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Quality of Life in Patients with Skin Disease and Their Cohabitants

Trinidad Montero-Vílchez, Manuel Sánchez-Díaz, Antonio Martínez-López and Salvador Arias-Santiago

Abstract

Health evaluation implies assess multidimensional aspects of a person's development, such as physical, social, psychological, and emotional features. It is important to consider all these factors to apply a needs-oriented each patient approach. Chronic skin diseases have a great impact on quality of life, even more than other chronic conditions. For example, hidradenitis suppurativa is estimated to impair quality of life more than cardiovascular disease, lung disease or endocrine diseases. Multiple tools have been developed to measure health-related quality of life in patient, being the Dermatology Life Quality Index (DLQI) the most used. Psoriasis, hidradenitis suppurativa, acne, atopic dermatitis and hair disorders are those with the greatest impact on patients' quality of life. Moreover, chronic skin conditions impair not only patients' quality of life, but also cohabitants. Nevertheless, there is scarce information regarding the impact on their cohabitants. So, the objective of this chapter is to review the literature to assess the psychological and social effects of dermatological conditions both on patients and cohabitants.

Keywords: Acne, Alopecia, Atopic Dermatitis, Cohabitants, Hidradenitis Suppurativa, Psoriasis, Quality of Life

1. Introduction

Health evaluation implies assess multidimensional facets of a person's development, such as physical, social, psychological and emotional aspects [1]. It is important to consider all these factors to apply a needs-oriented each patient approach. Chronic skin diseases have a great impact on quality of life, even more than other chronic conditions like asthma, epilepsy or diabetes [2]. Psoriasis, hidradenitis suppurativa, acne, atopic dermatitis and hair disorders are those with the greatest impact on patients' quality of life [2–4].

Multiple tools have been developed to measure health-related quality of life in patient, being the validated Dermatology Life Quality Index (DLQI) the most used. It evaluates the impact of skin symptoms of dermatological conditions and their treatment on patient's lives. The 10-item questionnaire covers the following aspects of patients' quality of life: symptoms and feelings, daily activities, leisure, work or school, personal relationships, and treatment. Each question is scored from 0 to 3 (not at all/not relevant (0), a little [1], a lot [2], and very much [3]) and

reflects the extent to which the person's life quality is adversely affected by the skin condition. The total score ranges from 0 to 30, and higher score reflects a greater impairment in patients' life [5]. The DLQI punctuation is interpreted 0–1 = no effect at all; 2–5 = small effect; 6–10 = moderate effect; 11–20 = very large effect; 21–30 = extremely large effect [6]. There are also other scales to assess anxiety, depression or sexual dysfunction that are also used to evaluate different aspects of patients' quality of life [6, 7]. The validated Hospital Anxiety and Depression Scale (HADS) is used to evaluate the prevalence of anxiety and depression. It is divided into two scales of seven items each. Scores equal or higher than 8 on the subscales are indicative of anxiety or depression [8]. The validated International Index of Erectile Function (IIEF-5) and the Female Sexual Function Index (FSFI-6) questionnaires are used to evaluate sexual dysfunction in men and women, respectively. Scores lower than 22 for IIEF-5 and lower than 20 are indicative of sexual dysfunction [9, 10]. Furthermore, to compare different diseases impact on quality of life or to compare several treatment improvements in patients' life, quality-adjusted life-year (QALYs) or global disability-adjusted life years (DALYs) are used [11, 12].

Chronic skin conditions impair not only patients' quality of life, but also cohabitants. In fact, it has been described caregiver burnout syndrome, expressing with stress, anxiety or depression what may impair people's life [13]. This means that the primary caregivers of a sick person are also affected by the disease. Although there is scarce information regarding the impact on cohabitants' quality of life, recently the Family Dermatology Life Quality Index (FDLQI) has been developed. It is a 10-item questionnaire that covers family member's perception of a certain specific impact on his/her quality of life over the last 1 month. Each item is scored on a four-point scale (0–3). The final score is calculated by summing the scores of individual items and ranges from 0 to 30. Higher total FDLQI scores indicate greater impairment of the family member's quality of life [14]. FDLQI could be interpreted similarly to DLQI: 0–1 = no effect at all; 2–5 = small effect; 6–10 = moderate effect; 11–20 = very large effect; 21–30 = extremely large effect.

The objective of this chapter is to review the literature to assess the psychological and social effects of dermatological conditions both on patients and cohabitants.

2. Material and methods

Search strategy. A literature search was performed using Medline, Scopus and Embase from conception to November 2020. The following search terms were used: ((Dermatology) OR (Skin diseases) OR (Alopecia) OR (Psoriasis) OR (Hidradenitis Suppurativa) OR (Acne) OR (Acne Inversa) OR (Atopic Dermatitis)) AND (Quality of Life).

Inclusion and exclusion criteria. The search was limited to: (i) human data, (ii) articles regarding impairment in quality of life in patients and cohabitants, (iii) articles written in English or Spanish. All types of epidemiological studies (clinical trials, cohort studies, case-control studies and cross-sectional studies) were included and analyzed. Reviews, guidelines, protocols, and conference abstracts were excluded. Skin conditions were selected regarding their high prevalence, their severity and their high impairment in quality of life. Psoriasis, hidradenitis suppurativa, atopic dermatitis, acne and alopecia were included. Only studies using validated scales to assess impairment in quality of life were included.

Study selection. Two researchers (TMV and MSD) independently reviewed the titles and abstracts of the articles obtained in the first search to assess relevant studies. The full texts of all articles meeting the inclusion criteria were reviewed, and their bibliographic references were checked for additional sources. The

articles considered relevant by both researchers were included in the analysis. Disagreements about inclusion or exclusion of articles were subjected to discussion until a consensus was reached. If not reached, resolution was achieved by discussion with a third researcher (SAS).

Variables. The variables assessed were number of participants and cohabitants, assent tools used to evaluate quality of life, risk factors associated with impairment in cohabitants' quality of life, general impairment in patients' quality of life.

Target audience. Clinicians and research are the main audience of this review. Doctors should be aware to consider patients and cohabitant impairment in quality of life when making treatment decisions. Moreover, research should include validate measure of patients and cohabitants quality of life in their investigations.

2.1 Psoriasis

Psoriasis is a chronic, recurrent, multi-systemic inflammatory disease that mainly affects the skin and the joints [15]. It is a multifactorial disease caused by a combination of immunological imbalance, genetic associations and environmental factors [16]. Its prevalence around the world has been estimated from between 0.51% and 11.43% [17], being more frequent in countries more distant from the equator [18]. In Europe, psoriasis prevalence is about 1.3% [19]. Furthermore, its incidence is increasing over the years [19, 20]. It has a bimodal age of onset (16 to 22 and 57 to 60 years) [21] and it affects both sexes similarly [18].

Psoriasis is considered a major global health problem [22]. Although, the skin manifestations are commonly the only recognized symptoms of psoriasis [20], this disease is associated with multiple comorbidities such as arthritis, cardiovascular disease, metabolic syndrome, depression, anxiety or inflammatory bowel disease [23–26]. All of them contribute to increase the morbimortality in these patients. In fact, similar to many chronic inflammatory diseases, the risk of early mortality in patients with psoriasis is increased, especially due to cardiovascular events [27]. Likewise, the risk of mortality from cardiovascular disease is higher in patients with more severe psoriasis [28]. Patients with psoriasis are also at increased risk of mental problems. Rates of anxiety, depression and even suicide are increased in these patients [29]. Psoriasis can also influence the interpersonal and sexual health of people with psoriasis [30]. Psoriasis therefore impacts on physical, emotional, and social patient's life [20]. Moreover, the economic burden of psoriasis is high, as in Europe the annual total cost per patient is between 6,000-12,000€ [31].

Furthermore, psoriasis has a great impact on cohabitants' life [6, 7, 32]. The presence of psoriasis impaired the quality of life in almost 90% of the cohabitants. FDLQI scores of cohabitants are associated with the DLQI scores of the patients. Moreover, an increased body surface area affected, and the genital and scalp location were associated with a higher FDLQI score while FDLQI scores were lower for cohabitants with higher professional/university education [6]. Disease severity and duration impact negatively on cohabitants' quality of life, anxiety and depression [6, 32]. In addition, after getting psoriasis, a reduction in the frequency of sexual intercourse occurred in more than 90% of the relationship and 40% of psoriasis partners suffer from sexual dysfunction [7, 32].

Multiple treatments are effective for treating psoriasis, including topical medications, phototherapy, oral systemic medications, and biologics [33]. Mild psoriasis can be treated with topical corticosteroids or corticosteroids plus vitamin D analogues. Moderate psoriasis needs to be treated with systemic treatments, such as methotrexate, acitretin or cyclosporine, or phototherapy. If psoriasis is severe or treatment-resistant, biologics are indicated. There is a wide range of biologics therapies for treating psoriasis: TNF α (etanercept, adalimumab, infliximab,

certolizumab), IL12/23 inhibitors (ustekinumab), IL23 inhibitor (guselkumab, risankizumab, tildrakizumab), IL17 inhibitors (secukinumab, ixekizumab, brodalumab) [34]. The economic outcomes of these targeted treatments have been compared with non-targeted ones. The incremental benefits compared with no targeted treatment are, in descending order: ixekizumab 1.68 QALYs, brodalumab 1.64 QALYs, secukinumab 1.51 QALYs, ustekinumab 1.43 QALYs, infliximab 1.27 QALYs, adalimumab 1.15 QALYs, etanercept 0.97 QALYs, and apremilast 0.87 QALYs. Initial targeted treatment with IL-17 inhibitors seems to be the most effective treatment strategy for plaque psoriasis patients who have failed systemics [11].

2.2 Hidradenitis suppurativa

Hidradenitis suppurativa (HS) is a chronic, recurrent, debilitating inflammatory skin disease of the hair follicle that usually presents after puberty with painful, deep-seated inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axillae, inguinal and anogenital regions [35]. A prevalence rate of around 1% has been estimated [36], of 0.03–1% in Europe [37–39] and of 0.053% in the USA [40].

Its etiopathogenesis is still elusive and may be of pivotal importance in improving patients and relative's quality of life. Genetic susceptibility, smoking, obesity and hormonal disorders are major risk factors for the development of HS [41]. Moreover HS, has been associated with multiple physical comorbidities such as spondylarthritis, inflammatory bowel disease and increased cardiovascular risk [42, 43]. Moreover, HS impairs patients' mental health. It has been related to higher levels of depression, anxiety, worse quality of life, sexual dysfunction and a higher suicide risk [44–47]. HS also has consequences on social relationships and professional careers, as high rates of absenteeism and unemployment have been reported in HS patients [43]. For all these reasons, HS is a stigmatizing and disabling disease that greatly impairs physical, emotional, and social patient's life. Moreover, the economic burden of HS is high [48]. Direct medical costs due only to surgery are around £2,000 per patient per year in the UK [49]. Indirect costs, for expel associated with frequent and long-term absenteeism and disability, have also a great impact on the health system [50].

Moreover, HS has a great impact on cohabitants' life as they are involved in patients' caregiving [51–53]. A positive association between the Dermatology Life Quality Index (DLQI) and the Family Dermatology Life Quality Index (FDLQI) has been observed [52]. The most affected areas are emotional distress (depression, anxiety, embarrassment), social life and routine household expenditure [53]. In fact, patient's anxiety and depression and higher score for negative affectivity are associated with a lower quality of life in their cohabitants [52]. Disease severity also impairs both patients and cohabitants life due to skin symptoms (disease duration, pain, more involved locations), the need of continuous care and more unpleasant treatments and a higher economic expenditure [51]. In addition, a great impact is found in partners or husband/wife compared with parents, leading to a potential effect on the couple relationships [51]. In fact, patient sexual dysfunction greatly impairs cohabitant's quality of life [52]. On the other hand, higher educational level and an early diagnosis and treatment have a positive impact on patients and their partners' life [51–53].

HS therapy is often challenging and requires the combination of medical and surgical treatments [54, 55]. Medical treatment of mild disease consists in topical clindamycin 1% solution/gel twice a day for 12 weeks or, for a more widespread disease, tetracycline 500 mg daily for 4 months. If patient do not respond or for moderate-to-severe disease, clindamycin 300 mg with rifampicin 600 mg daily for

10 weeks would be considered [56]. Adalimumab, a monoclonal antibody against tumor necrosis factor- α , is the only biologic agent currently available for treating moderate to severe HS, but a primary or secondary lack of response has been observed in some patients [57]. New insights into the pathogenesis of HS reveal an inflammatory cytokine profile including elevated levels of (TNF)- α , interleukin (IL)-1 β , IL-17 or interferon (IFN)- γ and other biologic treatments such as bimekimab, bimekizumab, brodalumab, guselkumab, risankizumab or secukinumab are being tested in clinical trials [58]. There is scarce evidence regarding cost-effectiveness therapies in HS. It has been estimated that the incremental cost-effectiveness ratio for adalimumab versus standard care was around £30,000 per QALY gained [59]. Nevertheless, its cost-effectiveness was highly susceptible to the health states' utility values, the treatment discontinuation and the resource utilization [60].

2.3 Acne

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit that usually presents at adolescence with comedones (blackheads and whiteheads), papules, pustules, nodules, cysts and scars. The most affected areas correspond to the highest density of pilosebaceous units (face, neck, upper chest, shoulders, and back) [61]. It is a prevalent condition that involves 85% of adolescents and 6–10% of the general population [62].

Acne is a multifactorial disease resulting from androgen-induced disturbed sebaceous gland activity associated with increased sebum production and alterations in sebum fatty acid composition, altered keratinisation, inflammation, *Propionibacterium acnes* colonization of hair follicles and dysfunction of the innate and adaptive immunity [63]. Genetic susceptibility, air pollution, aggressive skincare products, corticosteroids and hormonal products are risk factors to develop acne. The role of nutrition in acne pathogenesis is still controversial [64]. Acne is associated with physical disability due to painful skin lesions. Moreover, it usually affects visible areas, with risk of permanent scarring and aesthetic consequences. In fact, acne is associated with high rates of anxiety, depression and even suicide [65, 66]. People with acne are also more prone to have social phobia [67].

Acne not only impairs patients' life but also their cohabitants. More than 90% of people leaving with acne patients have impaired their quality of life. A positive correlation between FDLQI in cohabitants and DLQI in patients is observed. Furthermore, patients' level of depression and anxiety are also associated with their cohabitants' [68].

Acne treatment is based on disease severity, patient preference, site of involvement, age of the patient and tolerability. Topical therapies may be used as monotherapy, in combination with other topical agents or in combination with oral agents in both initial control and maintenance. The most employed topical products are benzoyl peroxide, salicylic acid, antibiotics, combination antibiotics with benzoyl peroxide, retinoids, retinoid with benzoyl peroxide, retinoid with antibiotic, azelaic acid, and sulfone agents. Systemic antibiotics are used in moderate to severe inflammatory acne and should be used in combination with a topical retinoid and benzoyl peroxide. Tetracycline, mainly doxycycline and minocycline, are the most effective antibiotics. Oral contraceptives can improve acne for many women, mainly in those with clinical or laboratory signs of hyperandrogenism. Oral isotretinoin is indicated for severe acne or moderate treatment-resistant acne [69]. The effectiveness and cost effectiveness of isotretinoin are well proven as its cost per QALY of £898 (\$US 1374) is affordable [70]. Dermatologist treatment appears cost-effective related to producing additional QALYs at a cost of \$40,000 per QALY gained [71].

2.4 Atopic dermatitis

Atopic dermatitis (AD) is a common and chronic inflammatory skin disease. It is characterized by recurrent eczematous lesions and intense itch which develop in people of all ages and ethnicities. The prevalence of AD has been estimated around 12% in children and 7% in adults in United States [72]. It is considered the leading non-fatal health burden attributable to skin diseases [73]. The etiopathogenesis of AD is not completely understood. However, most studies agree that skin barrier dysfunction and immune dysregulation play a key role in the development of AD [74, 75]. Genetic polymorphisms in the filaggrin gene, which encode a major structural protein in the stratum corneum, upregulation of Th2 cytokines, such as IL-4 and IL-13, changes in the skin microbiome and altered lipid composition are thought to be responsible for the appearance of pruritus and skin lesions in patients suffering from AD [75–78].

AD is frequently associated with food allergy, asthma and rhinitis, which is also known as the “atopic march”. This concept refers to the propensity for AD to begin early in life and be followed by the serial incidence of food allergy, asthma, and hay fever [79]. Other associated conditions include eosinophilic esophagitis [80], allergic contact dermatitis [81], cardiovascular disease [82] and infections [83, 84].

Skin lesions and severe symptomatology, including severe itch and skin pain, contribute to an impaired quality of life in patients suffering from AD. Psychosocial distress, stigma, sleep disturbance avoidance of social interaction are consequences of AD [85]. Significantly poorer dermatology-related quality of life scores have been found in patients with AD: higher DLQI [86] and Children’s DLQI [87], greater Skindex affectation [88] and itch-related quality of life [89]. Different general quality of life scores are also affected in patients with AD [86, 87, 89]. Furthermore, the impact on quality of life is not restricted to the patient itself, but also affects to their cohabitants. It has been shown that parents of children with AD have lower quality-of-life scores [90–92] and that AD influences marital conflicts [93]. Regarding the sexual health, there is evidence that AD have a strong impact in sexual behavior. The involvement of visible areas and sensual areas leads to lower quality of life indexes and higher burden scores in patients with AD [94]. Moreover, people with more severe AD have a greater impact on sexuality [94, 95].

Given its high burden, AD have been associated with high QALY loss, even higher than autoimmune disorders, diabetes, food allergy and heart disease in both males and female [96]. Moreover, six-dimensional health state short form (SF-6D) score, an utility score which ranges from 0 (worst health) to 1 (best health) was estimated to 0.63 in severe AD. This was lower than SF-6D in high blood pressure (0.63), diabetes (0.65) and similar to anxiety, depression and heart disease (0.63) [96].

The treatment of AD follows a stepwise approach that is tailored according to disease severity and extension [85, 97]. Patient’s education and basic skin care must be carried out in all patients, including those without active skin lesions. It consists of the frequent application of skin moisturizers, warm baths or showers using non-soap cleansers and avoidance of skin irritants. For mild and localized disease, treatment involves the use of topical corticosteroids (TCS) and topical calcineurin inhibitors (TCI). For moderate-to-severe and extensive disease, phototherapy or systemic drugs are indicated. Systemic immunosuppressants, such as cyclosporine, methotrexate, azathioprine and mycophenolate mofetil can be used [75, 85]. Dupilumab, a monoclonal antibody which acts as a targeted therapy for AD, is currently the most effective therapy for severe AD. It acts through the blockage of the IL-4 receptor alpha-chain [85, 98]. Emerging therapies include anti IL-13 and anti IL-31 antibodies, JAK inhibitors, and inhibitors of PDE-4 [85, 98].

Finally, AD places a high financial burden on patients, families and society through direct medical costs and decreased productivity. Taking this into account, a conservative estimate of the annual costs of atopic dermatitis in the United States (2015) is \$5.297 billion [99]. Regarding the current development of novel treatments, which involve higher costs [100], these costs are likely to increase over the time.

2.5 Alopecia

Alopecia is a heterogeneous group of common skin disorders. This group can be divided into two minor groups: a) Non-cicatricial alopecia: Follicular epithelium is not replaced by connective tissue, so it is potentially reversible; b) Cicatricial alopecia: Follicular epithelium is replaced by connective tissue, so it is assumed that permanent injury of the follicular stem cell region has occurred.

2.5.1 Non-cicatricial alopecia

Many different skin conditions can be classified into this category. Most common and most representative non-cicatricial alopecia will be reviewed below.

2.5.1.1 Androgenetic Alopecia (AGA)

AGA is an androgen-dependent hereditary disorder resulting from the conversion of scalp terminal hairs into miniaturized vellus hairs in a characteristic pattern. Androgens act on the epithelial cells of genetically susceptible hair follicles in androgen-dependent areas, leading to follicular miniaturization [101]. Its frequency and severity increase with age, with at least 80% of Caucasian men and 50% of women showing signs of AGA by age 70 years [102, 103]. In male pattern hair loss, there is a progressive loss of hair in the frontal and bitemporal line, and also in the vertex. In the female pattern hair loss, the frontal hairline is spared with a diffuse central thinning of the crown.

In some studies, AGA has associated to age and family history of AGA. Moreover, some factors related to metabolic syndrome have also been related to AGA in both genders: Hypertension, diabetes mellitus and waist circumference [104].

As AGA is frequent and affects a visible area such as the scalp, it can lead to a significant impairment in the quality of life and social inhibition in patients. There is evidence of the impairment in quality-of-life scores in both males and female suffering from AGA: DLQI [105–107], Hairdex scale [105] and Skindex-29 scale [106]. Moreover, AGA has a negative impact on sexual function in premenopausal women, reflected in a decreased FSFI compared to healthy females [108].

Only two therapeutic agents have been approved by the Food and Drug Administration and European Medicines Agency for the treatment of AGA: Topical minoxidil (in both males and females), and oral finasteride (in males) [109]. Minoxidil was first introduced as an oral treatment for severe hypertension in the 1970s [110]. When hypertrichosis was observed as a side effect of this medication, both topical and oral formulations of minoxidil were developed to treat alopecia. Minoxidil changes the micro-environment of the hair follicle, inducing a prolonged anagen phase and increased hair growth. Most common presentations of topical minoxidil include 2% and 5% lotions which are applied 1 ml/12 hours. Although oral minoxidil seems to be effective to treat AGA, it is not yet approved [111]. Oral finasteride is approved for AGA in men with a dosage of 1 mg/24 hours. It acts through the inhibition of 5- α reductase and is effective and safe [109] in the treatment of AGA.

2.5.1.2 Alopecia Areata (AA)

AA is a common inflammatory hair loss, characterized by an autoimmune-mediated hair follicle destruction, due to the upregulation of inflammatory pathways. The lifetime incidence of AA is approximately 2% worldwide [112]. The etiology is still not fully understood, but the loss of immune privilege in the hair follicle seems to play a crucial role in the development of AA [113]. Clinical features of AA vary from the appearance of small, well-circumscribed patches of hair loss to a complete absence of body and scalp hair.

As AA is an autoimmune disorder, patients suffering from AA have a higher risk of developing autoimmune diseases: thyroid disorders [112, 114], with an incidence in AA between 2,3-14,6%; diabetes mellitus, with an incidence in AA between 0,4-11,1% [115]; and vitiligo, with an incidence in AA between 1,8-7,0% [115] are some of the most common. AA have also been associated with atopic diseases, metabolic syndrome, *Helicobacter Pylori* infection, and vitamin D deficiency [116]. Moreover, a 66–74% of lifetime prevalence of psychiatric disorders have been reported in AA patients, with a 38–39% lifetime prevalence of depression and a 39–62% prevalence of generalized anxiety disorder [117–120].

Regarding the quality of life in people suffering from AA, there is increasing evidence of the strong impact of AA in quality-of-life scores, which affects up to 76.7% of children and 77.6% of adults [121]. Impairments in DLQI as well as in alopecia specific scores have been reported [115, 121, 122]. Role-emotional, mental health and vitality domains seem to be the most affected [121]. Moreover, scalp involvement, anxiety and depression have a negative impact on the quality of life of patients with AA [121]. AA also impacts on sexual quality of life [123]. One study showed that both males and females suffering from AA had decreased sexual quality of life with low Sexual Quality of Life for Females (SQOL-F) and Sexual Quality of Life for Males (SQOL-M) scores. In this study, men strongly identified with the statement “I fell anxious” and women with the statement “I feel embarrassed”.

Preliminary outcomes of a research conducted in the Hospital Virgen de las Nieves (Granada, Spain), which were presented at the national congress of the Spanish Dermatology Academy showed also a significant burden in cohabitants of patients with AA. Cohabitants of patients with AA had high FDLQI scores, which correlated to DLQI from patients. Anxiety in cohabitants also showed correlation with the time of evolution of the disease [124].

There are different therapeutic options for AA, depending on the age of the patient and the extension of the disease. Briefly, in adult patients suffering from isolated patches of hair loss or less than 25% of scalp hair loss are the best candidates to therapy with intralesional injections of potent corticosteroids (such as triamcinolone). In the case of adult patients who refuse the injections and children, potent topical corticosteroids (betamethasone, clobetasol) are considered the first-line therapy. An alternative for mild cases is the use of topical anthralin. When AA is extensive, systemic drugs are recommended. Systemic corticosteroids taken in low doses can be effective but involve serious long-term adverse events. Other systemic immunosuppressive agents can be useful in AA: methotrexate or azathioprine. JAK inhibitors (tofacitinib, baricitinib) are novel promising therapies for severe cases of AA [125, 126].

2.5.2 Cicatricial alopecia

A wide variety of diseases can be classified into this group, both primary skin diseases and secondary cicatricial alopecia. Given that most of cicatricial alopecia are relatively uncommon, there is scarce evidence regarding their comorbidities and

their treatment. Moreover, almost any studies report data about the impairment in quality of life associated with these skin disorders.

Few studies address the issue of quality of life in patients with Frontal Fibrosing Alopecia (FFA) [127]. FFA is a cicatricial alopecia, typically appearing in post-menopausal woman, characterized by slowly progression of hair loss in the frontal, temporal or frontotemporal scalp and eyebrows. Hair follicles show perifollicular erythema and scale. Patients with FFA have been found to show impairments in DLQI, and anxiety and depression scores [127].

Preliminary outcomes of a research conducted in the Hospital Virgen de las Nieves (Granada, Spain), which were presented at the national congress of the Spanish Dermatology Academy showed a significant burden in cohabitants of patients with FFA. Cohabitants of patients with FFA had high FDLQ) scores, which correlated to DLQI from patients. Anxiety in cohabitants also showed correlation with the time of evolution of the disease. However, the impact on the quality of life in cohabitants of patients with FFA was lower than the impact on the cohabitants of patients with AA [124].

3. Discussion

Skin diseases have a great impact on patients and cohabitants quality of life. Clinicians should be aware of this issue so they can provide an individualized medicine, targeting not only the visible symptoms of the disease but also the impact on quality of life. Researchers should also include quality of life impairment scales for patients and cohabitants to measure the effectiveness of treatments. Universal scales are needed to homogenize results. Further research regarding skin conditions should include the impact of both patients and cohabitants' quality of life assessed by validate scales. Moreover, healthcare policy should also consider not also patients' needs but also cohabitants'.

The most common tools to assess impairment in quality of life were the DLQI (for patients) and the FDLQI (for cohabitants), **Table 1**. HS and psoriasis are the diseases that have a greater impact on patients and cohabitant quality of life. The media DLQI scores for HS was 13.34 points and the media FDLQI was 9.76 points [51–53]. Psoriatic patients reported a media of 10.79 points in the DLQI and their cohabitants reported a media of 12.8 points in the FDLQI [6, 7, 32]. The greater impairment of this disease could be explained because of the symptoms, chronicity and comorbidities associated. The clinical manifestations of HS cause pain, itching, malodor and suppuration, among other symptoms, which make life difficult for patients [35]. Pain is one of the most important problems in patients with HS, usually related to the inflammation of the nodules. Psoriatic plaques are also associated with itching and pain what cause an important physical burden in patients [15]. The lesions of these disease frequently appear on the genital area, having an impact on sexual life [15, 35]. The sexual impairment could also explain the great cohabitants impairment of quality of life [6, 52], apart from the chronicity of this disease and the caregiver burnout syndrome. The following disease with higher points in the DLQI was AD (media of 10.78) [86, 87, 89]. This could also be explained because of the itching and the sleep disorder associated with this disease [79]. Acne and alopecia were scored with the lowest rate quality of life impairment. Acne patients scored a media of 7.56 points in the DLQI and their cohabitants a media of 6.46 in the FDLQI [68]. This could be explained because it is a disease that usually happens in adolescent and it is temporary [65]. Alopecia patients recorded a media of 6.1 points in the DLQI and their cohabitants a media of 6.13 points [124]. This might be explained because they are not usually associated with other symptoms and

Disease	Article	Number of patients/ cohabitants included	Assessment tools used to evaluate quality of life	Patients	Cohabitant	Risk factor associated with impairment in cohabitants’ quality of life	General impairment in patients’ quality of life
Psoriasis	Martinez-Garcia E et al. 2014	34/49	DLQI	12 (range 1–28)	—	Negative factors: DLQI, marital status, cohabitants’ anxiety, severe psoriasis, a long disease duration, genital and scalp location. Protective factors: Higher professional/university education	Increased risk of other diseases: arthritis, cardiovascular disease, metabolic syndrome, inflammatory bowel disease. Increased risk of mental problems: anxiety, depression, suicide. Impaired social life: interpersonal and sexual health., economic burden.
			FDLQI	—	8.82 (range 0–30)		
			IIEF-5/ FSFI-6 (sexual dysfunction, %)	79.1% females, 19.1% males	54.5% females, 59.2% males		
	Halioua, B et al. 2020	184/184	DLQI	9.57 (6.35 SD)	—	Negative factors: patients’ quality of life, cohabitants’ mental health, patient disease severity	
			FDLQI	—	16.78 (9.96 SD)		
	Hidradenitis suppurativa	Ramos-Alejos- Pita C et al. 2020	27/27	DLQI	13.88 (SD 9.53)	—	Negative factors: patients’ BMI, IHS4, impairment in patients’ quality of life, patients’ negative affectivity, patients’ depression, sexual dysfunction, partners’ sexual dysfunction
FDLQI				—	10.48 (SD 7.76)		
IIEF-5/ FSFI-6 (sexual dysfunction)				18.26 (SD 6.28)	20.82 (SD 6.51)		
Wlodarek K et al. 2020		50/50	FDLQI	—	8.7 (SD 6.8)	Negative factors: patient’s and partner’s age, Hurley stage, HSSI	
Marasca C et al. 2020		35/70	DLQI	12.8 (SD 4.48)	—	Negative factors: DLQI, Hurley stage, partner relationship Protective factors: Higher professional/university education	
			FDLQI	—	10.11 (range 0–19)		

Disease	Article	Number of patients/ cohabitants included	Assessment tools used to evaluate quality of life	Patients	Cohabitant	Risk factor associated with impairment in cohabitants' quality of life	General impairment in patients' quality of life
Acne	Martinez-Garcia E et al. 2014	62/66	DLQI	7.56 (range 0–29)	—	Negative factors: impairment in patients' quality of life, acne duration, cohabitant's anxiety level.	Physical disability: painful lesions. Mental health: high rates of anxiety, depression and suicide. Impaired social life: aesthetic consequences, social phobia.
			FDLQI	—	6.46 (range 0–26)		
Atopic dermatitis	Xu X et al. 2019	559 / 559	IDQOL	8.76 (SD 2.6)	—	Negative factors: Higher CDLQI and IDQOL, severity of the disease, and children's age.	Age and severity of the disease was related to lower quality of life in children. Patients have an increased risk of food allergies, asthma, hay fever, eosinophilic esophagitis, allergic contact dermatitis, cardiovascular disease and infections.
			CDLQI	8.76 (SD 2.2)	—		
			RAND-36	—	38.52 (SD 7.16)		
	Ezzedine K et al. 2020	399 / 399	CDLQI	8.7 (SD 7.1)	—	Negative factors: Children's age, higher CDLQI and DLQI, shorter disease duration, younger parents.	
			DLQI	12.8 (SD 11.1)	—		
			ABS-F	—	10.0 (SD 8.0)		
	Gieler U et al. 2017	64 / 64	GDS, QPCE.	—	.	Negative factor: Being a single mother of a child with atopic dermatitis led to higher perceived stress in the family and less life-satisfaction when compared to mothers with partners.	
	Jang HJ et al. 2016	78 / 78	DFI	—	—	Negative factors: Severity of the disease, children's female gender, parent's stress and negative affect led to lower family quality of life.	

Disease	Article	Number of patients/ cohabitants included	Assessment tools used to evaluate quality of life	Patients	Cohabitant	Risk factor associated with impairment in cohabitants' quality of life	General impairment in patients' quality of life
Alopecia Areata	Arias-Santiago S et al. 2020 (preliminary outcomes)	16 / 16	DLQI	6,5	—	Negative factors: The evolution time of the diseases led to higher anxiety and depression scores in cohabitants. Higher FDLQI correlates to higher anxiety and depression scores	Patients with AA have higher risk of thyroid disorders, diabetes mellitus, vitiligo, atopic diseases, metabolic syndrome, Helicobacter Pylori infection, and vitamin D deficiency. There is a 66–74% of lifetime prevalence of psychiatric disorders (depression and prevalence of generalized anxiety disorder).
			FDLQI	—	7,25 (SD 4,89)		
Frontal Fibrosing Alopecia	Arias-Santiago S et al. 2020 (preliminary outcomes)	15 / 15	DLQI	5,7	—	Negative factors: The evolution time of the diseases led to higher anxiety and depression scores in cohabitants. Higher FDLQI correlates to higher anxiety and depression scores	There is scarce evidence regarding the comorbidities of FFA. Patients with FFA have been found to show impairments in DLQI, and anxiety and depression scores.
			FDLQI	—	5		

ABS-F: Atopic dermatitis Burden Scale-Family; CDLQI: Children's Dermatology Quality of Life Index; DFI: Dermatitis Family Impact questionnaire; DLQI, Dermatology Life Quality Index; FDLQI, Family Dermatology Life Quality Index; GDS: General Depression Scale; HSSI, Hidradenitis Suppurativa Severity Index; IDQOL: Infant's dermatitis quality of life; IIEF-5, International Index of Erectile Function; QPCAE: Questionnaire for Parent so Children with Atopic Eczema; SFI-6, Female Sexual Function Index;.

Table 1.
Articles regarding quality-of-life impairment in patients with skin diseases and cohabitants.

some types of alopecia, such as alopecia areata, are not chronic and patients can be completely recovered from its disease [125].

Regarding psychological impact of patients and cohabitants, HADS-A and HADS-D are the most frequent scales used, **Table 2**. The highest rates of patient’s anxiety are reported for HS (9.51) and psoriasis (8.82), followed by frontal fibrosing alopecia (7.5), acne (6.9) and alopecia areata (6.6). The highest rates of cohabitants

Disease	Article	Number of patients/ cohabitants included	Assessment tools used to evaluate quality of life	Patients	Cohabitant
Psoriasis	Martinez-Garcia E et al. 2014	34/49	HADS-Anxiety	8.82 (range 1–18)	8.06 (range 0–16)
			HADS-Depression	6.15 (range 0–19)	4.73 (range 0–14)
			Rosenberg’s Self-Esteem Questionnaire (<15, %)	78.2% females, 31.8% males	56.6% females, 40.8% males
	Halioua, B et al. 2020	184/184	MCS-12	41.94 (SD 10.35)	45.50 (SD 11.00)
			PSC-12	45.57 (SD 5.63)	44.92 (SD 5.75)
	Alariny AF et al. 2019	120/120	HADS-A (> 7, %)	69.1% females, 39.1% males	63.6% females, 51% males
HADS-D (> 7, %)			39.1% females, 21.8% males	45.5% females, 34.7% males	
Hidradenitis suppurativa	Ramos-Alejos-Pita C et al. 2020	27/27	HADS-Anxiety	9.51 (SD 4.89)	7.22 (SD 4.20)
			HADS-Depression	7.70 (SD 5.11)	5.14 (SD 4.52)
Atopic Dermatitis	Gieler U et al. 2017	64 / 64	SSQ, SWLS.	—	—
	Jang HJ et al. 2016	78 / 78	SWLS, PANAS	—	—
Acne	Martinez-Garcia E et al. 2014	62/66	HADS-A	6.29 (range 0–15)	6.91 (range 1–19)
			HADS-D	2.47 (range 0–11)	4.23 (range 0–16)
Alopecia Areata	Arias-Santiago S et al. 2020 (preliminary outcomes)	16 / 16	HADS - Anxiety	6.6	6.5
			HADS - Depression	4.9	6
Frontal Fibrosing Alopecia	Arias-Santiago S et al. 2020 (preliminary outcomes)	15 / 15	HADS - Anxiety	7.5	4.5
			HADS - Depression	4.1	3

HADS, Hospital Anxiety and Depression Scale; MCS-12, Mental Health Subscale; PANAS: Positive Affect and Negative Affect Schedule; PCS-12, Physical Health Subscale; SWLS: Satisfaction With Life Score; SSC: Short Stress Questionnaire.

Table 2.
Articles regarding psychological impairment in patients with skin diseases and cohabitants.

anxiety are reported for psoriasis (8.06), followed by HS (7.22), acne (6.91), alopecia areata (6.5) and frontal fibrosing alopecia (4.5). Depression was rated lower than anxiety in all diseases. Patients reported the highest rates for HADS-Depression in HS (7.7) and psoriasis (6.15), followed by alopecia areata (4.9), frontal fibrosing alopecia (4.1) and acne (2.47). Cohabitants reported the highest rates for HADS-Depression in alopecia areata [6], HS (5.14), psoriasis (4.73), acne (4.23) and frontal fibrosing alopecia. Up to our knowledge, there are no reports regarding the impact of AD in cohabitants anxiety and depression. In agreement with DLQI and FDLQI scores, psoriasis and HS are the diseases that have the greatest impact on patients and cohabitants anxiety [6, 7, 32, 51–53]. Regarding depression, patients' reports are in agreement with anxiety and DLQI scores. Nevertheless, cohabitants reported the highest scores for anxiety in alopecia areata [124]. This might be due because most alopecia areata patients are children and their hair loss negatively affect their parent's psycho [112].

4. Conclusion

Since skin lesions are visible and can generate unpleasant sensations, such as itching or pain, skin diseases are a major cause of decreased quality of life. In addition, the involvement of areas with a high emotional burden, such as the genital area, scalp or facial area can lead to social inhibition, anxiety and depression. Studies focused on the evaluation of the quality of life of patients and cohabitants with skin diseases and their co-habitants are necessary to objectify the great burden they bear. Therefore, it seems necessary to make a comprehensive approach to skin diseases, taking into account not only the medical aspect, but also the emotional and the quality of life of both patients and cohabitants.

The holistic approach of the skin disease requires the complete evaluation of patients and cohabitants, from the biological, psychological and social point of view. This approach should include specific evaluations of quality of life and related disorders in all patients and cohabitants, which will lead to a better quality of the health of the populations. Moreover, therapeutic methods aimed at improving the quality of life such as patient schools, cognitive-behavioral strategies or mindfulness should be implemented in the daily clinical practice to treat not only the biologic, but also the social and psychologic manifestations of skin diseases.

Conflict of interest

The authors have no conflict of interest to declare.

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Author details

Trinidad Montero-Vílchez^{1,2}, Manuel Sánchez-Díaz^{1,2}, Antonio Martínez-López^{1,2}
and Salvador Arias-Santiago^{1,2,3*}

1 Dermatology Department, Hospital Universitario Virgen de las Nieves, Granada, Spain

2 Instituto de Investigación Biosanitaria IBS, Granada, Spain

3 Dermatology Department, Faculty of Medicine, University of Granada, Granada, Spain

*Address all correspondence to: salvadorarias@ugr.es; salvadorarias@hotmail.es

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