

CLINICAL REPORT

Family Burden in Epidermolysis Bullosa is High Independent of Disease Type/Subtype

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Epidermolysis bullosa is a rare, inherited group of disorders characterized by blistering of the skin following friction or mechanical trauma. The aim of this study was to assess the family burden of epidermolysis bullosa in children aged 0–7 years. A postal survey was conducted. The perceived severity of the disease was evaluated by the caregivers, using the Patient Global Assessment 5-point scale. The caregiver received the Family Strain Questionnaire and the 12-item General Health Questionnaire to assess the probable presence of depression/anxiety. A single-item analysis was also performed for questions related to the burden of disease. Forty-two families were invited to participate. Data from 28 young patients and their caregivers were analysed (response rate 66.7%). The family burden increased with increasing caregiver's perceived disease severity, with increasing patient's body surface involved, and if parents had depression/anxiety, reaching statistical significance in several Family Strain Questionnaire scales. The family burden due to epidermolysis bullosa is very high independent of disease type/subtype. Key words: epidermolysis bullosa; family burden; caregivers.

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Epidermolysis bullosa (EB) is a rare, inherited group of disorders clinically characterized by blistering of the skin following friction or mechanical trauma. The mode of inheritance is either autosomal dominant or recessive. Four major types of EB are currently distinguished, based on the ultrastructural level of separation of the epidermis from the underlying dermis: intra-epidermal in EB simplex (EBS), intra-lamina lucida in junctional (JEB), sub-lamina densa in dystrophic EB (DEB), and mixed in Kindler Syndrome (KS). The clinical course of these major types of EB is extremely variable, from fatal (severe forms involving various organs with early postnatal death or chronic progression) to relatively mild (skin fragility

with local blistering with little or no impact on life expectancy). EB types are thus further subdivided into major and minor subtypes based on clinical and laboratory findings (1)

EB has a significant clinical and socio-economic impact, both on patients and their families (2). Even though chronic skin blistering affects personal, physical, emotional and professional aspects of patients' life, only a few published studies to date have attempted to determine the specific impact of the different EB types and subtypes on patients' daily life and the strategies for coping with EB. These studies have addressed the assessment of mobility, activities and pain in the different EB types and the impact on parental, interpersonal relationships, marital status and family size (3, 4).

In addition, the main problems experienced by affected children and their parents have been described in a number of qualitative studies (5, 6).

The aim of this study was to assess the family burden in children aged 0–7 years affected by EB.

METHODS

For this observational, cross-sectional study, patients' names were obtained from the EB database of the Istituto Dermatologico Dell'Immacolata – Istituto di Ricovero e Cura a Carattere Scientifico (IDI-IRCCS) in Rome, a national reference centre for EB and other skin diseases in central and southern Italy. Only those patients with a diagnosis confirmed by immunofluorescence antigen mapping and/or transmission electron microscopy were included. The project was approved by IDI's ethics committee. The study was conducted in February–March 2008. The parents of 42 children aged 0–7 years were invited by telephone to participate in a postal survey about caregiver burden due to EB. Those who agreed to participate were sent study questionnaires, written information about the project and an informed consent form to be signed. The questionnaires had to be completed by the main caregiver. The signed consent forms and the completed questionnaires were returned in a pre-addressed stamped envelope. A reminder telephone call was made to carers who had not returned the questionnaire after one month. Information about the clinical EB type and subtype was obtained from the above-mentioned database.

The perceived severity of the disease was evaluated by the caregivers of the children with EB using the Patient Global Assessment (PGA) on a 5-point scale. Caregivers were asked to complete the Family Strain Questionnaire (FSQ), and the 12-item General Health Questionnaire (GHQ-12), as well as a short demographic questionnaire.

Study measurement tools

Patient Global Assessment. The PGA index consists of a 5-point scale, with scores from 0 to 4, corresponding to “very mild”, “mild”, “moderate”, “severe”, and “very severe” disease (7).

The first two and last two categories were pooled in the data analysis because of small numbers.

General Health Questionnaire-12. The GHQ-12 (8) is a self-administered 12-item questionnaire designed to measure psychological distress and detect current non-psychotic psychiatric disorders, such as depression and anxiety. The reliability and validity of the Italian version have been tested in several diseases, including dermatological conditions (9).

Answers are given on a 4-point scale; for instance, the item “in the last weeks, did you feel under strain?” envisages the following answers: “no”, “not more than usual”, “more than usual” and “much more than usual”. When scored with the binary method (0-0-1-1) the GHQ-12 can be used as a screening tool to detect minor non-psychotic psychiatric disorders, yielding final scores that range from 0 to 12. Operationally, patients scoring 4 or more were considered “GHQ-positive”, i.e. at risk of depression and anxiety.

Family Strain Questionnaire. The FSQ consists of a brief semi-structured questionnaire and 44 self-completed dichotomic items (10).

This is a validated instrument for the general screening of caregiving-related problems. It makes it possible to optimize administration and data analysis time, and to make comparisons between the extent of problems experienced by caregivers of patients with different diseases. The semi-structured interview collects information concerning the socio-economic status of caregivers and their beliefs/interpretations concerning the disease of their patients. Five areas are investigated: Emotional burden (Eb); Problems in social involvement (Si); Need for knowledge about the disease (Kd); Satisfaction with family relationships (Sfr); and Thoughts about death (Td). “Yes” answers are attributed a score of 1, thus the higher the score for each area, the greater the problems experienced, with the exception of Sfr, for which a high score indicates good relationships.

Collected information included patient’s personal data (e.g. age, gender, disease duration, days of hospitalization due to the disease, etc.) and the extent and distribution of the skin lesions as evaluated by the child’s caregiver (marked on a silhouette of the human body). A senior dermatologist then evaluated the patient’s representation of skin involvement, and coded it into three categories: < 10%; 10–30%; and > 30%.

A short demographic questionnaire was also used for caregivers, to collect information about gender, age, education level, income, and satisfaction with income. The annual income amount was used as a measure of economic status. Caregivers had to indicate their annual income (€) per household: (a) 6000–17,000; (b) 17,000–35,000; or (c) more than 35,000. For the analysis, the variable was dichotomized using €17,000 as a cut-off.

Statistical analysis

Mean values and standard deviation (SD) were calculated for all continuous variables, and values compared using the Mann-Whitney test. A *p*-value < 0.05 was considered significant. For the single-item analysis, given the small numbers, the exact χ^2 test was used.

All statistical analyses were performed with the STATA statistical package, release 9 (STATA, College Station, TX, USA).

RESULTS

A total of 42 families of children with EB aged 0–7 years were invited to participate in the study. Twenty-

eight (66.7%) replied. The characteristics of the children are reported in Table I.

The distribution of EB types and subtypes in the patients, according to the latest revision of EB classification was as follows: EBS (6 cases with EBS – Dowling-Meara [EBS-DM] –, one EBS localized, and 3 with other generalized EBS subtypes); JEB (one case non-Herlitz generalized subtype); one dominant DEB (DDEB) generalized, 3 recessive DEB (RDEB) severe generalized, 9 RDEB generalized other, and 4 RDEB other subtypes.

Fifty percent of the patients with EB had skin involvement of between 10 and 30% of their body surface area, while 43% had less than 10% involvement and only 7% had greater than 30% involvement. The characteristics of the caregivers are shown in Table II.

Results of the Family Strain Questionnaire, completed by the parents (82% of whom were mothers) for their children are shown in Table III. Although no significant differences were seen among EB types, the family burden increased significantly with increasing caregiver’s perceived disease severity (for Si, Kd, and Td scales) and increasing patient’s body surface involved (for Eb, Si, Kd, Td scales). FSQ data are reported only for EBS-DM and RDEB (the two subtypes with more cases). The emotional burden was higher in caregivers of RDEB children; however, this difference did not reach statistical significance. The high Eb score in the EBS group was probably due to the fact that it included two

Table I. Characteristics of the children with congenital epidermolysis bullosa (EB) (n = 28)

Variables	
Gender, n (%)	
Male	12 (42.9)
Female	16 (57.1)
Age, years, mean \pm SD	3.0 \pm 1.7
range	0–7
Area of body surface involved, n (%)	
< 10%	12 (42.9)
\geq 10 \leq 30%	14 (50.0)
> 30%	2 (7.1)
Length of hospitalization due to EB in the last year, n (%)	
0 days	14 (50.0)
\leq 7 days	9 (32.1)
> 7 days	5 (17.9)
EB type/subtype ^a , n (%)	
EBS-DM	6 (21.4)
EBS, localized	1 (3.6)
EBS, other subtypes	3 (10.7)
JEB n-H, generalized	1 (3.6)
DDEB, generalized	1 (3.6)
RDEB, severe generalized	3 (10.7)
RDEB, generalized other	9 (32.1)
RDEB, other subtypes	4 (14.3)

^aEBS: epidermolysis bullosa simplex; EBS-DM: EBS, Dowling-Meara; JEB: junctional epidermolysis bullosa; JEB n-H: JEB non-Herlitz; DEB: dystrophic epidermolysis bullosa; DDEB: dominant DEB; RDEB: recessive DEB. EB types and subtypes are in accordance with the latest revision to EB classification (1).

SD: standard deviation.

Table II. Characteristics of the caregivers of children with epidermolysis bullosa (n = 28)

Variables	
Gender, n (%)	
Male	5 (17.9)
Female	23 (82.1)
Age, years, mean ± SD	34.4 ± 4.9
Education, n (%)	
Medium	6 (21.4)
High	22 (78.6)
Family annual income (€), n (%)	
≤17,000	16 (57.1)
>17,000	12 (42.9)
Satisfaction with income, n (%)	
Satisfied	10 (35.7)
Dissatisfied	18 (64.3)
Support by other family members, n (%)	
Yes	22 (81.5)
No	5 (18.5)
Perceived disease severity, n (%)	
Low	14 (51.9)
Medium	8 (29.6)
High	5 (18.5)
Patient's health conditions, n (%)	
Fine	11 (40.7)
Quite good	13 (48.2)
Bad	3 (11.1)

Totals may vary because of missing values.
SD: standard deviation.

patients in the “EBS other subtypes” generalized forms, with very high family emotional burden.

Concerning the single FSQ questions, almost 90% of the parents who had returned the questionnaires reported that they needed more information; 82% believed they had a strong and very compact family; and 79% relied on their family to face the disease; 72% were disappointed about their child's disease; and 61% were worried about EB chronicity.

Table IV shows the association of some variables of interest (e.g. GHQ status, age, education, working conditions, marital status, religion and perceived sufficiency of income) with the single items of the FSQ. All values with *p* < 0.10 obtained from an exact χ^2 test were reported.

GHQ-positivity is the condition most often associated with the different FSQ items, and a strong association with the more burdensome aspects of caregiving are seen also for single parents, for those who report a disadvantaged economic situation, and for those who are not affiliated with any religion.

Among the FSQ items, the ones about the difficulty to contain anger, to speak to the patient about the disease, capability of coping with problems, about not having time for other family members, and the one about feelings of guilt about the child's disease, are those more frequently associated with the above-mentioned variables.

Five out of 26 mothers were GHQ-positive (19.2%), and the family burden was significantly greater among GHQ-positive caregivers (for Eb and Si scales).

Table III. Mean values and statistical assessments of each Family Strain Questionnaire scale in the caregivers of children (0–7 years) with epidermolysis bullosa (EB), according to disease- and caregiver-related variables

	Family Strain Questionnaire scales					
	n	Eb	Si	Kd	Td	Sfr
Overall	28	5.54	2.75	2	1.54	3
<i>Disease-related variables</i>						
<i>EB types/subtypes</i>						
EBS	10	6.5	3.4	2	1.9	3
DEB	17	5.1	2.5	2.1	1.3	3.1
<i>Subtypes:</i>						
EBS-DM	6	4.3	3	1.3	1.5	3.7
RDEB	9	6.1	2.6	2.3	1.4	2.8
<i>Disease severity as evaluated by the caregiver</i>						
Low	14	3.9	1.7*	1.6*	1.1*	2.9
Medium/High	13	7.6	3.9	2.5	2.1	3.0
<i>Patient's health conditions</i>						
Fine	11	4.4	2.0	1.5	1.3	2.6
Quite good/bad	16	6.5	3.3	2.4	1.7	3.2
<i>Body area involved</i>						
<10 %	12	2.2*	1.0*	1.4*	0.8*	3.2
≥10 %	16	8	4.1	2.4	2.1	2.8
<i>Hospitalization due to EB (last year)</i>						
Yes	14	5.6	3.8*	2.0	1.9	2.9
No	14	5.5	1.7	2.0	1.2	3.1
<i>Caregiver-related variables</i>						
<i>General Health Questionnaire (GHQ)-12 status</i>						
GHQ-positive	5	10.6*	5.4*	2.8	2.2	2.2
GHQ-negative	21	4.2	2.1	1.8	1.4	3.1
<i>Family annual income (€)</i>						
<17,000	16	5.6	2.6	1.9	1.5	3.1
≥17,000	12	5.5	3.0	2.1	1.6	2.8
<i>Satisfaction with income</i>						
Satisfied	10	4.8	2.4	2.0	1.3	3.0
Dissatisfied	18	5.9	2.9	2.0	1.7	3.0

**p* < 0.05 Mann-Whitney *U* test (SD omitted to enhance readability).

Totals may vary because of missing values.

As references for Family Strain:

FSQ in EB adults (our data not shown n. 84): Eb 6.3 ± 4.4, Si 2.9 ± 2.3, Kd 2.5 ± 1.3, Td 2.0 ± 1.3.

Oncological diseases: Eb 7.6 ± 3.8, Si 3.5 ± 2.1, Kd 2.3 ± 1.4, Td 3.3 ± 1.6 (10).

Vascular leg ulcers: Eb 7.0 ± 3.7, Si 4.3 ± 1.8, Kd 2.7 ± 1.0, Td 2.2 ± 1.5 (15).

Eb: emotional burden; Si: problems in social involvement; Kd: need for knowledge about the disease; Td: thoughts about death; Sfr: satisfaction with family relationships; EBS: epidermolysis bullosa simplex; EBS-DM: epidermolysis bullosa simplex Dowling-Meara; DEB: dystrophic epidermolysis bullosa; RDEB: recessive dystrophic epidermolysis bullosa.

Considering the family income, however, no significant differences in the FSQ scale scores were found between the group with an income of less than €17,000, and the group with an income of ≥ €17,000. No differences in the FSQ scales were observed between satisfied and dissatisfied children's carers, with respect to household income.

DISCUSSION

Family members play a major role in providing care and assistance to elderly and unwell relatives (11). The effect

Table IV. Single-item analysis of the Family Strain Questionnaire, in 28 caregivers of children with epidermolysis bullosa: p-values for selected variables of interest

Item #	Item content (summary)	Answers % Yes	GHQ (n=5)	Age (n=16)	Education (n=6)	Work (n=13)	Single (n=7)	Religion (n=6)	Money (n=8)
1	Can rely on someone	78.6				<0.01			
2	Tiredness	50.0	0.02	0.05			0.08	0.08	
3	United family	82.1		0.05				<0.01	
5	Insomnia, headache ...	46.4				0.09	0.06		0.09
6	Less visits to friends	35.7	0.06	<0.01					
10	Doctors stress me	28.6			0.04				
12	Too much to think about	57.1	0.04				0.02	0.02	
14	Unsure about overcoming hardships	35.7	0.03			0.07			0.07
15	Often feel like crying	28.6	0.01						
16	Can't cope with problems	34.3	<0.01				<0.01		0.03
17	Very stressed	42.9	0.08					0.03	
18	Difficult to contain anger	46.7	<0.01				<0.001	0.02	0.04
21	Abandoned interests	42.9	0.08	0.02		0.04			
22	Worried	60.7	0.07			0.07			0.09
23	Would like to control emotions	33.3			0.03				
25	No time for other family members	28.6	0.01		0.04		<0.001		0.03
27	Need to talk to experts	32.1			0.06	0.01	0.02		
28	Annoyed by requests	14.3			0.02				
29	Think about how things will go	50.0	0.02				0.08	0.08	
33	Feelings of guilt	32.1	0.02				<0.01	0.04	
34	Always supported by other family	71.4						0.04	
38	Annoyed by patient's symptoms	10.7			<0.01				
42	I can speak to patient about disease	55.6	<0.01	<0.01			0.02		0.09

Numbers in each column refer to: GHQ, positive; age >34 years; education <9 years; work: yes; religion: no; money, self perceived presence of economical problems. *p*-values are from the Pearson's two-sided exact χ^2 test. Items were selected according to the following criteria: either at least one variable significant at the 0.05 level, or at least three variables significant at the 0.10 level. Values in **bold** denote *p* <0.05. GHQ: General Health Questionnaire.

of stressors on family members caring for a physically or mentally ill relative has been referred to as the caregiver burden. The scientific literature is rich in reports, particularly concerning persons involved in caring for patients with cancer or schizophrenia (12), or other chronic diseases (13, 14); however, not many reports compared the family burden in different diseases.

The present study of family burden in EB children highlights the need to provide these families with support interventions, including management of relatives' psychological reaction to patient illness; provision of information on the nature, course and outcome of the patient's disease; training for relatives in the management of patient symptoms, and reinforcement of relatives' social networks. In fact, we showed that EB imposes a heavy burden on the caregiver. The FSQ scores were similar to those observed in caregivers of cancer patients (10) and of patients with leg ulcers (15). A higher family burden was also associated with a greater child's body surface involved by blisters, and a higher psychological distress of the caregiver, as measured by the GHQ-12.

Considering income, it is interesting to note that no significant differences between groups with different annual income were noticed. A possible burden reduction could have been expected in terms of facilities or human resources availability where the income was higher, but surprisingly this was not the case. However, the self-reported information of "having economic problems"

was associated with several aspects of caregiving (e.g. coping, anger, lack of time for other family members) in single-item analysis.

Such analysis provides further insight into specific problems of caregiving, even considering the small number of subjects in this study (Table IV). For instance, the problem of the difficulty of managing anger is highlighted by its association with probable depression/anxiety (as measured by the GHQ-12), being single, having no religious affiliation, and having economic problems; or the need for support in order to be able to devote more time to other family members, or to be able to discuss the disease and its implications with the patient.

The present study has some limitations. First, the IDI-IRCCS Institute is a national reference centre for skin diseases, and in particular for EB laboratory diagnosis, thus our sample is not a good representation of the Italian general EB population. Severe and rare forms of EB are over-represented, because serious or unusual cases are often referred to our institute from central and southern Italy. More patients are needed in order to obtain more consistent results for this rare disease. Secondly, this study was conducted in winter, which is the best period of the year for patients with EB and, finally, the clinical assessment of the amount of skin involved was based exclusively on self-reported data.

In conclusion, the results of the study showed that the main determinants of family burden in families with

children with EB were the perceived severity and extent of the patients' disease, and, surprisingly that family income did not have an influence on family burden.

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