Assessment of Quality of Life in Patients with Acne Vulgaris and Its Consequent Disabilities in Qom, 2018

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**A-R-T-I-C-L-E**

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**A-B-S-T-R-A-C-T**

\textbf{Background & Aims of the Study:} Acne is a chronic inflammatory disease characterized by comatose lesions and cysts that can be accompanied by scarring in some cases. The physical and psychological effects of acne include deformities, scarring, depression, impaired social relationships, and discontentment. Moreover, the affected people experience social isolation, and they engage in social activities less frequently due to embarrassment and fear of being excluded from the community. Some studies reported that the prevalence of acne is 10 times higher in males, as compared to females. With this background in mind, the current study aimed to assess quality of life in patients with acne vulgaris and its consequent disabilities in Qom, 2016.

\textbf{Materials and Methods:} This is a cross-sectional (descriptive-analytical) study and the statistical population included acne patients who were referred to dermatological clinics in Qom. Therefore, 147 patients were selected by convenience sampling. Data collection tools were the Cardiff Acne Disability Index (CADI) and Dermatology Life Quality Index (DLQI) questionnaires. CADI is a questionnaire which is specific for acne consisting of five questions about feelings, interference with social life, and interaction with the opposite gender, avoidance of public places, the appearance of the skin, and perceived severity of the disease over the last month. DLQI consists of 10 items covering symptoms and feelings (items 1 and 2), daily activities (items 3 and 4), leisure (items 5 and 6), work and school (item 7), personal relationships (items 8 and 9) and treatment (item 10). Data were analyzed in SPSS software (version 21) using descriptive statistics and independent t-test, ANOVA, and Pearson correlation coefficient. A p-value less than 0.05 was considered statistically significant.

\textbf{Results:} 83% of the cases were female and 35.4% of them had a family history of acne. 26.5% of patients had less than a high school diploma degree and the average score of quality of life in acne patients was 7.32 and the mean score of acne-related disability index was reported as 5.86. The results of the statistical tests demonstrated no significant difference in the mean score of quality of life and acne-related disability in terms of gender and family history of acne (P>0.05). Moreover, the results of the ANOVA test indicated no difference in mean scores of quality of life and acne-related disability index in terms of education (P>0.05). In addition, the Pearson correlation coefficient result revealed that the relationship of age and duration of illness with the mean score of quality of life and disability index was not significant (P>0.05). Nonetheless, this test demonstrated a direct and significant relationship between the mean score of quality of life and acne-related disability (P<0.05; r = 0.73).

\textbf{Conclusion:} As evidenced by the obtained results, there was a significant relationship between quality of life and acne-related disability (P<0.05). Acne can affect different aspects of patients’ lives in a myriad of ways. Accordingly, their social, educational, and recreational activities, as well as their mental and psychological health are adversely affected by this disease.

Background

Acne is the most prevalent skin disorder occurring during the second and third decades of life. Acne lesions chiefly appear on the face and back but can also occur in other areas, such as chest and upper arms (1). Increased secretion of skin fat along with increased bacterial proliferation are some factors that cause acne. Predisposing factors for acne include genetics, hormonal factors, and stressors (2-4). The average age of onset of acne in adolescent girls and boys is reported to be 12-15 and 16-18 years, respectively (1). Acne is so prevalent that some people have recognized it as a physiological state during adolescence and puberty.

The prevalence of acne in men is less but more severe; nonetheless, it is less common but less resistant to treatment in women. In general, 10% of men and 50% of women continue to be plagued by acne by the age of 40. This disease is likely to occur earlier in girls than boys since girls start puberty earlier than boys. Acne is observed in 40% of 17-year-old girls and 25% of 18-year-old boys. After this age, its prevalence decreases, and the patients would be on the road to recovery. In general, acne affects about 85% of people aged 12-24 years; however, the number of people with persistent or adult-onset acne is increasing.

Based on a new definition which was introduced in 2011, acne is considered a chronic inflammatory disease of the pilosebaceous units in adolescence with a reported prevalence of 40-95% in adults with a preference for males. Androgen increases the effects of acne, on the contrary estrogens control the incidence of acne. Gastrointestinal disorders, hypovitaminosis, avitaminosis, or anemia are involved in the development of this complication. In addition, severe cases of acne can also cause scarring (5). Mental stress can extend the time required to heal wounds by up to 40%, which can also be an influential factor in delayed or inadequate treatment and healing of acne lesions (6).

Numerous cases of recurrence of acne have been reported in young women following the stress of marriage and marital life (7). The assessment of quality of life in patients with skin diseases is of utmost importance. Although skin diseases do not reduce survival in most cases, they can affect quality of life in other ways. They can cause unpleasant symptoms, such as itching, pain, mental stress, lack of self-confidence, and embarrassment. In addition, these diseases can adversely affect social and family relationships, waste time, and impose financial and medical burdens on the affected patients (8, 9).

Although acne is a self-limiting disease, it assumes significance in human life since it plagues the face, and the effects of these skin lesions last for years and even to the end of life. Therefore, this disease can play a key role in people’s lives, especially at the age of the importance of self-confidence and social activities.

Therefore, many patients will have low self-esteem and difficulty in building relationships. Studies conducted on skin diseases have indicated that the psychosocial effects of acne are more devastating than psoriasis and eczema (10). Moreover, it has been found that patients with severe acne are easier to set off than others which can affect quality of life on one hand and treatment satisfaction on the other and. In people with low self-esteem and mental image, acne can exert a profound effect on people in puberty which is associated with vulnerability (11).

The results of a study suggested that about 30% of people believed that acne was caused by poor skin health and hygiene (12). Another study was performed on the prevalence of depression and suicidal ideation among about 480 skin patients. The results of the mentioned study indicated that these mental conditions were manifested much more severely in acne patients, as compared to those with alopecia.
areata, dermatitis, alopecia, and mild to moderate psoriasis (13). In another study, depression and suicidal ideation were reported in 7.2% of acne patients(14).

Nimir et al. (2006) equated psychosocial and emotional problems of acne with such debilitating illnesses as eczema, seizure, diabetes, backache, and arthritis. They added that these emotional problems were not associated with the severity of acne, and even mild to moderate acne can lead to severe depression and suicidal ideations. In addition, severe degrees of anxiety have been observed which were provoked by failure in social interactions.

The results of the study performed by Nimir et al. demonstrated a significant decrease in anxiety in these patients after the treatment (15). In the same vein, a study was carried out by Gorel et al. (2005) on the effects of skin diseases on the quality of life. The results of the mentioned study pointed to the significant relationship of acne with anxiety and depression (16). With this background in mind and considering the undeniable effects of acne on affected patients, the present study aimed to assess quality of life in patients with acne vulgaris and its consequent disabilities in Qom, 2018.

**Materials & Methods**

The present study was a cross-sectional study. The statistical population was calculated at a minimum of 147 cases using sample size formula infinite population, probability of type 1 error of 0.05, the standard deviation of 0.59, and study accuracy of 0.02 d. Consequently, patients with acne vulgaris who were referred to Qom medical centers were selected through convenience sampling with their full knowledge and consent.

Inclusion criteria entailed: acne patients aged 11-50 years, patient consent to participate in the study, and no history of psychiatric problems. On the other hand, the exclusion criteria included: incorrect response to questions, noncooperation of patients, and the use of topical and systemic medications that may interfere with the assessment of acne. Data were collected using two valid and reliable questionnaires, namely CADI (Cardiff Acne Disability Index) and DLQI (Dermatology Life Quality Index) (18).

The DLQI is a compact self-reported questionnaire which measures quality of life over the previous week in patients with skin diseases. It consists of 10 items covering symptoms and feelings (items 1 and 2), daily activities (items 3 and 4), leisure (items 5 and 6), work and school (item 7), personal relationships (items 8 and 9) and treatment (item 10). Each item is scored on a four-point scale, with higher scores indicating greater impairment. It ranges from zero (no effect on the quality of life) to 3 (high impact on the quality of life) with a higher score indicating a worse quality of life. Results within the range of 0-1 signify that acne did not affect patient quality of life, scores of 2-5 indicate low impact, scores of 6-10 demonstrate moderate impact, scores of 20-11 illustrate a high impact, and scores of 21-30 suggest an extremely high impact on the quality of life.

CADI is a questionnaire which is specific for acne and contains five questions about feelings, interference with social life and interaction with the opposite gender, avoidance of public places, the appearance of the skin, and perceived severity of disease over the last month. Each question has four options to choose from and is rated from 0-3 giving the total score. The final score ranges from 0-15. CADI scores were graded as low (0-4), medium (5-9), and high 10-15. High scores indicate a higher level of disability. Therefore, the scores of DLQI and CADI questionnaire range from 0-30 and 0-15, respectively.

Both DLQI (19) and CADI (20) questionnaires have Persian versions with confirmed validity and reliability. To comply
with ethical considerations, the participants were ensured of the confidentiality of their responses and written consent was obtained from all of them. Moreover, the approval was obtained from the Ethics Committee of Qom University of Medical Sciences under the ethical code of IR.MUQ.REC.1395.120. Data were collected by written consent. On a final note, the data were analyzed in SPSS software (version 20) using descriptive statistics and independent T-test, ANOVA, and Pearson correlation coefficient. A p-value less than 0.05 was considered statistically significant.

**Results**

According to data analysis, 83% (n=122) of the participants were females and 17% (n=25) were males. The mean age of subjects was 22.60±6.41 years with the age range of 11-50 years. Considering the educational level, 26.5% (n=39), 34% (n=50), 33.3% (n=49), 5.4% (n=8), and 0.7% (n=1) of cases had below diploma, diploma, master's, and higher degrees, respectively. The mean scores of treatment duration, participants' quality of life, and acne-related disability were obtained at 3.89±2.51, 7.32±5.67, and 5.86±2.93 years, respectively. Moreover, 35.4% (n=52) of patients had a family history of acne vulgaris.

As evidenced by the analysis, in the independent t-test, gender showed no significant relationship with quality of life score and acne-related disability index (P>0.05; Table 1). Moreover, in the current study, according to independent T-test, family history demonstrated no significant relationship with quality of life score and acne-related disability (P>0.05; Table 1).

In addition, the results of the ANOVA test showed no significant relationship between educational level and the mean quality of life score (P=0.556). In the same vein, this test did not find any significant relationship between educational level and acne-related disability (P=0.35)(17). Furthermore, Pearson's correlation coefficient revealed no significant relationship between age and the mean quality of life score (P=0.483; r = 0.058) and no significant relationship between age and mean score of acne-related disability (P= 0/766; r=0.025).

This coefficient also demonstrated no significant relationship between treatment duration and mean score of quality of life (P=0.063; r=0.154) and no significant relationship between treatment duration and mean score of acne-related disability (P=0.068; r=0.151). Nonetheless, this test showed a direct correlation between quality of life and the index of acne-related disability (P<0.001; r=0.73) (Table 2)

As illustrated by the obtained results, acne vulgaris had no, low, moderate, high, and extremely high effect on quality of life in 14.3% (n=21),34.7% (n=51),27.9% (n=41), 18.4% (n=27), and 4.8% (n=7) of It is noteworthy that patients reported acne-related shyness and low self-esteem (78.2%) as the most serious problem caused in their quality of

<table>
<thead>
<tr>
<th>Table 1) Relationship of gender and family history with the mean score of quality of life and mean score of acne-related disability index</th>
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<tbody>
<tr>
<td><strong>Demographic characteristics</strong></td>
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<tr>
<td><strong>Gender</strong></td>
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<tr>
<td>Male</td>
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<tr>
<td>Female</td>
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<td><strong>Family history</strong></td>
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<tr>
<td>No</td>
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<tr>
<td>Yes</td>
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</table>
Table 2) Relationship between mean quality of life score and the index of acne-related disability

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean±SD</th>
<th>P-value</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatology Life Quality Index</td>
<td>7.32±5.87</td>
<td>&lt;0.001</td>
<td>0.73</td>
</tr>
<tr>
<td>The Cardiff Acne Disability Index</td>
<td>5.86±2.93</td>
<td></td>
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</tbody>
</table>

Table 3) Frequency and percentage of types of acne-related problems in affected patients during the past week (n=147)

<table>
<thead>
<tr>
<th>Acne related problems</th>
<th>Frequency (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itching, burning, pain (symptoms)</td>
<td>23.1(34)</td>
</tr>
<tr>
<td>Anger and embarrassment (self-esteem)</td>
<td>21.8(32)</td>
</tr>
<tr>
<td>Preventing daily activities</td>
<td>60.5(89)</td>
</tr>
<tr>
<td>Effect on clothing</td>
<td>50.3(74)</td>
</tr>
<tr>
<td>Impact on social and recreational activities (entertainment)</td>
<td>49.0(72)</td>
</tr>
<tr>
<td>Sport problems</td>
<td>76.2(112)</td>
</tr>
<tr>
<td>Working/schooling problems</td>
<td>66.0(97)</td>
</tr>
<tr>
<td>Problems in relationship with spouse and relatives</td>
<td>51.0(75)</td>
</tr>
<tr>
<td>Sexual problem</td>
<td>80.3(118)</td>
</tr>
<tr>
<td>Treatment problems</td>
<td>54.4(80)</td>
</tr>
</tbody>
</table>

Table 4) Frequency and percentage of specific responses from Acne Cardiff Disability Index (n = 147)

<table>
<thead>
<tr>
<th>Acne-related disability</th>
<th>Frequency(percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Aggression, embarrassment</td>
<td>20.4 (30)</td>
</tr>
<tr>
<td>2. Interference with social life</td>
<td>30.6 (45)</td>
</tr>
<tr>
<td>3. Avoidance of public changing facilities</td>
<td>57.8 (85)</td>
</tr>
<tr>
<td>4. Patient mental state</td>
<td>4.8 (7)</td>
</tr>
<tr>
<td>5. Perceived severity of acne</td>
<td>7.5 (11)</td>
</tr>
</tbody>
</table>

life (Table 3). Moreover, the results also showed that 35.4% (n=52), 52.4% (n=77), and 12.2% (n=18) of reported low, moderate, and severe acne-related disorder, mental distress (95.2%), including acne-related anxiety and grief was reported as the most serious disability and disorder (Table 4).

Discussion

The present study investigated the quality of life in acne patients referred to dermatological clinics in Qom using DLQI and CADI questionnaires. Although there were some differences between the two questionnaires, the correlation coefficient was obtained at r=0.73 in the current study. In the study conducted by Beheshi et al. (21) on students, the correlation coefficient was reported as r=0.72 (P<0.001). Moreover, in the study performed by Durai et al. (22), the correlation coefficient was estimated at r=0.73 (P<0.0001). The findings of the two above-mentioned studies were consistent with the results of our study signifying that acne-related disability increases with a more disrupted quality of life.

The results of the present study indicated the considerable impact of acne on patients’ quality of life. As revealed by the DLQI questionnaire, acne exerted major impacts on quality of life in 85.7% of cases. These complications had extremely high, high, moderate, low, and no effect on quality of life in 4.8%, 18.4%, 27.9%, 34.7%, and 14.3% of cases, respectively. The mean DLQI and CADI scores were obtained at 7.32 and 5.86, respectively, while the results were different in similar studies in other...
countries. In a study conducted by Inwalker et al. (23) in Scotland, the mean DLQI and CADI scores were measured at 1.7 and 1.9, respectively. In a study carried out by Hanisah et al. (24) on Malaysian students, the maximum CADI score was 13 with an average of 4. In the same vein, in a study conducted in Hong Kong (25), the mean score was reported as 2.56. Moreover, it is worthy to note that the quality of life was better in all of the three abovementioned studies.

The CADI score in the study performed by Safi Zadeh et al. (26) was 5.97 which is almost similar to the mean score of the present study. These differences can be ascribed to the sampling process which was based on those who referred to dermatology clinics. There is no doubt that a more severe disease or different behaviors can be expected from those patients who refer to physicians for the treatment of acne. On the other hand, in a study conducted by Abdul Hafiz et al. (27) in Egypt, the mean DLQI scores in men and women were reported as 11.9 and 15 demonstrating a worse quality of life, as compared to the current study. These differences can be attributed to differences in disease severity, cultural differences, and differences in expectations.

In the present study, no significant difference was found between quality of life and disease duration. This result indicates that the effect of acne on quality of life is not affected by disease duration, rather it depends on personal traits and the ability of patients to accept this disease and its associated problems. The results of a study conducted by Kokandi et al. (28) and Safi Zadeh et al. (26) were in agreement with the results of our study in this respect. Nevertheless, the results of the study performed by Hazarika et al. (29) were inconsistent with the results of the present study.

In the current study, gender showed no significant relationship with quality of life and acne-related disability which is consistent with the result of the studies conducted by Hanisah et al. (24), Yazici et al. (30), and Safi Zadeh et al. (26). Nonetheless, quality of life was reported to be better in males in a study performed by Law et al. (25) (16), while in the study conducted by Abdul Hafiz et al. (27), women had a higher quality of life. It is a dramatic result since it challenges the widely held belief that acne has less effect on boys. On the contrary, boys experience psychological problems and are worried about acne. Nevertheless, these results are inconsistent with previous studies which revealed more serious psychological disorders in girls (31,32).

In the current study, no significant relationship was observed between quality of life and educational level which is in contrast to the results of the study conducted by Safi Zadeh et al. (26). The mentioned study suggested that people with higher education had a better quality of life which can be ascribed to their better economic conditions. In other words, educated people are able to accept this disease and cope with its consequences due to their financial status. It is worth noting that this study may be affected by selection bias.

Acne can affect mood, self-esteem, and interpersonal relationships and can lead to depression and suicidal ideation (14, 33, 34). CADI subscales include aggression, frustration, interference with social life, avoidance of public changing facilities, and the appearance of the skin. In the current study, subscale analysis demonstrated that 79.6% of patients were confronted with special emotional problems (aggression/rage), and 69.4% of cases were faced with social problems.

In the study conducted by Hanisah et al. (24), 71.1% and 58.7% of adolescents were faced with problems in sensory logic (aggression) and social interventions/problems, respectively, which is relatively similar to the results of the present study. Notably, acne can exert profound effects on people’s emotions and interfere with their social lives. It is due to the fact that acne patients usually feel embarrassed and are less self-confident, as
compared to their peers or their opposite sex. Accordingly, they cannot fulfill their true potentials in everyday activities.

The results of the present study demonstrated that acne affects quality of life in 85.7% of patients based on the DQLI score. On the other hand, Safi Zadeh et al. (26) reported that acne exerted an effect on quality of life in 51.8% of patients based on the DQLI score. This difference can be attributed to race, demographic characteristics, study design, and questionnaires. Other studies have also revealed that acne can have a serious impact on body image, self-esteem, and socialization and may even trigger anger, anxiety, depression, and social dysfunction (15, 35, 36). The present study reported 76.8% of physical symptoms (itching, burning, pain), and 64.2% of acne patients reported physical symptoms in another study (21).

Reich et al. (36) attributed 50% of acne cases to itching, and Tasoula (37) pointed to itching as a physical symptom of acne in 25% and 33% cases of acne lesions on face and back, respectively. In the mentioned study, 78.2% of patients reported acne-related anger and embarrassment, while in the study conducted by Hazarika (29), 88% of cases reported anger and embarrassment. In the study carried out by Ogedegbe (38), 64.4% of patients were mentally impaired due to their skin flaws. The affected people may feel a sense of embarrassment and anger when comparing themselves to those without this disease.

In the present study, daily activity problems (e.g., shopping, house chores) were reported by 39.5% of acne patients. This value is much less than those reported by Hazarika et al. (29) who found that 69% of acne patients had difficulties in their daily activities. Nonetheless, it was in agreement with the results of a study performed by Beheshti et al (21). They reported that 39% of people were faced with problems in their daily activities and friendly relationships. Therefore, problems in daily activities may be attributed to avoidant behaviors, anger, and frustration. It can also impose more serious restrictions on the patients and increases the severity of the disease (29).

The image of everyone is judged by their clothing, and clothes are an important part of community acceptance. In our study, 49.6% of patients reported difficulty in choosing proper clothing to wear due to acne, whereas 21.3% of adults reported this difficulty in a study conducted in Greece (37). Along the same lines, in a study performed by Beheshti (21), 43.4% of patients had difficulty in choosing the proper clothing.

Acne patients attempt to minimize the appearance of their perceived flaw by covering it with clothing. In the present study, most women pointed out that they try to hide their disease with clothing. One of the reasons for the high impact of the disease on clothing in the current study is that affected people could not accept their disease and often try to cover it up. In the present study, 51% of patients reported that acne affects their social activities. This finding is less than the value reported in the study performed by Hazarika (29) who found that acne had a negative impact on social activities and leisure time in 68% of patients. Nonetheless, in a study conducted in Greece, 19.2% of students were influenced by acne in their social lives(37).

Another study performed on Scottish students showed that the personal and social lives of 20% of students were affected by acne (23). It would seem that acne may indirectly affect people's social activities by reducing self-esteem and self-confidence. In the present study, 23.7% of patients reported acne-related sports problems in agreement with the study conducted by Alazani (39) in which 23% of students had difficulty exercising. However, in a study conducted in Scotland, 10% of affected students were reluctant to go swimming or play other sports due to embarrassment (23). In the same sense, 14.4% of cases had difficulty with sport and exercise in a study.
performed by Tasula (37). Acne exerted a more profound effect on playing sport in the mentioned study, as compared to the other three studies. It can be attributed to the stigma surrounding the contagious nature of this disease in swimming pools.

In the present study, 34% of people referred to the negative effect of acne on work and study. On the other hand, in an Indian study, 57% of cases reported a negative effect (29), and 21% of patients reported that acne affected their work, schooling, and personal activities (27).

Walker et al. (23) also reported similar results in their study which investigated the negative effects of acne on work and education. The results of the mentioned study indicated a significant statistical relationship between this negative effect and the degree of acne (P<0.05). In this study, patients pointed out that they were constantly suffering from acne, which affected their ability to focus on study/work, thereby diminishing their concentration.

In the present study, 49% of cases reported serious problems in their relationships with their spouse and relatives, while this value was reported as 19.2% and 75% in studies conducted in Greece (37) and performed by Hazarika (29), respectively. Patients reported being constantly asked about their acne, even being abused by their peers and relatives. Accordingly, acne exerted a greater impact on life relationships in the current study, as compared to the Greek study. It can be due to the fact that acne patients exaggerate their disease and give greater importance to opinions and acceptance of others.

In the current study, 19.7% of people reported acne-related sexual problem; nonetheless, in a study conducted by Hazarika (29), only 5% of patients reported acne-related sexual problems. A statistically significant relationship was observed between sexual problems and the severity of acne in the mentioned study (P<0.05).

In the present study, 45.6% of people reported that home remedies were time-consuming and could interrupt their daily lives. In the same vein, in a study performed by Beheshti et al. (21), 45.2% of people pointed out that home remedies would waste time and disrupt life. In other words, people with acne vulgaris get immersed in the treatment of their diseases and spend most of their time on the treatment. Consequently, they become exhausted and withdraw from their treatment after a while.

The strengths of this study include the substantial number of individuals within the age range of 11-50 years and the use of self-report questionnaires. Most of the studies were conducted on high school or university students within a specific age range. In addition, these studies did not use self-report questionnaires. The answers in the current study are more reliable since patients would be embarrassed and avoided honesty if the questions were organized in an interview.

Finally, it is worth noting that the present study may have been influenced by selection bias since our sampling framework was limited to skin clinics rather than the general population. Furthermore, the majority of our study population were those with a high school diploma or higher who came from urban areas. Accordingly, the results of the study can be attributed to such factors as workplace environment urban life patterns which raise further concern about appearance. Therefore, this can be regarded as one of the limitations of the current study.

It is suggested that further studies be performed with a larger sample size. Moreover, given the high prevalence of acne, it is suggested that the investigation of psychiatric disorders in affected patients be practiced and performed in dermatology clinics.

### Conclusion

As evidenced by the obtained results, there is a significant relationship between quality of life and acne-related disability. The present study...
indicated the significant impact of acne and its complications on physical symptoms, emotions, daily and social activities, working/schooling, and interpersonal relationships.

Considering the abovementioned issues and the necessity of devoting special attention to this problem, it is recommended that health professionals and physicians be provided with necessary training on acne-related psychosocial and negative effects on quality of life. Moreover, it is suggested that they identify and track acne patients due to the side effects of low quality of life and self-esteem. The timely diagnosis and treatment of acne by physicians and dermatologists can be an important factor in the reduction of mental disorders and, in turn, the improvement of the quality of life in acne patients.

This article was extracted from a research project conducted in Qom University of Medical Sciences (ethical code: IR.MUQ.REC.1395.1200).

Footnotes

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Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this article.

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