

## CLINICAL REPORT

# Severe Impairment of Quality of Life in Hailey-Hailey Disease

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**Hailey-Hailey disease (a skin fragility disorder) runs a chronic course and may cause important disability. However, little has been formally investigated concerning the quality of life (QoL) of patients affected by this disorder. We studied the impact of Hailey-Hailey disease on the QoL of 22 consecutive patients seen at our dermatological clinic. Patients were examined by a dermatologist, and they were asked to complete two self-administered questionnaires: the Skindex-29, in order to determine their QoL, and the 12-item General Health Questionnaire, to evaluate psychological distress. Completed questionnaires were returned by 20 patients. Even in patients with few body sites involved, median overall QoL scores were much higher than those observed in other skin conditions in all three domains investigated by the Skindex-29 (i.e. symptoms, emotions and social functioning). This was true also for the levels of psychological distress. QoL impairment was substantial irrespective of the number of body sites involved. Our findings document a great impact of Hailey-Hailey disease on patients' QoL. Therefore, a more aggressive therapeutic approach may be warranted in all patients, including those with few lesions. *Key words: Hailey-Hailey disease; familial benign chronic pemphigus; skin diseases; quality of life.***

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Hailey-Hailey disease (familial benign chronic pemphigus), first described by Hailey & Hailey in 1939 (1), is a rare blistering disorder characterized by recurrent vesicles and erosions particularly involving the flexural areas. The underlying gene defect has been localized to chromosome 3q21 with mutations in the gene ATP2C1 encoding a novel Ca<sup>2+</sup> pump (2, 3). The mechanism by which mutant ATP2C1 causes acantholysis is unknown, but it may be through abnormally elevated cytoplasmic calcium or abnormally low Golgi Ca<sup>2+</sup> levels. The disease is dominantly inherited and a great variation in the pattern and severity within families is observed. Generally, patients first experience lesions in the second to third decade of life. The disease runs a chronic relapsing course with attenuation at older age. Most

individuals have a disease of relatively limited extent, although widespread and severe involvement can occur. The most commonly affected sites are the folds such as the axillae, groin, neck and sub-mammary regions; however, lesions can also occur on extra-fold areas such as the trunk and abdomen. Mucosal surfaces are only exceptionally involved. The presence of longitudinal white streaks in the nails has recently been emphasized (4). The mainstays of therapy include anti-infective agents administered either topically or systemically combined with topical corticosteroids. Recently, topical tacrolimus ointment, photodynamic therapy with 5-aminolevulinic acid, and injection of botulinum toxin type A have been shown to be effective in some cases (5–9).

Although the clinical features of this condition are well known, only rarely has a description of the burden that this disease places on the patients been attempted (10). In this article, we investigated how Hailey-Hailey disease affects quality of life (QoL) in terms of symptoms, emotions and social functioning, and psychological well-being.

## METHODS

All patients hospitalized in our institute between January 2001 and February 2003 for whom a diagnosis of Hailey-Hailey disease was ascertained were included in the study. They were examined by a dermatologist, and underwent a routine haematological analysis, a histological examination of a cutaneous specimen, direct and indirect immunofluorescence studies, and other instrumental examinations (e.g. chest X-rays) whenever required from the clinical investigation. Age and sites affected at onset and at hospitalization, as well as every associated disease, trigger factors (e.g. friction, heat, sweat), and all therapies administered were also recorded.

To measure QoL we chose a dermatology-specific instrument because a disease-specific scale for rare diseases is not available (11), and also because we wanted to allow comparisons with other well studied skin disorders. We assessed the impact of Hailey-Hailey disease on patients' health-related QoL using the self-administered questionnaire Skindex-29, which has been shown to be a valid tool for measuring health-related QoL of dermatological patients (12, 13). The Italian version of the Skindex-29 has been developed following the guidelines for the cross-cultural adaptation of health-related QoL measures and has been validated in a previous survey (14). It measures QoL on three scales: the emotions scale, the symptoms scale and the social functioning scale. Higher scores indicate a poorer QoL. Psychological distress was assessed using the 12-item General Health Questionnaire (GHQ-12). This self-administered questionnaire is considered a valid and reliable tool to measure psychological distress, and it has been recently used and validated in a

dermatological setting (14, 15). We scored the GHQ-12 using the continuous Likert method (16). Comparisons of the QoL and psychological distress scores between subsets of patients were performed using the Mann-Whitney non-parametric U test. The study was approved by the Institute Review Board.

## RESULTS

### *Clinical characteristics*

During the study period we collected information on 22 patients with Hailey-Hailey disease (14 women and 8 men, age range 30–84 years, with a mean of 52.4 years). The age at onset ranged from 20 to 67 years, with a mean of 35.2 years, and the duration of disease was 1 to 53 years (mean 17.3 years). A positive family history was reported by 10 patients (45.4%). Five patients reported that their condition worsened in summer, due to heat and/or sweating.

At the time of examination, the disease was localized on several body sites in most of the patients: women had an average of 3.6 involved sites, while men had 2.8. As for the involved body sites, we observed that in addition to the classical flexural localization, the back and the shoulders and, to a lesser extent, the trunk were also frequently involved (Fig. 1). No patient presented lesions in the oral cavity or other mucous membranes. All cases were confirmed histopathologically. Direct immunofluorescence was negative in all cases. As regards associated conditions, we found hypercholesterolaemia in four patients, essential hypertension in three patients, and thyroid nodules, tinea cruris, discoid lupus erythematosus and genital herpes simplex in one patient each, respectively. Topical therapies consisted of steroid plus antibiotic cream in 12 patients, topical antiseptic agents in 5 patients, steroid alone in 4 patients and zinc oxide paste in 1 patient. Nine patients also received systemic therapy: doxycycline (100 mg/day) in four cases, dapsone (100 mg/day) in three cases and corticosteroids in two cases.

### *Questionnaire study*

Completed questionnaires were returned by 20 patients (Table I). Median overall QoL scores were well above the threshold we have previously used to classify 'very

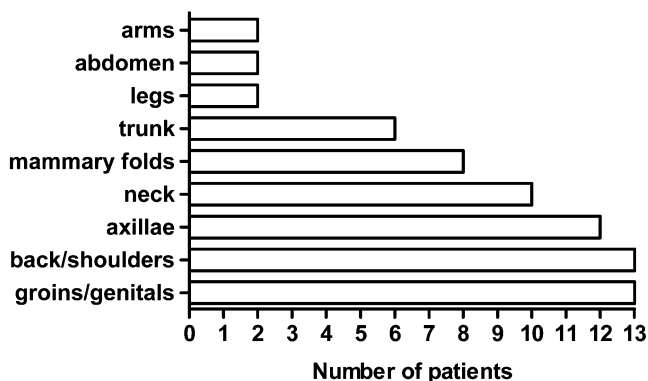


Fig. 1. Body sites involved in 22 patients with Hailey-Hailey disease.

poor' QoL (i.e. Skindex-29 scores  $\geq 35$ ) (17) in all three domains investigated by the Skindex-29 (i.e. symptoms, emotions and social functioning). Moreover, the levels of psychological distress were higher than those we have previously reported in other dermatological patients (15). Skindex-29 and GHQ-12 scores were not significantly different among subsets of patients for most of the considered variables (i.e. gender, age, age at onset, duration of disease, family history and number of body sites involved). The exceptions were higher scores in the Skindex-29 emotions scale for younger patients, and for patients with four or more body sites involved, and higher scores in the symptoms scale for subjects with a disease history longer than 12 years. Symptoms scores appeared to be independent of which body sites (e.g. groin, axillae, etc.) were involved and whether  $< 4$  or  $\geq 4$  body sites were involved. No significant differences were observed for GHQ-12 scores.

## DISCUSSION

Individual lesions of Hailey-Hailey disease consist primarily of flaccid vesicles and blisters on an erythematous background evolving into eroded patches with a fissured appearance. The disease is generally considered as affecting mainly folds; however, we found that back/shoulders and trunk were also as frequently involved as the groin/genital area and the mammary folds, respectively. It is known that most patients complain of significant discomfort and some find that the condition severely restricts their work and leisure activities. In our study, we found that, irrespective of the number and type of body sites involved, patients had a poor QoL, in all three domains investigated by the Skindex-29 (symptoms, emotions and social functioning). The only previous study investigating the impact of Hailey-Hailey disease on QoL (10) assessed handicap in 66 patients using the self-administered questionnaire Dermatology Life Quality Index (DLQI) (18). That study reported that the mean DLQI score was 6.06, corresponding to 20.2% of the maximum score, similar to the DLQI score of 29.7% obtained in patients with psoriasis, but lower than the atopic eczema score (47.1%) (18). Our findings seem to document a greater impairment in QoL than reported by Harris et al. (10). However, it should be considered that in the latter British study patients were interviewed at home using a mailed questionnaire and asked to consider their condition over the previous week, while we studied hospitalized patients, presumably in a more severe period of their disease. In fact, the observed Skindex-29 scores were similar to those of adults hospitalized with severe atopic dermatitis (Abeni et al., unpublished observations). In addition, Skindex-29 and GHQ-12 scores in our study were twice as high as those we previously reported for urticaria pigmentosa (19), and

Table I. *Quality of life and psychological distress median scores among 20 patients with Hailey-Hailey disease*

		No. of patients	Quality of life (Skindex-29 scale scores)			Psychological distress (GHQ-12 score)
			Symptoms	Emotions	Social functioning	
Gender	Overall	20	58.9	53.8	53.1	16.0
	Male	7	53.6	50.0	43.8	16.0
	Female	13	67.9	55.6	56.2	16.0
Age	≤ 55 years	12	57.1	57.5	56.2	16.0
	> 55 years	8	67.9	40.8*	42.7	16.0
Age at onset	≤ 30 years	7	57.1	52.5	43.8	16.0
	> 30 years	13	64.3	55.0	56.2	16.0
Duration	≤ 12 years	9	53.6	52.5	50.0	16.0
	> 12 years	11	67.9 <sup>a</sup>	55.0	56.2	16.0
Family history	Yes	10	58.9	51.2	50.0	16.0
	No	10	62.5	56.5	53.1	15.5
No. of body sites involved	<4	13	60.7	50.0	43.8	16.0
	≥4	7	57.1	60.0 <sup>a</sup>	56.2	17.0

\* $p < 0.05$ , Mann-Whitney non-parametric U test.

similar to those of 20 in-patients with pemphigus vulgaris seen at our institute (55.4, 55.0 and 50.0 in the symptoms, emotions and social functioning Skindex-29 scales; and 14.5 in the GHQ-12) (Abeni et al., unpublished observations). The GHQ-12 scores found in our patients indicate a great negative impact of Hailey-Hailey disease on psychological well-being. This is of some concern because we have previously shown in a dermatological setting that treatment adherence is significantly lower in patients with minor anxiety and depression problems (20). Furthermore, it has recently been reported that psychological distress impairs clearance in psoriasis patients undergoing photochemotherapy (21).

A previous study in psoriasis has shown that the physician's assessment of clinical severity does not necessarily correlate with the degree of handicap experienced by the patient (22). Patients with a disease that appears mild to the clinician may in fact be suffering from considerable handicap. This appears to be true also for patients with Hailey-Hailey disease. Therefore, a more aggressive therapeutic approach may be advisable also in patients with only few body sites involved.

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