels, dot vessels, and glomerular vessels were not significantly different.

Information on the dermoscopy of the labial mucosa is limited, and in the literature, dermoscopic examination has been performed in several dermatological diseases of the labial mucosa.[19-21] According to our previous dermoscopic experience of labial mucosa, we observed that hairpin vessels occur both in the normal labial mucosa and in the vicinity of any lesion localized to this region. In our study on oral mucocele dermoscopy, we detected hairpin vessels in 57.1% of the lesions.[21] However, these vessels were rather large, prominent, and focusable than the chain and grouped hairpin vessels in the lesion-free labial mucosa.[21]

**Table 1: Dermoscopic features of smoker and nonsmoker group**

| Dermoscopic structures | Smoker group, *n* (%) | Nonsmoker group, *n* (%) | *P* |
|---|---|---|---|
| Deep vascular network | 76 (92.7) | 79 (96.3) | 0.304 |
| Superficial vascular network | 74 (90.2) | 79 (96.3) | 0.119 |
| Mixed reticular arrangement | 68 (82.9) | 61 (74.4) | 0.182 |
| Clear reticular arrangement | 13 (15.9) | 22 (26.8) | 0.086 |
| Grouped hairpin vessels | 58 (70.7) | 51 (62.2) | 0.247 |
| Dot vessels | 45 (54.9) | 39 (47.6) | 0.349 |
| Chain hairpin vessels | 20 (24.4) | 14 (17.1) | 0.248 |
| Microaneursym | 29 (35.4) | 15 (18.3) | 0.014 |
| Matchstick hairpin vessels | 31 (37.8) | 13 (15.9) | 0.002 |
| Glomerular vessels | 2 (2.4) | 5 (6.1) | 0.246 |
| Yellow background areas | 78 (95.1) | 75 (91.5) | 0.349 |
| Purple areas | 17 (20.7) | 21 (25.6) | 0.459 |
| Hemorrhagic dot | 40 (48.8) | 22 (26.8) | 0.004 |
| Targetoid brown round areas | 31 (37.8) | 16 (19.5) | 0.010 |
| Yellowish-white streaks | 25 (30.5) | 22 (26.8) | 0.604 |
| Hyperkeratosis | 31 (37.8) | 15 (18.3) | 0.005 |
| White dot | 18 (22) | 8 (9.8) | 0.033 |
| Honeycomb appearance | 7 (8.5) | 3 (3.7) | 0.192 |
| Microulceration | 8 (9.8) | 4 (4.9) | 0.230 |

In this study, targetoid brown round areas were significantly higher in smokers (37.8% vs. 19.5%, *P*: 0.010) than nonsmokers. While the center of these dermoscopic structures was brown, there was a white ring surrounding it. We think that these structures are improving microulceration.[18] However, there was no significant difference between the two groups in terms of newly developed microulcerations. We think that the white dots and honeycomb appearance found in our study are different variants of hyperkeratosis. However, it was significant that hyperkeratosis and white dots were higher among smokers. Hyperkeratotic structures were sometimes linear.

There was no significant difference between the groups in terms of yellowish white streaks (30.5% vs. 26.8%, *P*: 604). We conclude that these structures are cicatricial structures secondary to trauma. These structures, which are generally linear, can be multiple and rarely in starburst pattern.

## Conclusion

In this study, the effect of smoking on vascular and nonvascular structures such as microcirculation of labial mucosa was evaluated dermoscopically. In this study, we think that structures such as hemorrhagic dot, matchstick hairpin vessels, and microaneursym, which are significantly higher in smokers, may be caused by microcirculation disorders. In addition, we believe that the possibility of smoking to make similar changes in other tissue and organ microcirculation should be considered in patients with these structures.

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## Conflicts of interest

There are no conflicts of interest.

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Original Article

# Tattoos: Why Do We Get? What Is Our Attitude?

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## Abstract

**Background:** The inclination to get tattoos has been increasing in our country. While its history depends on the ancient past, feelings and thoughts of tattooed people about tattoos, and their awareness on complications and removal methods has not been investigated completely. Aims: Our aim is to learn the approach of individuals on tattoos and getting tattoos. **Settings and Design:** We have planned a cross-sectional survey study for tattooed and non-tattooed people. **Materials and Methods:** Twenty four multiple-choice and one open ended question were prepared for people with tattoos, and seven questions were prepared for people who don't have tattoos. Four questions were common in both groups. **Statistical Analysis Used:** For statistical analyses, SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) was used. Statistical significance of the difference between common questions was determined with chi-square test, and the effect of different groups on answering the question was analyzed with Cramér's V test. p values below 0.05 were recognized as statistically significant. **Results:** About half of people with tattoos had their first tattoo when they were between ages 18-29, and 38.2% had a single tattoo. 16.7% of individuals got their first tattoo below age 18. Women often preferred their wrists and ankles for tattoos, while men preferred arms, neck, legs and trunk. While women preferred to get a tattoo about a loved one, men rather got tattoos to look cool. 37.7% of people who don't have tattoos said they did not get one since they might regret it later, 25.4% stated they did not get one since it did not comply with the rules of their religion. 20.2% did not like seeing tattoos in others. **Conclusion:** The rate of getting tattoos in minors is higher in our country compared to other countries. The majority of people who want their tattoos to be removed got tattooed when they were minors. There is a higher rate of men than women who want to get their tattoos removed. 4.2% of tattooed people regret their tattoos in the process of getting them. It was observed that tattooed people were not aware of the risk of disease transmission by getting tattooed.

**Keywords:** Attitude, personality, psycho-dermatology, tattoo

## Introduction

Tattooing involves the placement of dye into the dermis with the help of a needle, and it is permanent. Getting tattoos have become increasingly popular all over the world in the last decade.[1] The same trend has been observed in our country as well.

The possession of the oldest known tattoo belongs to Ötzi, the Iceman, who lived 5300 years ago and is recognized as the oldest mummy of the world.[2] Throughout history, tattoos have been used for various purposes. Convicts were marked with tattoos in the old ages, whereas Nazis marked Jews with tattoos in concentration camps in the Second World War.[3,4] In our day, there are recommendations for people with disabilities who cannot express themselves to get tattoos for this purpose. These numeric tattoos carry the person's identity information and it is possible to reach the disabled person's family when they are lost. Tattoos are also used for permanent makeup, reconstructing the appearance of nipples after mastectomy or disguise pigment disorders like vitiligo.[5]

Although the history of tattoos goes back to ancient ages, it is still not investigated why people get tattoos, what kinds of tattoos they prefer, what do they feel during and after getting tattoos, the complications of tattoos, and their awareness on removal methods. It is also not known how nontattooed people see tattooed people, their opinions about them, the reasons underlying their choice of not getting tattoos, and

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how will they react if one of their loved ones wanted to get a tattoo. Furthermore, there is no detailed investigation on whether there are differences on people's opinion about tattoos with regard to age, gender, or educational status. We have planned a cross-sectional survey study to learn the opinions and approaches of individuals in our country on tattoos and getting tattooed.

## Methods

The approval of the Istanbul Medeniyet University Göztepe Training and Research Hospital Ethics Committee was taken for the study (2019/0065).

Survey questions about tattoos were formed by the investigators by reviewing and discussing literature about the subject. Survey form included participants' sociodemographic characteristics, why, where, when, how and in what way people get tattoos, how they feel after, reactions of their loved ones, their opinions about tattoos and their awareness on the complications of tattoos, the reason why people do not get tattoos and whether they want to get tattooed, and their perspective on tattooed people. Twenty-four multiple choice and one open-ended question were prepared for people with tattoos, and seven questions were prepared for people who do not have tattoos. Four questions were common in both groups. The common questions were the reactions of people who are dependent on them after they got their tattoo, and their reactions when they saw tattoos in public officers. Survey was answered by the participants without any time limitation, independently, and without getting any help.

For statistical analyses, SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA: IBM Corp) was used. Statistical significance of the difference between common questions was determined with the Chi-square test, and the effect of different groups on answering the question was analyzed with Cramér's V-test. Values of $P < 0.05$ were considered as statistically significant.

**Table 1: Distribution of age, gender, and education status in tattooed and nontattooed groups**

| | Tattooed individuals | Nontattooed individuals |
|---|---|---|
| Mean age | 31±12.5 | 36±12.5 |
| Minimum and maximum age | 16-88 | 16-74 |
| Gender, *n* (%) | | |
| Female | 81 (56.3) | 68 (59.6) |
| Male | 63 (43.7) | 46 (46.4) |
| Educational status, *n* (%) | | |
| Primary education graduate | 51 (35.4) | 43 (37.7) |
| Higher education graduate | 93 (64.6) | 71 (62.3) |
| Total number | 144 | 114 |

Primary education graduate represents high school and below, while higher education graduate represents college and above

## Results

The survey was applied to literate people with or without tattoos who have applied to Istanbul Medeniyet University Göztepe Training and Research Hospital Dermatological and Venereal Diseases Clinic for various reasons between March and August 2019, and accepted to participate in the study.

There was no statistically significant difference in the distribution of age, gender, and education level between tattooed and nontattooed groups [Table 1].

About 38.2% of the study participants had 1 tattoo, 29.9% had 2–3 tattoos, 23.6% had 4–9 tattoos, 4.8% had 10–19 tattoos, and 3.5% had at least 20 tattoos. The person with the highest number of tattoos had 85 tattoos in total and got his/her first tattoo at the age of 30 years. The earliest age to get the first tattoo was 11, whereas the latest age was 70 in our study. The mean age for getting the first tattoo was 27.6. 16.7% of individuals got their first tattoo below age 18. 29.2% was female while 70.8% was male among the people who got their first tattoo when they are minors ($P = 0.003$). 72.9% had a black tattoo, 16.7% had a mixed-color tattoo, and it was followed by blue, red, brown, and green, respectively.

When they first decided to get a tattoo, 45.1% faced no family intervention, families of 30.5% supported them, and families of 21.5% of individuals warned them or did not want them to get a tattoo. About 92.4% had their tattoo performed by a professional tattoo artist. 37.5% stated that they got a tattoo to remember nice memories, 31.9% stated that they wanted to carry something they liked on their body, whereas 22.2% stated that they got a tattoo because they wanted to do a different thing. Getting a tattoo of the name of someone they loved was determined to be significantly higher among women ($P = 0.028$), while getting tattoos to be cool was significantly higher among men ($P = 0.025$), and getting tattoos to remember good memories was significantly higher among higher education graduates ($P = 0.004$).

It was stated by 91% that they paid attention to hygiene rules while getting a tattoo, and 77.8% stated that they paid attention to the environmental conditions of the tattoo saloon. Only four people experienced itching and redness on the tattoo area after getting their tattoo. Three of the people who underwent magnetic resonance test had a burning feeling on the tattoo site.

The rate of people who thought they might get their tattoo removed at a later date even while getting tattooed was 38.2%. About 53.5% stated that they received positive comments from other people about their tattoo, 35.4% stated that they received both positive and negative comments. Fourteen people regretted getting a tattoo, and six regretted it in the process of getting the tattoo. About 15.3% covered or wanted to cover their tattoo with another tattoo. Those who felt regret were statistically significantly higher among men (11 people), compared to women (3 people) ($P = 0.009$). Among people who regretted their tattoos, the mean age of getting the first tattoo was 21.2% and 50% had their first tattoo before coming

of age. The mean period between getting a tattoo and wanting to get the tattoo removed was 7.4 years. 38.9% had a single tattoo and the color of tattoo was black in 77.8%. 66.7% of these people had tattoos in visible areas, 21.2% had tattoos in half-visible areas. 27.8% tried to cover their tattoo with another tattoo in the past. 55.6% of people who considered removing their tattoo had applied to a doctor, and 70% of people who applied were male, whereas 30% were female. 60% of people who have applied had tattoo removal procedure done. 32% of people with tattoos did not know how tattoos were removed. In our study, 19.4% of tattooed people, mostly males, considered having a tattoo may cause a problem in the workplace or while seeking employment in future. Moreover, 8.8% of the nontattooed group said that they did not get a tattoo since it might cause a problem while seeking employment.

When the reason of not getting a tattoo was asked to nontattooed group, 37.7% said that they did not get a tattoo since they might regret it later, 25.4% said that it did not comply with the rules of their religion, 20.2% said that they did not get one since they did not enjoy it, and 21.5% said there was no reason. When asked the possibility of getting a tattoo in future, 44.7% said no, 21.1% said yes, while 25.4% replied maybe. 20.2% of the nontattooed group said that they did not enjoy the sight of tattoos in other people. About 55.3% said that their feelings will change depending on the fact that whether or not they will like the person's tattoo.

Among the responses to the question "what would you feel if you saw a tattoo on a public officer" in the common questions, the responses "I would like that" by 47.22% and "I would trust them better if they had tattoos" by 9.03% were significantly higher in the tattooed group than the nontattooed group ($P < 0.000$; $P = 0.039$, respectively). In the nontattooed group, the responses "I would not care" by 73.68%, and "I would not like that" by 14.91% were significantly higher ($P < 0.000$; $P < 0.000$, respectively). Furthermore, the response "I would trust them better" was significantly higher in males ($P = 0.036$). When asked in what body part did they have a tattoo or would want to get a tattoo, both tattooed people and nontattooed people said they preferred/would prefer arms and wrists. However, the neck, torso, arms, legs, and hands were statistically higher in tattooed people. Meanwhile, torso, arms, legs, and neck were significantly higher in men ($P = 0.032$, $P < 0.000$, $P = 0.025$, and $P = 0.049$, respectively). Wrists and ankles were statistically significantly higher in women ($P = 0.019$, $P < 0.000$, respectively), whereas hands were statistically significantly higher in primary education graduates $P = 0.026$ [Table 2].

## Discussion

While the prevalence of tattoos varies in Europe, depending on the country, it is known to be between 15% and 25%.[6] About 21%–29% of population in the USA has at least one tattoo, and about 15%–20% has at least two tattoos and higher. It was determined that 31% of women and 27% of men had tattoos.[1] The prevalence of tattoos in our country is not known.

In this study, 16.7% of individuals got their first tattoo below the age of 18 years. This rate was higher compared to other countries. The rate of people who got their first tattoo below the age of 18 years was 4.6% in the USA, 11.3% in Europe, and 8% in Canada.[7-9]

**Table 2: The differences between the tattooed and nontattooed individuals; the attitude for a loved one getting tattoo and the favorite part of the body for getting tattoos**

| | Number of people, *n* (%) | | *P* |
|---|---|---|---|
| | Tattooed individuals | Nontattooed individuals | |
| What would your reaction be if one of your loved ones got a tattoo? | | | |
| It's their decision and none of my business | 78 (54.17) | 40 (35.09) | 0.003 |
| I would prevent them if they are minor | 45 (31.25) | 37 (32.46) | 0.893 |
| I would warn them | 10 (6.94) | 40 (35.09) | <0.000 |
| I would forbid it | 1 (0.69) | 10 (8.77) | 0.003 |
| I would encourage them | 22 (15.28) | 3 (2.63) | 0.001 |
| I would warn them, if they still want it I would support it | 12 (10.53) | 7 (4.86) | 0.096 |
| What kind of a tattoo did/would you get? | | | |
| About a loved one | 50 (34.72) | 38 (33.33) | 0.895 |
| A tattoo of an animal I love | 33 (22.92) | 7 (6.14) | <0.000 |
| A beautiful word or text | 30 (20.83) | 19 (16.67) | 0.428 |
| A tattoo that would describe me | 53 (36.81) | 34 (29.82) | 0.289 |
| About my profession | 13 (9.03) | 11 (9.65) | 1 |
| Meaningful text | 54 (37.5) | 42 (36.84) | 1 |
| Pastoral drawing | 21 (14.58) | 14 (12.28) | 0.715 |
| The team I support | 9 (6.25) | 9 (7.89) | 0.630 |

Among responses to questioning their reaction if a loved one got a tattoo, the option "I would prevent them if they are minor" was significantly higher in higher education graduates compared to primary education graduates $P$=0.008. There was no significant difference in other options. Among responses to "What kind of a tattoo did/would you get," tattoo of a beautiful word and a tattoo about their profession or their team were significantly higher in men ($P$=0.024, $P$=0.004, $P$=0.002, respectively), while getting a pastoral tattoo was significantly higher in women ($P$=0.016)

We have determined that the mean age to get a tattoo was 27.6. This was nearly similar to other studies. Mean age was found to be 30 in a study performed on 3411 tattooed people.[10] It was determined that 73% of those had 1–3 tattoos on average, whereas 63% got a single color, generally black, tattoo (59%). It was found in our study that single-color, particularly black tattoos were preferred, but the number of tattoos was lower.

It was seen that 54% of women mostly got a tattoo on their torso, while 48% of men mostly got their tattoo on their arms in a study.[10] While men preferred similar areas, women in our country were different in selecting tattoos on visible areas such as the wrists and ankles.

There is a wide variety of reasons for getting tattoos. While there may be religious or traditional reasons, it may be due to social status or fashion, or an indicator of power.[11] In this study, individuals generally got tattoos to remember nice memories, carry something they liked on their body, and for wanting to be different.

A lower rate of tattooed individuals (9.7%) in our study regretted their tattoos compared to other studies, while 4.2% stated that they regretted it even while getting it done. The rate of regret was higher in men. 11.4%–14% of tattooed people regretted getting a tattoo in previous studies.[12,13] Tattooed individuals have stated that they had difficulty in getting a job due to visible tattoos in a study.[14] In our results, the rate of individuals who faced or thought they would face difficulties in finding a job was also quite high.

It was reported in recent years that a higher rate of women applied for tattoo removal in particular.[15] In this study, 12.5% of tattooed people considered tattoo removal and a higher rate of men (78.5% of those who regret their tattoos) regretted getting tattoos. 58% of participants stated that they removed their tattoos only for the fact that they wanted them removed, 57% stated that they were embarrassed, 38% said that their perception of their body changed, 38% said that they were considering a new career, 37% said that they had difficulty in selecting clothes, and 32% said that they received a negative opinion from another person.[15] These last two reasons were striking particularly in women.[15] Differently, men regretted getting tattoos at a higher rate in our study. The majority of these people had tattoos on visible areas and they had shorter time before applying to a doctor for tattoo removal, compared to other studies.

Nontattooed individuals in our study stated that their feelings against tattooed individuals would depend on the fact that whether or not they liked the tattoo. About 50% of nontattooed individuals stated that they found tattooed individuals more rebellious, 45% less attractive, 27% less healthy and 25% said that they found tattooed individuals less spiritual.[16] The view on nontattooed individuals was negative, particularly for women with tattoos in visible areas, and they were viewed as less attractive. Indeed, with the increasing trend, it may be argued that young people's view on tattooed individuals will be more neutral; however, new studies performed with young people show their view on tattooed individuals are still negative. The interesting difference here is that while young people thought that tattooed women were stronger and freer, this view did not apply to tattooed men.[17]

## Conclusion

Our study has shown that the rate of getting tattoos in minors was higher in our country compared to other countries, and the majority of people who want their tattoos removed got their tattoo at this age interval. For this reason, parents in our country should be warned about the fact that individuals below the age of 18 need their parents' permission to get tattoos. Differently from other countries, women rather had their tattoos on visible areas. While women preferred a tattoo about a loved one, men rather got tattoos to look cool. Nevertheless, regretting their tattoo and applying to a doctor for tattoo removal were more common in men. Therefore, it is necessary to raise awareness about tattoos and possible health problems they might induce. There is a need for further studies with a higher number of individuals and centers in order to attract attention to these problems in our country.

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### Conflicts of interest

There are no conflicts of interest.

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Case Report

# Chronic Tophaceous Gout Manifesting with Bilateral Diffuse Pedal Swelling: Cytology Revisited with an Update in Its List of Differentials

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## Abstract

Gout, a disorder of purine metabolism, presents with acute or chronic arthritis and deposition of urate crystals in connective tissue and kidneys. Rarely, patients progress into chronic tophaceous gout (CTG). We emphasize on a 74-year-old male patient, who developed multiple gouty tophi over both his hands. In addition, both his feet were diffusely swollen. On detection of characteristic urate crystals from both his hands and feet lesions, the diagnosis of CTG was confirmed.

**Keywords:** Chronic tophaceous gout, cytology, diffuse pedal swelling, urate crystals

## Introduction

The diagnosis of chronic tophaceous gout (CTG) is favored from its initial clinical presentation and subsequent biochemical profile of the patient. In general, the patients are hyperuricemic. The tophi are girdled around the joints only. Rheumatoid nodules, tendinous xanthomas, synovial cysts, sarcoidosis, granuloma annulare, and multicentric reticulohistiocytosis are its closest possible differentials. Furthermore, the likely coexistence of other multifocal cutaneous cysts or tumors within the milieu needs to be excluded. However, the cytological demonstration of urate crystals from gouty tophi forthwith establishes its definite diagnosis.[1]

## Case Report

A 74-year-old male presented with a history of recurrent asymmetric arthralgia involving both his hands and feet for the past 8 years. Later on, he gradually developed multiple painful subcutaneous nodules over both his hands, along with aching diffuse swelling of both feet over the past 1 year. His feet appeared edematous at both its plantar and dorsal aspects. On palpation, these were noncompressible hard as seen with nonpitting edema. All the small joints there exhibited negligible range of mobility. A deeply burrowing ulcer was noticed across the inner border of the left foot. Proximal parts of all limbs above the wrist or ankle joints maintained its normal morphology [Figure 1]. Fine needle aspiration cytology (FNAC) was performed from his hand nodules and the most eminent areas on the feet. Exfoliative samples were obtained from the ulcer. Under microscope, all the smears appeared indifferent. It featured shaggy tangles of brown-colored, long and slender, needle-like crystals, i.e., morphologically reminiscent of classic urate crystals from the gout. Brisk lymphohistiocytic inflammatory infiltrate and foreign body reaction was present [Figure 2]. His serum biochemical investigations revealed hyperuricemia at 12.2 mg/dl (normal: 4–7 mg/dl). The patient was then instituted upon hypouricemic therapy alongside other supportive management.

## Discussion

Diffuse pedal swelling is commonly observed in congestive cardiac failure, renal failure, erysipelas, cellulitis, deep

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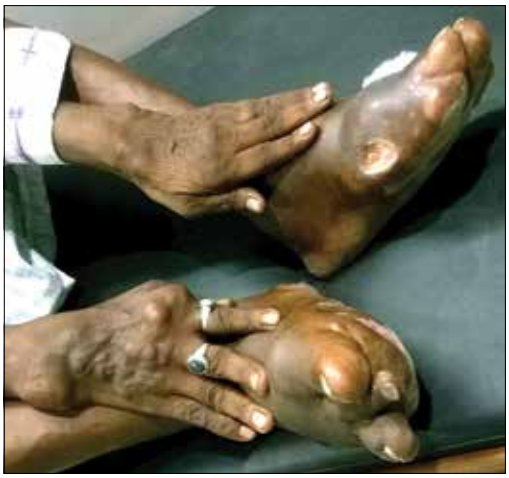

**Figure 1:** Clinically, multiple nodules over the dorsum of the right hand and a few around the left wrist joint. Bilateral diffuse pedal swelling at both plantar and dorsal aspects, with an ulcer on the left foot

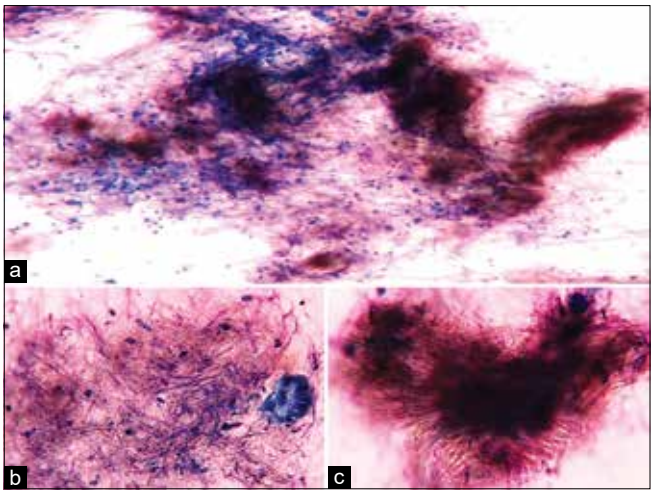


**Figure 2:** Cytologically, clumps of amorphous brown-colored crystals intermingled with lymphohistiocytic cells ([a] Pap, ×100) and foreign body giant cells ([b] Pap, ×400); on magnification, the crystals appear needle-shaped slender with pointed both ends ([c] Pap, ×400)

vein thrombosis (DVT), and lymphedema from filariasis or any other cause. Bilateralism is usually observed with cardiac or renal ailments, but the edema in association is pitting by nature. Localized tenderness along with fever and cutaneous rash/blisters are features of cellulitis and erysipelas. DVT-related pain or swelling tends to extend far more proximally than described in the present case. Filariasis precipitates into nonpitting limb edema, but symmetrical involvement is unlikely.[2,3] However, generalized diffuse enlargement of both feet caused by precipitation of urate crystals is also unusual. No such description of CTG could be traced from the already published literatures even after careful scrutiny. In the present case, the pedal lesions were readily approached by cytological techniques, and the pathology came out as same as the hand nodules. Thereby, the diagnosis of CTG was established with an ease.

Like in the discussed report, an unorthodox presentation of CTG requires demonstration of urate crystals for confirmatory diagnosis, which can be performed through synovial biopsy, joint fluid analysis, or biopsy from the tophi. The signature monosodium urate crystals are best visualized under polarized microscopy and smear preparations, as on routine processing for histology, these crystals often disintegrate. Cytological detection of the crystals from the tophi is also a useful alternative.[4] In the discussed patient, all his pathological lesions were sampled very well with FNAC and scrape cytology. He was detected hyperuricemic as well. From such an overall presentation, CTG was the diagnosis of choice. The present case reconciles about an uncommon pedal manifestation in CTG and therefore an updated consideration to its related differential diagnoses.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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Case Report

# A Psoralen and Ultraviolet A-Aggravated Dermatosis: Grover's Disease

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## Abstract

Grover's disease (GD) is an acquired dermatosis called transient acantholytic dermatosis. The exact cause is unknown, but the factors blamed for the etiology include ultraviolet (UV), sweating, temperature rise, radiation, medications, and malignancies. Topical corticosteroids, topical retinoids, and topical calcipotriol are usually sufficient for treatment, and systemic retinoids, systemic steroids, phototherapy, and methotrexate are rarely used. The current report describes the case of GD in a female patient, which was aggravated by the psoralen and UVA phototherapy.

**Keywords:** Grover's disease, phototherapy, treatment

## Introduction

Grover's disease (GD) is a pruritic, papular, or papulovesicular dermatosis which is histopathologically characterized by acantholysis and dyskeratosis. It often shows spontaneous regression within weeks or months, although it may sometimes have a course with relapses and remissions.[1] The etiology and pathogenesis of this condition are still unclear; however, the disease has been associated with triggering factors, including high body temperature, sweating, acute ultraviolet (UV) exposure, drug use, and internal malignancies.[1,2] Topical treatment involves corticosteroids, calcipotriol and retinoids, and systemic treatment involves the use of vitamin A, synthetic retinoids, corticosteroids, methotrexate, and photo (chemo) therapy.[1] GD is one of the skin conditions, which is sometimes aggravated by the UV light exposure.[3]

## Case Report

A 76-year-old female patient presented at our clinic with itchy lesions located under both breasts and in the lumbar region. These lesions were present for 2 years with exacerbation occurring in the summer season. The dermatological examination revealed erythematous, red-brown, papulovesicular lesions under both breasts and in the lumbar region [Figure 1a and b]. The patient's systemic examination and laboratory tests were unremarkable. Histopathological evaluation of the biopsy specimen taken from the lesion revealed hyperkeratosis, acanthosis, spongiosis, suprabasal acantholysis, superficial dermal edema, perivascular neutrophilic, and eosinophilic inflammatory cell infiltrate [Figure 2]. The direct immunofluorescence examination did not reveal any particular findings. With the existing findings, the patient was diagnosed with GD. Topical clobetasol propionate 0.05% and topical calcipotriol cream were initiated. In the 3rd month of this treatment, no remission was detected and topical pimecrolimus 1% was initiated, but she could not use this therapy because of irritation. We started oral methylprednisolone 0.5 mg/kg/day but no remission was detected after 2 months of therapy. Thereafter, oral acitretin 0.5 mg/kg/day therapy was initiated. However, no remission was detected with oral acitretin therapy after 3 months. Thereafter, psoralen and UVA (PUVA) phototherapy three times weekly was initiated. Oral 8-methoxalene was given 0.5 mg/kg, 2 h before PUVA treatment. The initial

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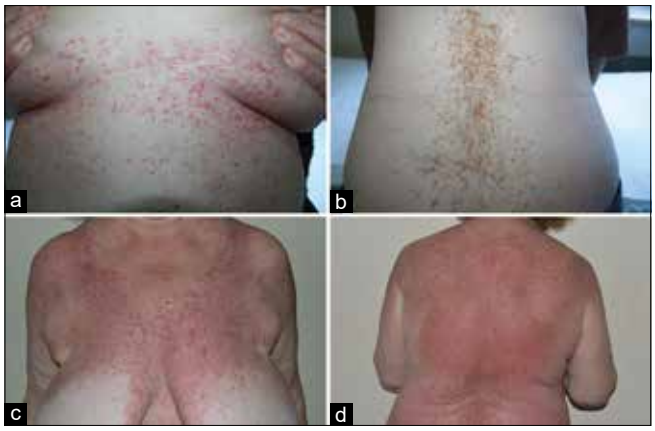


**Figure 1:** Erythematous, red-brown papulovesicular lesions under both breasts (a) and lumbar region (b). Generalized erythema and had aggravation of lesions on the chest (c) and back (d)

doses were applied 0.5 joule/cm$^2$. The patient developed generalized erythema and had aggravation of lesions after five sessions of PUVA phototherapy; therefore, the treatment was discontinued [Figure 1c and d].

## Discussion

GD is often a benign, self-limiting disease; however, it may sometimes occur as a resistant and difficult to control dermatosis.[4] The etiology of the disease is unknown, although several factors have been proposed to be associated with the disease, including the UV exposure, exposure to extreme temperature, and sweating.[5] The distribution of the skin lesions and seasonal variations highlight the importance of the UV exposure, although rare occurrence of this condition suggests that other structural and environmental factors may play a role in the disease pathogenesis.[1] Malignancies are one of the major causes of the etiology in patients with atypical and severe disease course; it has been suggested that the underlying malignancy contributes to the development of the disease by modifying the immune responses.[5] The development of GD following transplantation, chemotherapy, and radiotherapy and atypical and severe disease course may support this hypothesis.[5] In addition, Paslin reported a case of GD triggered by varenicline which acts as a nicotine antagonist.[6] The lesions in the present case occurred in the summer months; however, further investigations did not show any malignancy or immunosuppression, and there was no history of drug use which might induce the disease.

In clinical practice, GD is characterized by papulovascular lesions with recurrent erythema which rapidly turn into crusted and keratotic erosions. Itching is one of the main symptoms of the disease which leads to severe distress.[4] In addition, several conditions presenting with generalized papular lesions may mimic GD. The disease has four histopathological patterns, including Darier disease-like, Hailey-Hailey disease-like, pemphigus vulgaris-like, and spongiotic type. The most commonly reported subtypes are Darier disease-like and pemphigus vulgaris-like.[1]

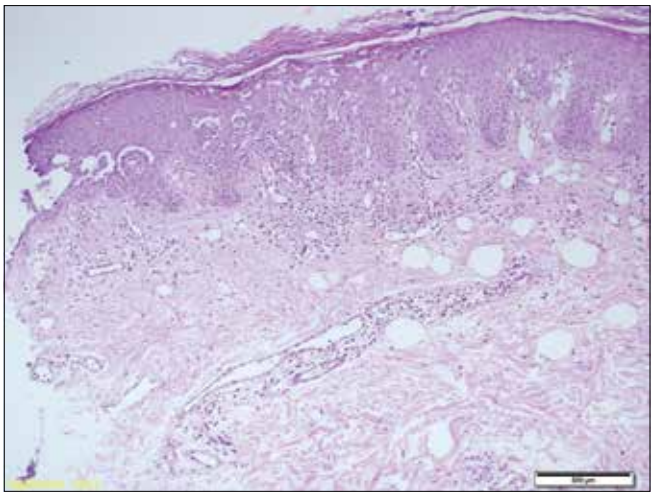

**Figure 2:** Hyperkeratosis, acanthosis, spongiosis, suprabasal acantholysis, superficial dermal edema, perivascular neutrophilic, and eosinophilic inflammatory cell infiltrate (H and E, ×40)

For the treatment of GD, UV phototherapy is a cost-effective modality which is successfully used in the treatment of many conditions in the practice of dermatology.[7] The UV exposure is among the prominent triggering factors in etiopathogenesis of GD; however, the reports interestingly suggest that phototherapy can be also effective in the treatment of GD. The exact mechanism of action of phototherapy in GD is unknown.[1] The reports have suggested that bathing and oral PUVA, particularly, can be effective in refractory cases.[8,9] Furthermore, moderate-dose UVA-1 therapy has been demonstrated to be successful in cases in whom PUVA is unable to be administered.[10] Liu and Letada[4] reported a dramatic improvement in disease symptoms in a resistant case of GD using red light 5-aminolevulinic acid-photodynamic therapy. In the present case, the lesions spread to the whole trunk following five sessions of PUVA phototherapy, and therefore, therapy was discontinued.

In conclusion, GD is a dermatosis triggered by UV exposure; phototherapy is included in the treatment options. However, aggravation was observed soon after the treatment in the present case. Therefore, while treating GD with PUVA phototherapy, we suggest that clinicians should be aware of the possibility of aggravating lesions.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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