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Serum ferritin levels amongst individuals with acne

Ouissal Essadeq, Hyba Taounza, Narjess Er-rachdy, Anas Ahmed Mountassir and Laila Benzekri

Ouissal Essadeq
Dermatology Venerology Department, Ibn Sina University Hospital, University Mohammed V in Rabat, Morocco

Hyba Taounza
Dermatology Venerology Department, Ibn Sina University Hospital, University Mohammed V in Rabat, Morocco

Narjess Er-rachdy
Dermatology Venerology Department, Ibn Sina University Hospital, University Mohammed V in Rabat, Morocco

Anas Ahmed Mountassir
Laboratory of Community Health, Preventive Medicine and Hygiene, Department of Public Health, Faculty of Medicine and Pharmacy, University Mohammed V in Rabat, Morocco

Laila Benzekri
Dermatology Venerology Department, Ibn Sina University Hospital, University Mohammed V in Rabat, Morocco

Corresponding Author:
Ouissal Essadeq
Dermatology Venerology Department, Ibn Sina University Hospital, University Mohammed V in Rabat, Morocco

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Abstract
Acne vulgaris is a widespread dermatological condition with a multifactorial etiology. Emerging research highlights the potential role of micronutrients, particularly iron, in acne pathogenesis. This study investigates serum ferritin levels, a key biomarker of iron status, in individuals with acne compared to healthy controls.
Conducted as a hospital-based cross-sectional study over 18 months, the research included 70 acne patients and 70 age- and sex-matched controls. Participants' dietary habits, stress levels, physical activity, and acne severity were assessed, alongside serum ferritin and hemoglobin measurements.
The median ferritin level in the acne group was 19.0ng/mL, significantly lower than the control group, which had a median serum ferritin level of 30.4 ng/mL. Among acne patients, 55.7% exhibited ferritin deficiency (≤20 ng/mL), with 21.4% having very low levels (<10 ng/mL). In contrast, ferritin deficiency was less common in the control group. A significant difference in ferritin levels was observed between males and females, with males displaying higher ferritin levels in both groups. Additionally, lifestyle factors such as high-glycemic-index food consumption, stress, and physical inactivity were significantly associated with acne. Hemoglobin levels were slightly lower in the acne group compared to reference values and was statistically correlated with the GEA acne grade.
These findings highlight a potential link between serum ferritin levels and acne. Iron, as a critical micronutrient, influences skin health through its role in oxidative stress and immune response. The study also underscores the importance of considering dietary and lifestyle factors in acne management.
Further research is warranted to explore the complex interplay between iron metabolism, inflammation, and acne pathogenesis. Dietary interventions and iron supplementation could represent complementary strategies for managing acne, potentially improving patient outcomes.

Keywords: Acne vulgaris, serum ferritin, iron metabolism, anemia, inflammation, oxidative stress, dietary habits, lifestyle factors.

Introduction

Acne vulgaris, commonly referred to as acne, is a multifactorial skin condition characterized by chronic inflammation of the pilosebaceous unit. As one of the most prevalent dermatological disorders worldwide, it affects approximately 9.4% of the global population and ranks as the eighth most common disease globally. Interestingly, its prevalence is notably higher among females, affecting nearly 80% of them at some point in their lives [1].
Recently, the connection between nutrition and skin health has garnered significant attention, particularly the role of micronutrients in the onset and severity of acne. Among these micronutrients, iron stands out as a key element essential for cellular metabolism and immune regulation. Serum ferritin, a protein responsible for storing iron in the body, is widely recognized as a reliable biomarker for evaluating iron reserves [2].
Despite its importance, research examining serum ferritin levels in individuals with acne remains limited and, at times, inconclusive. Some studies hint at a potential link, suggesting that imbalances in iron-whether in excess or deficiency-may contribute to inflammatory processes and oxidative stress, both of which are key factors to acne development [3]. Additionally, the role of ferritin has been reported in patients with rosacea [4] and alopecia [5].
This study aims to evaluate serum ferritin levels in individuals with acne compared to healthy controls. By doing so, we aim to uncover potential interactions between micronutrient status, inflammation, and skin health.
A deeper understanding of this relationship could open doors to complementary treatment strategies for acne.

Materials and Methods: This was a hospital-based cross-sectional study conducted over 18 months (from February 2023 to August 2024) at the dermatology department of Ibn Sina University Hospital in Rabat, Morocco.
A total of 70 participants of both sexes, with varying degrees of acne severity, were included. An equal number of age- and sex-matched healthy individuals without acne were recruited as the control group. To ensure the integrity of the study, individuals with other inflammatory conditions, those who had undergone iron therapy, blood transfusions, or blood donations in the six months prior to the study, as well as pregnant or lactating women, and those with malabsorption syndrome or malnutrition, were excluded.
Informed consent was obtained from all participants before their inclusion in the study.
Healthy volunteers for the control group were selected using a purposive sampling technique, ensuring they matched the cases in terms of age and sex. The responsible physician conducted face-to-face interviews with all participants to collect necessary information, and informed consent was obtained from each participant before their inclusion in the study.
During the interviews, the physician documented dietary habits (including weekly consumption of dairy, high-glycemic-index foods, whey protein, and red meat), stress levels, and physical activity. Acne severity was graded using the Global Acne Evaluation (GEA) score which classifies acne into five stages: very mild (1), mild (2), moderate (3), severe (4), and very severe (5).
Blood samples were collected and analyzed for serum ferritin levels using chemiluminescent immunoassay (CLIA) and for complete blood count (CBC) using automated hematology with VCS technology. Serum ferritin levels were categorized as follows: normal (>20 ng/mL), low (10-20 ng/mL), and very low (<10 ng/mL).
The collected data were analyzed using Excel and Jamovi 2.3.28 software.
Qualitative variables were expressed as frequency and percentage, while quantitative variables were presented as mean ± standard deviation (SD) if they followed a normal distribution; otherwise, they were expressed as median and interquartile range (IQR). Comparisons between groups were performed using the Chi-square test when conditions were met; if expected counts were less than 5, the Fisher's exact test was applied instead. Comparisons across acne severity groups were conducted using one-way analysis of variance (ANOVA) for normally distributed data and the Kruskal-Wallis test for non-normally distributed data, as appropriate. Paired samples t-test was used for the analysis of paired groups when data were normally distributed, while the Wilcoxon rank test was applied for non-normally distributed data.
A p-value of < 0.05 was considered statistically significant.

Results: We included a total of 140 individuals in this study, divided into two groups: a patient group consisting of 70 individuals with acne and a control group of 70 age- and sex-matched individuals without acne. Each group represented 50% of the study population.
The mean age of participants was 23.6 ± 6.14 years, reflecting a symmetrical age distribution. The age range spanned from 12 to 43 years. Female participants comprised the majority of the population (64.3%), while males represented 35.7%. Both patient and control groups were well-balanced in terms of age and sex (Table 1). Phototype IV was predominant, observed in 72.1% (49 participants), followed by phototype III in 25% (17 participants), and phototype V in 2.9% (2 participants).

Table 1: Characteristics of the study participants

Variable	Patient group (n=70)	Control group (n=70)
Age[a] (year)	23.1 ± 4.21	23.1 ± 4.21
Gender[b]		
Female	45 (64.30)	45 (64.30)
Male	25 (35.70)	25 (35.70)
Phototype[b]		
III	17 (25.00)	15 (21.42)
IV	49 (72.10)	52 (74.28)
V	2 (2.90)	3 (4.30)

a) Mean± standard deviation (SD) b) Expressed as n (%)

Lifestyle and behavioral factors in acne patients

Regarding dietary habits, 88.6% of participants followed a balanced diet, while 7.1% adhered to a high-protein diet, and 4.3% followed a restrictive one.
The weekly consumption of high-glycemic index (GI) foods among the study participants showed considerable variability, with a median intake of 3 times per week (table2). A notable proportion of participants (31.4%, 22 individuals) reported no consumption of high-GI foods.
When stratified by acne severity (Grade GEA), the weekly intake of high-glycemic index (GI) foods varied across groups. Participants with mild acne (GEA 2) had the highest intake, with a median of 6 times per week (table 3) with a significant association (p=0.045).
Dairy intake had a median consumption of 4 times per week (Table 2), while a small subset (8.5%) consumed dairy more than 10 times weekly. Participants with very mild acne (Grade 1) reported the lowest intake, while those with very severe acne (Grade 5) had the highest median intake of 5 times per week (Table 3).
Red meat consumption varied, with 12.9% of participants reporting no intake, 78.5% consuming it 1 to 5 times per week, and 8.6% consuming it 6 to 10 times weekly (table 2).
Whey protein consumption was reported by only 5.7% of participants, exclusively males. When stratified by acne severity (Grade GEA), the proportion of participants consuming red meat more than 5 times per week remained low across all groups, with a slight increase in mild acne cases (Grade 2) (Table 3).

Table 2: Dietary and lifestyle characteristics of the patient population

Variable	Patient group (n=70)
Dietary pattern[a]	
Balanced	62 (88.6)
High-protein	5 (7.1)
Restrictive	3 (4.3)
Weekly intake of high-glycemic index (GI) foods[b]	3 [0;5]

Weekly dairy intake[b]	4 [2;6]
Weekly red meat consumption[a]	
0	9 (12.9)
1-5	55 (78.5)
6-10	6 (8.6)
WHEY protein consumption[a]	4 (5.7)
Use of occlusive cosmetics[a]	25 (35.7)
Physical inactivity[a]	46 (65.7)
Perceived stress[a]	62 (88.6)

a) Variables expressed as n (%) b) Variables expressed as median [25th percentile; 75th percentile]

Among lifestyle factors, stress was commonly reported, affecting 88.6% of participants. Physical inactivity was prevalent in 80% of participants. The use of occlusive cosmetics was noted in 35.7% of cases, exclusively among females (Table 2).

Table 3: Association between acne severity (GEA grade) and dietary and lifestyle factors

	GEA Grade					p-value
	1	2	3	4	5	
Weekly intake of high-glycemic index (GI) foods[a]	3 [3; 3]	6 [4.25; 7]	4 [0; 5.75]	1 [0; 3]	2.5 [0.75; 5]	**0.045**
Weekly dairy intake[a]	1 [1; 1]	4 [2; 7]	4 [2; 5]	3 [1; 6.5]	5 [3.75; 5.25]	0.749
Weekly red meat consumption[a]	0 [0; 0]	3.5 [2.5; 5]	3 [2; 3]	3 [1.5; 3.5]	3 [2; 4]	0.349
WHEY protein consumption[b]						
Yes	0 (0)	0 (0)	1 (25)	1 (25)	2 (50)	0.479
No	1 (1.5)	12 (18.2)	25 (37.9)	18 (27.3)	10 (15.2)	

a) Variables expressed as median [25th percentile; 75th percentile] b) Variables expressed as n (%)

Impact of Acne on Quality of Life

The acne significantly affected the quality of life of the participants, with 78.6% of individuals reporting either a significant (27 participants) or very significant (28 participants) impact. Moderate and mild impacts were reported by 17.1% and 4.3% of participants, respectively. Notably, no participants indicated no impact, emphasizing the substantial psychosocial burden of acne.

Acne types, classification & severity: The distribution of acne types revealed a predominance of the inflammatory form, affecting 48.6% (34 participants), followed by the mixed type (32.9%, 23 participants). Severe conglobata acne was observed in 10% (7 participants), while retention acne was the least common, found in 8.6% (6 participants).

A significant gender-based difference was observed in the distribution of acne types (Table 4). Conglobata acne was exclusive to male participants (7 cases). The inflammatory form was more common in females, with 25 cases compared to 9 in males. Similarly, the mixed type was predominantly observed in females (16 cases vs. 7 in males). Retention acne was less common, with 4 cases in females and 2 in males.

The grade of acne varied significantly by age (Table 4). The average age at GEA 5 stage was the lowest, at 19.7 ± 5.05 years.

The distribution of acne severity according to GEA grade also varied significantly by gender (Table 4). In females, grade 3 was the most frequent (21 cases), followed by grade 4 (12 cases) and grade 2 (10 cases). In contrast, male participants exhibited a higher frequency of grade 5 acne (11 cases), with fewer cases in grades 4 (7 cases), 3 (5 cases), and 2 (2 cases). Grade 1 was seen in only one female participant, with no males in this category.

Table 4: Distribution of acne severity (GEA grades) by gender and age

	GEA Grade					p-value
	1	2	3	4	5	
Gender[a]						
Female	1 (2.2)	10 (22.2)	21 (46.7)	12 (26.7)	1 (2.2)	<0.001
Male	0 (0.0)	2 (8.0)	5 (20.0)	7 (28.0)	11 (44.0)	
Age[b] (years)	36.00	22.10 ± 4.76	23.90 ± 5.53	25.80 ± 6.83	19.70 ± 5.05	**0.011**

a) Variables expressed as n (%), b) Mean± standard deviation (SD)

Ferritin and Hemoglobin Levels

The analysis of ferritin levels in the acne group revealed a median of 19.0 ng/mL, with values ranging from 1.94 to 133 ng/mL. Among the participants, 44.3% (n=31) had normal ferritin levels (>20 ng/mL), while 34.3% (n=24) had low ferritin levels (10-20 ng/mL), and 21.4% (n=15) presented with very low ferritin levels (<10 ng/mL). These findings suggest a notable prevalence of reduced ferritin levels in individuals with acne (Table 5). However, this result was not statistically correlated with the GEA acne grade (p=0.218).

The mean hemoglobin level was 12.3 ± 1.69 g/dL, with values ranging from 9.00 to 16.0 g/dL (Table 5). This was statistically correlated with the GEA acne grade (p=0.027).

On the other hand, the control group had a median serum ferritin level of 30.0 ng/mL, with minimum and maximum values of 9 ng/mL and 107 ng/mL, respectively.

Table 5: Serum ferritin and hemoglobin levels among the acne group of the study

Variable	Valeur
Ferritin (ng/mL)[a]	19.0 [10.3; 26.0]
Hemoglobin (g/dL)[b]	12.30 ± 1.69

a) Variables expressed as median [25th percentile; 75th percentile] b) Mean± standard deviation (SD)

Comparison of Ferritin and Hemoglobin Levels between the Acne and Control Groups

The analysis revealed significant differences in ferritin levels between the acne and control groups. The median ferritin level in the acne group was 19.0 ng/mL, markedly lower than the control group's median ferritin level of 30.0 ng/mL. Additionally, 55.7% of individuals in the acne group exhibited ferritin deficiency (≤20 ng/mL), with 21.4% having very low ferritin levels (<10 ng/mL), compared to the control group where ferritin deficiency was less prevalent. Statistical analysis confirmed a significant association between ferritin deficiency and acne (Table 5).

The hemoglobin levels were also slightly lower in the acne group, with a mean of 12.3 g/dL, compared to the control group (12.5g/dL). These findings may indicate a higher prevalence of iron storage deficiency in the acne group, potentially linking lower ferritin levels to acne severity.

Table 6: Comparison of Ferritin and Hemoglobin levels between the Patient and Control Groups

Variable	Patient group (n=70)	Control group (n=70)	p-value
Ferritin level[a] (ng/mL)	19.0 [10.3; 26.0]	30.0 [19.0; 71.8]	**< 0.001**
Hemoglobin level[b] (g/dL)	12.30 ± 1.69	12.50 ± 1.13	0.353

a) Variables expressed as median [25th percentile; 75th percentile] b) Mean ± standard deviation (SD)

Discussion

Over the past decade, the importance of skin health and appearance has gained significant attention, prompting numerous studies on its influencing factors. Skin health is affected by a wide range of external and internal elements, with micronutrients playing a crucial role in preserving the skin's structure, function, and overall integrity.

Recent clinical investigations and meta-analyses have revealed a compelling correlation between serum mineral concentrations and the pathogenesis of chronic inflammatory dermatological conditions [6]. Among these micronutrients, iron (Fe) is essential for normal skin function. It contributes to the transcription of growth factors and cytokines, supports collagen synthesis, maintains oxidative balance, and facilitates wound healing [7]. Furthermore, the skin, for its part, plays a dual role in iron regulation, functioning as both a storage site and a route for its elimination [8].

Iron concentration varies across the different layers of the epidermis, with the highest levels found in the basal layer. It is eliminated through the stratum corneum as part of the epidermal exfoliation process [9].

As a transition metal, iron is integral to oxidative stress mechanisms in the skin, particularly through the production of reactive oxygen species (ROS). When the skin is exposed to UVA radiation, ROS are generated, especially in fibroblasts, causing oxidative damage to vital cellular components, such as mitochondrial, lysosomal, plasma, and nuclear membranes. This damage weakens the integrity of cell membranes, hampers mitochondrial ATP production, and can ultimately result in necrotic cell death within the skin [2].

This process not only accelerates skin aging but also contributes to inflammatory skin conditions like acne. Inflammation, a central factor in acne pathogenesis, operates alongside mechanisms such as follicular hyperkeratinization, excessive sebum production, variations in Cutibacterium acnes phylotypes, and exposome influences. The exposome encompasses environmental and lifestyle factors such as pollution, diet, stress, and hormonal fluctuations, all of which contribute to acne onset and exacerbation [10].

Excessive ROS, mediated by iron-related Fenton reactions, exacerbate inflammation by activating pathways like NF-κB and inducing the release of pro-inflammatory cytokines such as IL-1β and TNF-α. This interplay between ROS, inflammation, and exposome-driven factors creates a complex network driving acne lesion formation and progression [6, 11].

To further understand the role of oxidative stress and inflammation in acne, it is essential to examine the role of ferritin—a protein at the intersection of iron metabolism and immune response. Beyond its well-known function as an iron storage molecule, ferritin is also recognized as an acute-phase protein (APP) and an inflammatory marker. In inflammatory conditions, serum ferritin levels may reflect ongoing inflammation rather than true iron stores, as they tend to rise during acute infections and systemic inflammation, thereby complicating its interpretation as a reliable marker of iron status [12]. Ferritin levels have been investigated in various dermatological conditions, such as female-pattern hair loss [13], systemic lupus erythematosus (SLE) [14], and chronic spontaneous urticaria [15], highlighting its potential involvement in inflammatory skin diseases.

In the context of acne vulgaris, our findings on ferritin and hemoglobin levels reveal a more nuanced perspective. Ferritin levels in acne patients were significantly lower (median of 19.0 ng/mL) compared to controls (median of 30.0 ng/mL), with a notable prevalence of ferritin deficiency. Specifically, 55.7% of acne patients exhibited ferritin deficiency (≤20 ng/mL), including 21.4% with very low levels (<10 ng/mL), in contrast to the control group, where ferritin deficiency was less prevalent. Statistical analysis confirmed a significant association between ferritin deficiency and acne ($p<0.001$).

Our findings are consistent with those of Alharbi *et al*., who reported lower ferritin, hemoglobin, and mean corpuscular volume (MCV) levels in acne patients, though their results did not reach statistical significance. They also noted a higher prevalence of vitamin B12 deficiency in acne patients, a factor not assessed in our study but potentially relevant to acne pathogenesis[3]. Similarly, studies by Balta *et al*. and El-Saaiee *et al*. found no significant differences in ferritin, hemoglobin, or iron levels between acne patients and controls, but they acknowledged the potential role of iron metabolism in acne [18, 19].

Conversely, other studies have reported conflicting findings. El-Taweel *et al*. observed slightly elevated ferritin levels in acne patients compared to controls, though this difference was not statistically significant. This discrepancy may stem from ferritin's role as an acute-phase reactant, which complicates its interpretation in inflammatory conditions such as acne [12]. Similarly, Leyden found significantly elevated ferritin levels in acne patients, suggesting a potential link between ferritin and acne-associated inflammation. Additionally, Leyden reported reduced serum iron levels in patients with severe nodulocystic acne, highlighting inflammation-driven alterations in iron metabolism [16].

These findings align with broader observations of inflammatory reactions that decrease transferrin and serum iron levels while increasing ferritin, as noted by DiBaise and Tarleton [17].

Alam *et al*. also demonstrated that metabolic factors, particularly obesity, independently influence ferritin levels. Their study found that obese individuals exhibited higher ferritin and CRP levels regardless of iron stores, underscoring the need to consider metabolic factors when analyzing ferritin levels in acne patients [20].

Interestingly, Wu *et al*., using Mendelian randomization analysis, concluded that no causal relationship exists between markers of iron metabolism, including ferritin, and acne development. This finding highlights the complexity of the relationship between iron metabolism, inflammation, and acne pathogenesis [6].

While our study underscores a significant prevalence of ferritin deficiency in acne patients, the precise role of ferritin in acne-related inflammation remains uncertain. Larger, well-controlled studies are needed to clarify the interplay between iron metabolism, oxidative stress, and acne severity.

Conclusion: This study explored the relationship between serum ferritin levels, iron metabolism, and acne, aiming to shed light on the notable prevalence of ferritin deficiency in acne patients compared to controls. Our findings revealed a significant association between lower ferritin levels and acne, with 55.7% of patients showing ferritin deficiency ($\leq$20 ng/mL), including 21.4% with very low levels (<10 ng/mL). These results emphasize the potential role of iron storage deficiency in acne pathophysiology.

Our findings are in agreement with studies that identified reduced ferritin and hemoglobin levels in acne patients, though discrepancies with other reports underline the complexity of ferritin's dual role as an iron storage marker and acute-phase reactant in inflammatory conditions.

Future research should prioritize larger, well-controlled studies to better understand the contribution of iron metabolism to acne pathogenesis and to evaluate the potential benefits of dietary interventions and iron management as complementary strategies in acne treatment. This study provides a foundation for further investigation into the broader implications of micronutrient deficiencies on skin health and acne severity.

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