Original Article

# Role of Fatty Acids Intake in Generalized Vitiligo

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## Abstract

**Background:** Previous studies indicated the effect of fat on autoimmune diseases. The present study was aimed to investigate the association between fat intake and vitiligo. **Methods:** This case–control study was conducted in the Skin and Leishmania Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. Intakes of fatty acids were examined for their relation to risk of vitiligo among 100 cases and 110 controls. We included patients who suffered from generalized or localized vitiligo for <5 years that was approved by a dermatologist via the Vitiligo European Task Force criteria and the vitiligo area scoring index. Fat intake was assessed through individual interviews by a standardized food frequency questionnaire. **Results:** Vitiligo group consumed more saturated fatty acid (SFA) and less eicosapentaenoic acid and docosahexaenoic acid than control group, while other fatty acids were not significantly different among two groups ($P > 0.05$). Crude analysis showed that total fat (odds ratio [OR] = 3.33, 95% confidence interval [CI]: 1.46–7.58) and SFA (OR = 2.22, 95% CI: 1.04–4.90) intakes were associated with an increased risk of vitiligo (for highest quartile vs. lowest quartile). Results demonstrated a decrease in the risk of vitiligo for those within the highest quartile of monounsaturated fatty acids intake (OR = 0.41, 95% CI: 0.18–0.92). However, this relationship disappeared after adjustment for confounders as energy, age, sex, and body mass index, except for total fat (OR = 2.84, 95% CI: 1.63–5.44). Crude and adjusted analyses for polyunsaturated fatty acids and cholesterol intake were not statistically significant. **Conclusions:** Total-fat content of the diet had more impressive role than the specific subclasses of fats on the incidence risk of vitiligo. High-fat diet escalated the vitiligo risk. Regarding the role of fats on skin autoimmune diseases especially vitiligo, future studies are crucial.

**Keywords:** *Autoimmune diseases, fatty acids, vitiligo*

## Introduction

Vitiligo is one of the skin diseases that cause white spots due to loss of skin pigment cells, which is considered as an autoimmune disease.[1] Melanocytes, mucous membrane, and retina are damaged and lead to white spots in different areas of the skin.[2] The face, lips, hands, arms, feet, and the genitals are commonly affected skin area. Moreover, the color of the hairs in affected areas is usually white.[3] The prevalence of vitiligo is various between 0.38% and 2.9% in worldwide that affect all races and two genders. Other autoimmune disorders enhance the prevalence of this disease.[2,4,5] The exact etiopathogenic mechanism of vitiligo is not understood.[6] Loss of melanocytes may be associated with autoimmune cytotoxic T-cells, oxidant-antioxidant imbalance, genetic factors, neural mechanisms, or multifactorial mechanisms.[7-10] Cellular autoimmunity plays a major role in vitiligo pathogenesis.[11,12]

Functions of immune system may be influenced by the nutritional status; lipids as crucial components in diets have important effect on the modulation of the immune system. It has been demonstrated in the numerous experimental studies.[13] Therefore, a strong relationship between dietary fat and modulation of immune response could be established. Several studies revealed the importance of fatty acids in the diet and their application on the reduction of typical symptomatologies in autoimmune diseases.[14,15] Dietary fat has different effects on immune system based on the type of fat. N-3 fatty acids that commonly exist in fish oil have shown a significant reduction of inflammation in patients suffering from rheumatoid arthritis, psoriasis, systemic lupus erythematosus, multiple sclerosis (MS), etc.[16-19]

Other findings have indicated that different fats such as olive oil, oleic acid, eicosa



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pentaenoic (EPA), or docosahexaenoic (DHA) acids modulated the function of immune system.[20-23] However, according to some findings, polyunsaturated fatty acids (PUFAs) had more immunosuppressive effect than saturated fatty acids (SFA). Others showed that dietary PUFAs may interfere in the reduction of lymphocyte proliferation, cytokine synthesis, natural killer cell (NK) activity, antibody production, membrane surface molecules synthesis, etc.[24-28]

Findings about the association between dietary fat and autoimmune disease are controversial. Studies on dietary intake and vitiligo are less and investigation in this regard is necessary. The aim of the present study was investigation the association between fat intake and vitiligo.

## Methods

### Participants

A total of 147 vitiligo patients referred to Skin and Leishmania Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. In this case–control study, we recruited 100 vitiligo patients and 110 healthy subjects among eligible volunteers. We included individuals who those suffered from generalized or localized vitiligo for <5 years after their condition was approved by a center dermatologist. Other inclusion criteria were no positive family history of vitiligo, no use of systemic or topical treatment, anti-inflammatory or immunosuppressive drugs, corticosteroids, augmenter or depressor of lipid profile for at least 1 month before the study, no concomitant dermatological or systemic diseases, lack of underlying illnesses which demand special diet such as diabetes, hypertension, or renal disease, lack of heavy exercises, special diet, smoking, pregnancy, or lactation. The exclusion criteria were pregnancy or lactation during the study, diagnosis of disease such as bacterial or viral infections, or acute illnesses and start drug therapy during the study, mental disability to fill out the questionnaire, and lack of interest to continue cooperation.

### General characteristic survey

General characteristics including sex, age, smoking, medical history (medication use and history of diseases such as diabetes, cancer, and cardiovascular disease), physical activity, anthropometric data (weight, height, and body mass index [BMI]), presence of food limitation, and list of restricted foods were obtained by questionnaire.

The list of restricted foods in the present study included eggs, milk and dairy products (milk, cheese, plain yogurt), grains (wheat), fish (white flesh fish, red flesh fish), meats (beef, chicken), oily or spicy foods (soda, food additives, tinned foods or drinks, sour or pickled food items, tamarind,), citrus fruits and juices, grapes, pears, tomatoes, cherries, mangoes, chocolate and cocoa products, coffee, and others which could possibly aggravate vitiligo patches of depigmentation areas. Furthermore, the list of drugs was as follows: steroids, Ultraviolet B Light (either broadband or narrowband), psoralen and ultraviolet A light, tacrolimus (immunosuppressive), pimecrolimus (immunomodulator), skin camouflage solutions, depigmenting drugs such as (monobenzone, mequinol, or hydroquinone). All participants signed the consent form consciously; furthermore, patients were allowed to withdraw the study at any time that they were not willing to continue working with the team.

### Vitiligo severity indices and treatment evaluation criteria

Over the past decade, two methods of evaluation, while differ in their approach and outcomes, have been recognized as validated standards for the comparative evaluation of vitiligo and vitiligo treatments under clinical conditions: (1) the vitiligo area scoring index and (2) the Vitiligo European Task Force (VETF) system. Similarly, in both assessments, the body is separated into five different sites, specifically the head/neck, trunk, arms, legs, and hands/feet. In the present study, the center dermatologist used VETF as diagnostic method. The VETF evaluation system seeks to add more specific parameters to the quantitative measurement of depigmentation. Indeed, the VETF assesses the three dimensions of the disease (extent, staging, and spreading/progression). In VETF method, in each site, the largest lesion within each specific body site is clinically evaluated by visual and photographic assessment for the extent or percentage of vitiligo involvement (depigmented skin), staging, and spreading of vitiligo. In VETF method, staging is assessed from 0 (normal pigmentation) to 4 (complete hair whitening) grades. Spreading is assessed using the following scores: 0 (stable disease), −1 (regressive disease), and +1 (progressive disease).

### Dietary assessments

Each participant's usual food intake over the previous year was obtained through individual interviews by standardized food frequency questionnaire (FFQ) that contained 136 food items. Validity and reliability of questionnaire were approved.[29,30] Administered interviewer collected dietary information via face-to-face interview. All of the foods that were consumed at least twice a month were registered. The portions of each consumed food (g/d) were quantified by household measures, standard measures, and 35 sets of pictures with simple foods, food mixtures, and drinks. Questionnaire had an open-ended section where respondents recorded consumption of other foods not included on the food list and we ensured that the total diet of the individual was captured. In addition, FFQs include supplementary questions about cooking methods and specific types of fat and milk. A food composition table was used for mixed foods ingredients. Food items were converted to gram. Nutritionist 4 software (First Data Bank, San Bruno, CA) was used for nutrient analysis.

### Statistical analysis

Results were expressed as percentage (qualitative variables) and mean ± standard deviation (quantitative variables). Dietary total fat, PUFA, monounsaturated fatty acids (MUFA), SFA, linoleic acid, linolenic acid, oleic acid, EPA, DHA, and cholesterol variables were adjusted for total energy intake using the residual method. Independent *t*-test was used to compare the amount of total fat, PUFA, MUFA, SFA, linoleic acid, linolenic acid, oleic acid, EPA, DHA, and cholesterol intake between two groups. Multiple logistic regression models were used to analyze the association between dietary intake of fatty acids and occurrence of vitiligo with adjusting of potential confounders (age, sex, BMI, physical activity, and energy). Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) for the risk of vitiligo at different quartiles of dietary total fat, PUFA, MUFA, SFA, and cholesterol intake were computed in unadjusted and adjusted analyses. Quartile cut-points were based on the distribution of variables among controls. All analyses were performed with SPSS version 20.0 (SPSS, Chicago, IL, USA). Results with a value of $P < 0.05$ were considered statistically significant.

## Results

Data of 100 vitiligo patients (67 women, 38 men) and 110 healthy volunteers (33 women, 62 men) were analyzed. We found no significant differences between the cases and the controls in terms of age, sex, and BMI, but there was a significant difference in weight ($P = 0.009$) [Table 1].

Results from the independent *t*-test showed that consumption of SFA, EPA, and DHA significantly differed between the cases and the controls. Vitiligo group intakes more SFA and less EPA and DHA than control group. The intakes of energy, total fatty acids, MUFAs, PUFAs, cholesterol, oleic acids, linoleic acids, and linolenic acids were not significantly differed among two groups [Table 2].

Table 3 presents the results of the multiple logistic regression models regarding the relationship between quartiles of fatty acids intake and risk of vitiligo as ORs, 95% CIs, and *P* values for trend.

According to Table 3, crude analysis showed increase in the risk for those with high intakes of total fat (OR = 3.33, 95% CI: 1.46–7.58) and SFA (OR = 2.22, 95% CI: 1.04–4.90) and decrease in the risk for those with high intakes of MUFA (OR = 0.41, 95% CI: 0.18–0.92). However, this relationship disappeared after adjustment for confounders such as energy, age, sex, and BMI except for total fat (OR = 2.84, 95% CI: 1.63–5.44). Crude and adjusted analyses for PUFA and cholesterol intake were not statistically significant [Table 3].

**Table 1: Characteristics of participants**

| | Vitiligo | Control | *P* |
|---|---|---|---|
| Age | 20.71±6.19 | 23.22±5.39 | 0.07 |
| Gender (%) | | | |
| Male | 38 | 62 | 0.052 |
| Female | 67 | 33 | |
| Weight | 57.31±8.9 | 65.87±2.66 | 0.009 |
| BMI (kg/m$^2$) | 21.48±2.68 | 23.31±5.86 | 0.051 |

BMI=Body mass index

**Table 2: Dietary fat intake in two groups of study**

| | Control (*n*=110) | Vitiligo (*n*=100) | *P* |
|---|---|---|---|
| Energy | 2453.93±984.10 | 2147.35±874.38 | 0.21 |
| Total fat | 71.37±20.46 | 76.87±19.72 | 0.053 |
| SFA | 22.41±7.52 | 25.35±8.14 | 0.008 |
| MUFA | 23.81±14.78 | 22.39±12.27 | 0.46 |
| PUFA | 18.13±8.60 | 17.90±6.80 | 0.08 |
| Linoleic acid | 16.27±11.57 | 14.25±9.24 | 0.17 |
| Linolenic acid | 0.42±0.32 | 0.35±0.25 | 0.11 |
| Oleic acid | 18.4±13.25 | 16.43±9.83 | 0.23 |
| EPA | 0.03±0.04 | 0.01±0.01 | 0.001 |
| DHA | 0.07±0.12 | 0.04±0.03 | 0.004 |
| Cholesterol | 229.36±88.77 | 252.31±120.64 | 0.82 |

SFA=Saturated fatty acid, MUFA=Monounsaturated fatty acid, PUFA=Polyunsaturated fatty acid, EPA=Eicosapentaenoic acid, DHA=Docosahexaenoic acid

## Discussion

In the present case–control study, analysis confirmed that higher total fat intake associated with higher incidence risk of vitiligo. Although an unfavorable association was shown between the higher intake of SFA and lower intakes of EPA or DHA and vitiligo, these associations disappeared after adjustment with confounders.

Limited studies assessed the relationship between dietary fat intakes and the incidence or severity of vitiligo.

In clinical studies, significant benefits for systemic lupus erythematosus patients were achieved after consuming a low-fat diet plus n-3 fatty acid-rich fish oil supplement.[18] Studies showed that high saturated fat diets have deleterious effects on both macrophage phagocytosis and NK cell activity in autoimmune disease.[31] Autoimmune model study reported that a high-fat diet consisting of equal amounts of lard and soybean oil (rich in linoleic acid) developed disease and animals had a shortened lifespan.[32,33]

The composition of dietary fatty acids influenced the tissue phospholipids which in turn determine the amounts and types of precursor acids eicosanoids. There are two ways in which dietary fatty acids can modulate the biosynthesis of eicosanoids from arachidonic acid, the major 20-carbon PUFAs of the human monocytes and lymphocytes: (1) Essential fatty acids deficiency and high levels of trans-isomers of linoleic acid in the diet decrease tissue arachidonic acid and the biosynthesis of eicosanoids derived from arachidonic acid. (2) Dietary PUFA can modulate the biosynthesis of eicosanoids via the cyclooxygenase step.[34,35] It has been speculated that

**Table 3: Multiple logistic regression and 95% confidence interval across quartile of fat intake**

| | Q1 | Q2 | Q3 | Q4 | *P* trend |
|---|---|---|---|---|---|
| Total fat | | | | | |
| Crude | 1 | 2.33 (1.03-5.26) | 1.91 (0.84-4.34) | 3.33 (1.46-7.58) | 0.01 |
| Adjusted | 1 | 1.99 (1.21-2.45) | 1.03 (0.54-3.55) | 2.84 (1.63-5.44) | |
| SFA | | | | | |
| Crude | 1 | 0.75 (0.28-1.47) | 0.87 (0.54-1.61) | 2.22 (1.04-4.90) | 0.06 |
| Adjusted | 1 | 0.27 (0.04-1.67) | 0.37 (0.07-1.91) | 0.59 (0.09-3.57) | |
| MUFA | | | | | |
| Crude | 1 | 0.18 (0.07-0.43) | 0.78 (0.35-1.73) | 0.41 (0.18-0.92) | 0.001 |
| Adjusted | 1 | 0.14 (0.01-1.09) | 0.51 (0.12-2.22) | 0.23 (0.04-1.10) | |
| PUFA | | | | | |
| Crude | 1 | 1.08 (0.49-2.35) | 0.67 (0.30-1.47) | 0.85 (0.39-1.86) | 0.45 |
| Adjusted | 1 | 0.99 (0.54-2.04) | 0.53 (0.23-1.74) | 0.79 (0.48-1.78) | |
| Cholesterol | | | | | |
| Crude | 1 | 0.85 (0.38-1.86) | 0.95 (0.43-1.23) | 1.60 (0.73-3.50) | 0.25 |
| Adjusted | 1 | 0.75 (0.15-3.67) | 0.82 (0.19-3.50) | 0.88 (0.14-5.32) | |

SFA=Saturated fatty acid, MUFA=Monounsaturated fatty acid, PUFA=Polyunsaturated fatty acid

changes in membrane fatty acid composition via dietary lipids can alter membrane fluidity, which in turn can change activities of antigen receptors, membrane-bound enzymes, and membrane permeability to ions, particularly $Ca2^{++}$.[36,37]

Regarding the effects of SFAs on autoimmune system, Park *et al*.[38] investigated the impact of high-fat diet (HFD), partially substituted with pine nut oil and lard for 12 weeks. They claimed that the production of IL-1 β by splenocytes was augmented in HFD mice; thus, IL-1 β triggers the immune responses. Furthermore, Jahromi *et al*.[39] conducted a study to find the relation of dietary pattern and the risk of MS with factor analysis. They observed that traditional pattern high in low-fat dairy products and red meat was inversely associated with the risk of MS. Ghadirian *et al*.[40] found that pork and hotdog intakes escalate the risk of MS. They also suggested a positive relation between energy and animal fat intake and the risk of MS.

Previous studies investigated the effect of omega-3 (ω3) PUFA on autoimmune diseases. Ghorbanibirgani *et al*.[41] indicated that *Nigella sativa* oil and fish oil reduced the size of vitiligo's lesions. In a study that was performed on 39 chronic psoriasis patients in Birjand, Iran, the fish oil had the same impact in reducing the size of skin lesions in comparison to a combination of salicylic acid and betamethasone.[14] In another clinical study, the positive effect of fish oil on skin autoimmune diseases such as vitiligo was confirmed in India.[42] Löfvenborg *et al*.[15] showed that fatty fish consumption might reduce the risk of latent autoimmune diabetes in adults, possibly through effects of ω3fatty acids. Regarding the effects of ω3 fatty acids on the formation of eicosanoids from arachidonic acid, Lands *et al*.[43] demonstrated that n-3 PUFA competitively inhibits the oxygenation of arachidonic acid by cyclooxygenase. Hwang *et al*.[44] claimed that among different PUFAs, EPA (20:5 [*n*-3]) and DHA (22:6 [*n*-3]) are more effective than 18:3 (*n*-3) in suppressing tissue levels of arachidonic acid and the formation of eicosanoids from arachidonic acid. On the other hand, Ochi *et al*.[45] indicated that EPA was a poorer substrate for cyclooxygenase than arachidonic acid although it can be converted to thromboxane 3 and triene prostaglandins to a limited extent in tissues.

Some experimental studies assessed that the effect of ω6 PUFAs on autoimmune disorders showed sunflower oil, rich in linoleic acid, decreased relapse rate and severity of MS.[46,47] However, another study did not find this effect.[48]

Findings showed that high n-3 fatty acid diets increased the survival and reduced disease severity in spontaneous autoantibody-mediated disease, while linoleic acid-rich diets appear to increase disease severity. The underlying involved mechanisms were (1) regulation of gene expression, (2) signal transduction pathways, (3) production of eicosanoids and cytokines, (4) and the action of antioxidant enzymes.[13]

Reasons for different results are the impact of dietary fatty acids on animal autoimmune disease models appears to depend on the animal model and the type and amount of fatty acids fed, effect of other environmental factor and genetic factors.

Vitiligo is considered as rare diseases or diseases with a long latency period between exposure and disease manifestation, and this is the first study that assesses the relation of dietary fats with vitiligo.

## Conclusions

We conclude that the protective or detrimental effects of the dietary fatty acids on the risk of vitiligo are more dependent on the total fat content of the diet than the specific subclasses of fats or fatty acids. EPA and DHA may have beneficial effect on the treatment of vitiligo patients.

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## Conflicts of interest

There are no conflicts of interest.

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