

Women with Ehlers-Danlos Syndrome Experience Low Oral Health–Related Quality of Life

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***Aims:** To investigate the perceived impact of oral health–related quality of life problems in individuals with Ehlers-Danlos syndrome. **Methods:** Members of the Swedish Ehlers-Danlos Syndrome Association completed the Oral Health Impact Profile (OHIP-14). Of the 250 participating individuals, 223 were women, and they were the main focus of the analyses. The results were compared with a previous study of the oral health impact on quality of life in the Swedish population. Statistical methods used for comparison were the Student *t* and chi-square tests. **Results:** The mean OHIP-14 value for the entire Ehlers-Danlos syndrome group was 11.1. The mean for women was 11.8, which was significantly higher than 6.8 of the comparison group. The OHIP-14 score varied among age groups, and the highest mean value was found in the age group between 56 and 65 years of age. The most statistically significant differences between the subjects with Ehlers-Danlos syndrome and the comparison group were found for OHIP items 3, 4, and 8: “I have had pain in the mouth,” “I have had discomfort when eating,” and “I have been forced to interrupt meals.” **Conclusion:** It is well-known that Ehlers-Danlos syndrome has a considerable impact on health-related quality of life, and this study is the first to reveal that women with Ehlers-Danlos syndrome report a low oral health–related quality of life as measured with the OHIP-14. Dimensions that were particularly relevant were physical pain, psychologic discomfort, and handicap. J OROFAC PAIN 2012;26:307–314*

Key words: disability, Ehlers-Danlos syndrome, functional limitation, OHIP-14, oral health, quality of life

Ehlers-Danlos syndrome is an inherited, lifelong, and potentially disabling connective tissue disorder¹ that is characterized mainly by joint hypermobility, tissue fragility, skin laxity, and chronic joint and limb pain. It has a broad phenotypic spectrum, which can make diagnosis difficult.² According to the Berlin classification of 1986, the disorder can be divided into 10 entities, EDS I to X.³ The current classification suggests six main types of the disorder based on clinical, genetic, and biochemical features: classical type, hypermobility type, vascular type, kyphoscoliosis type, arthrochalasia type, and dermatosparaxis type.⁴ All forms that did not fit into this scheme have been clustered as “other forms.” The hypermobility and classical types are most common, with an estimated prevalence of 1:5,000 to 1:20,000.⁵ All other types are rare, with an estimated prevalence of less than 1:100,000. It is well established that the disorder is more common in women, although the reason for this is

Table 1 Type of Ehlers-Danlos Syndrome and OHIP-14 Scores

	Female (n %)	OHIP mean	Male n (%)	OHIP mean	All n (%)	OHIP mean	SD	CI (95%)
EDS types								
Classical	37 (17)	8.6	8 (29)	6.1	45 (18)	8.0	7.9	5.6–10.4
Hypermobility	72 (32)	12.7	4 (15)	2.5	76 (30)	11.7	10.3	9.3–14.0
Vascular	9 (4)	10.4	1 (4)	3.0	10 (4)	9.7	7.7	4.2–15.2
Arthrochalasia	2 (1)	12.0	0 (0)	0	2 (1)	12.0	16.9	NC
Mixed types	21 (9)	13.9	1 (4)	21.0	22 (9)	14.2	13.4	8.3–20.2
Unknown	82 (37)	12.3	13 (48)	4.4	95 (38)	11.4	12.1	9.0–13.9
All					250 (100)	11.1		9.7–12.4
Sex								
Males			27 (100)			5.2	6.1	2.8–7.6
Females	223 (100)					11.8	11.1	10.3–13.2

SD, standard deviation; CI, confidence interval; NC, not calculated.

unknown.^{1,2} Apart from hypermobility and chronic limb/joint pain, a variety of other manifestations may also be present, such as slow wound healing, dislocation of joints, bleeding tendency, hernias, fatigue, bowel problems, food hypersensitivity, muscle cramps, and pregnancy complications.^{6–8}

Although oral problems are often reported by individuals with Ehlers-Danlos syndrome, oral manifestations are not included in the diagnostic criteria for the six main types of the syndrome. The periodontitis type, formerly known as EDS type VIII, is currently clustered within the “other forms” of Ehlers-Danlos syndrome. Since the current diagnostic criteria were set in 1997,⁴ there have been several reports in the literature of oral manifestations in patients with Ehlers-Danlos syndrome. Reported oral features of Ehlers-Danlos syndrome are an absence of permanent teeth, pulp calcification in permanent teeth, abnormal pulp shape, short or deformed roots and crowns, mandibular bone loss, high caries frequency, and increased mucosal fragility.^{9,10} Recently, Klingberg et al¹¹ reported hypomineralized enamel in primary teeth. A limited effect of local anesthesia during dental treatment has also been reported.¹²

Research on Ehlers-Danlos syndrome has been impeded by the heterogeneity of the disorder, as well as the fact that the majority of the Ehlers-Danlos syndrome diagnoses are based solely on subjective clinical features. As a consequence, the general knowledge of Ehlers-Danlos syndrome is limited, and this pertains especially to oral and facial manifestations of the disorder and the perception of oral health-related quality of life in individuals with Ehlers-Danlos syndrome. The aim of the present study was to investigate the oral health-related quality of life in individuals with Ehlers-Danlos syndrome.

Materials and Methods

Study Population

In 2008, 365 members of the Swedish Ehlers-Danlos Syndrome Association were invited to participate in the study (332 females and 33 males). Through mail, members received information about the study and two questionnaires: the Oral Health Impact Profile (OHIP-14) and a background form. After 14 days, a reminder was sent to nonresponders. The inclusion criteria were a diagnosis of Ehlers-Danlos syndrome, age older than 18 years, and completed questionnaires. Of the original 365 invitations, 76 did not respond, 18 did not have a diagnosis of Ehlers-Danlos syndrome, 15 invitations were returned due to a wrong address, 5 were too young, and 1 was deceased. Thus, 326 members were eligible for the study and 250 (77%) (mean age, 46.1 years; standard deviation [SD], 12 years; range, 18 to 84 years) responded to the questionnaires (Table 1). Since very few responders were men, they were omitted from most analyses due to the fact that there were not enough data to generate reliable results.

The results were compared with a previous study of the oral health impact on the quality of life of a group of the Swedish population, referred to as the comparison group ($n = 259$). The comparison study consisted of a random selection of inhabitants of a Swedish city. They were 20, 30, 40, 50, 60, 70, and 80 years old; and 519 individuals responded to the OHIP-14 questionnaire.¹³

Questionnaires

The OHIP-14 was developed as a short version from the original OHIP-49.¹⁴ The OHIP is based on the

World Health Organization's International Classification of Impairments, Disabilities, and Handicaps,¹⁵ is widely used, and has been shown to have valid and reliable measures in different populations and cultural settings.^{14,16} OHIP-14 measures the frequency of 14 functional and psychosocial impacts of oral problems on peoples' health-related quality of life and is intended to measure the discomfort, dysfunction, and disability resulting from oral disorders.¹⁴ The rationale behind using the OHIP-14 instead of OHIP-49 was that it has been translated and validated in a Swedish context.¹⁶ Another reason for choosing the short version was that holding a pen and writing may sometimes be tiresome and painful for individuals with Ehlers-Danlos syndrome because of muscle cramps. OHIP-14 covers seven dimensions of oral health, each represented by two items.¹⁴ The dimensions are functional limitation (items 1 and 2), physical pain (items 3 and 4), psychologic discomfort (items 5 and 6), physical disability (items 7 and 8), psychologic disability (items 9 and 10), social disability (items 11 and 12), and handicap (items 13 and 14) (Table 2). All items in the OHIP-14 were introduced with this question: "During the past week, how often have you, as a result of problems with your oral cavity, teeth, jaw or prostheses, experienced the following situations?" The answers were coded in a 5-point ordinal scale as 0 (never), 1 (hardly ever), 2 (occasionally), 3 (fairly often), and 4 (very often). The scores were then added to make up the OHIP-14 score (range 0 to 56). A high total score indicates poor health-related quality of life.¹⁴

In the background form, the respondents were asked about their age, sex, and type of Ehlers-Danlos syndrome. The background form also included questions about whether they had perceived mucus problems in any body region. These regions were oral, nasal, eyes, or genitals. There was also an option to fill out other regions. The response format was "yes" for each body location. The number of areas involved was then added for each individual.

Statistical Analysis

SPSS for Windows 18.0 (IBM) was used for statistical analysis. To make the results comparable with the comparison group,¹³ the age groups were centered on ages 20, 30, 40, 50, 60, 70, and 80. The Student *t* test and chi-square test were used for comparison. In Tables 1 and 3, both SD and 95% confidence intervals (CI) were used. SD was used to compare with other studies, while CI illustrated the fact that the number of individuals in each group influences the relevance of the results. No further analyses were made on men since there were not

enough male responders to generate reliable results. The Chronbach alpha for the total scale was 0.93. Statistical significance was considered at a level of $P < .01$. To evaluate the correlation between OHIP-14 and the number of areas involved, the Pearson correlation coefficient was calculated.

The study was performed in accordance with the 1964 Declaration of Helsinki. Informed consent was obtained from all participants. The study was approved by the Regional Ethics Committee, Stockholm, Sweden (2008/2:4).

Results

In the entire Ehlers-Danlos syndrome group, the mean OHIP-14 value was 11.1: 5.2 for men and 11.8 for women. Men reported significantly fewer oral complaints than women. Individuals with mixed Ehlers-Danlos syndrome types had the highest OHIP-14 scores, while the classic type had the lowest scores (Table 1). The highest OHIP scores were seen in women between 56 and 65 years of age (Table 4). Only 15% ($n = 38$) of respondents reported an absence of oral problems (Fig 1).

Women with Ehlers-Danlos syndrome reported significantly higher OHIP-14 scores than the comparison group for ages 26 to 65 years of age, and no difference was seen for ages younger than 26 years or older than 65 years. The Ehlers-Danlos syndrome group reported statistically significantly higher OHIP-14 scores for items 2 to 6, 8, 10, 13, and 14 than the comparison group, with the most statistically significant differences for items 3, 4 and 8: "I have had pain in my mouth," "I have had discomfort when eating," and "I have been forced to interrupt meals." Additional items in which more than 10% reported problems fairly often or very often were items 5, 6, 9, 10, and 13: "I have felt insecure," "I have felt tense," "I have had difficulty relaxing," "I have felt embarrassed," and "I have felt that life in general has been less satisfactory" (see Table 2). Dimensions in which both items were significantly higher in the Ehlers-Danlos syndrome group were physical pain, psychologic discomfort, and handicap, with the highest percentage reported for physical pain (see Table 2).

Since the OHIP-14 is a self-reported questionnaire, no detailed information of the type of oral or orofacial conditions was obtained through the questionnaire.

Mucosal problems were reported by 206/223 (92%) of women and 23/27 (85%) of men. Among the women, 144 (65%) reported oral problems, 128 (57%) reported nasal problems, 143 (64%) reported

Table 2 OHIP-14 Scores in Ehlers-Danlos Syndrome (n = 223) and a Comparison Group (n = 259)¹³

OHIP item	Statement	Dimension	0 points		1–2 points
			Ehlers-Danlos syndrome (%)	Comparison group (%)	Ehlers-Danlos syndrome (%)
1	I have difficulty pronouncing words	Functional limitation	76	81	21
2	I feel my sense of taste has deteriorated	Functional limitation	63	80	29
3	I have had pain in my mouth	Physical pain	23	58	57
4	I have had discomfort when eating	Physical pain	34	68	46
5	I have felt insecure	Psychologic discomfort	45	61	41
6	I have felt tense	Psychologic discomfort	50	54	34
7	My diet has been unsatisfactory	Physical disability	61	63	31
8	I have been forced to interrupt meals	Physical disability	55	79	39
9	I have had difficulty relaxing	Psychologic disability	53	54	33
10	I have felt embarrassed	Psychologic disability	58	66	29
11	I have been somewhat irritated with other people	Social disability	73	67	22
12	I have had difficulty performing my daily tasks	Social disability	78	82	18
13	I have felt that life in general has been less satisfactory	Handicap	55	65	31
14	I have been totally incapable of functioning	Handicap	82	90	14

*Chi-square test; ** $P < .01$. NS, not significant.

0 points, never; 1 to 2 points, hardly ever/occasionally; 3 to 4 points, fairly often/very often.

Table 4 Comparison of Mean OHIP-14 Between Ehlers-Danlos Syndrome and the Comparison Group¹³ Stratified by Age Groups

Age	Ehlers-Danlos syndrome			Comparison group			<i>P</i> *
	n	Mean	SD	n	Mean	SD	
Men (all ages)	27	5.2	6.1	260	5.9	7.1	NS
Women	223	11.8	11.1	259	6.8	7.2	**
18–25 y	7	8.9	3.9	37	9.3	8.2	NC
26–35 y	38	11.9	10.7	46	4.6	6.2	**
36–45 y	71	11.3	10.6	28	6.5	6.6	**
46–55 y	53	11.1	9.5	41	6.2	7.2	**
56–65 y	38	16.3	14.5	38	6.7	6.1	**
66–75 y	14	7.1	10.5	38	7.7	7.2	NS
76–84 y	2	0.5	.7	31	7.6	8.0	NC

SD, standard deviation; NS, not significant; NC, not calculated. *Student *t* test; ** $P < .01$.

eye problems, and 149 (67%) reported genital problems. The women reporting oral problems had a mean OHIP-14 of 13.3 (SD, 11.5). Problems from the oral region were reported by 75% of the hypermobility type, 73% of the mixed type, 59% of the unknown type, 50% of the arthrochalasia type, and 40% of the vascular type. In women, the OHIP-14 values were positively correlated to the number

of mucosal areas involved ($r = .35$, $P < .01$) (see Table 3).

Discussion

Since hypermobility, skin hyperextensibility, and tissue fragility are acknowledged as the main

	1-2 points		3-4 points		<i>P</i> *
	Comparison group (%)	Ehlers-Danlos syndrome (%)	Comparison group (%)		
	15	4	4		NS
	16	8	4		**
	38	21	4		**
	27	20	5		**
	30	13	9		**
	40	17	6		**
	31	7	5		NS
	20	5	1		**
	39	14	7		NS
	31	13	3		**
	29	4	4		NS
	16	4	2		NS
	33	14	2		**
	9	4	0		**

Table 3 Number of Reported Involved Mucosal Areas and Mean OHIP-14 Scores in 223 Women with Ehlers-Danlos Syndrome

Areas (n)	Individuals n (%)	OHIP-14 mean	SD	CI (95 %)
0	17 (8)	3.4	4.6	1.2–5.6
1	33 (15)	6.2	8.0	3.5–9.0
2	43 (19)	11.7	11.2	8.3–15.0
3	54 (24)	11.9	10.1	9.3–14.6
4	60 (27)	15.6	12.5	12.4–18.7
> 5	16 (7)	17.6	10.4	12.5–22.7

SD, standard deviation; CI, confidence interval.

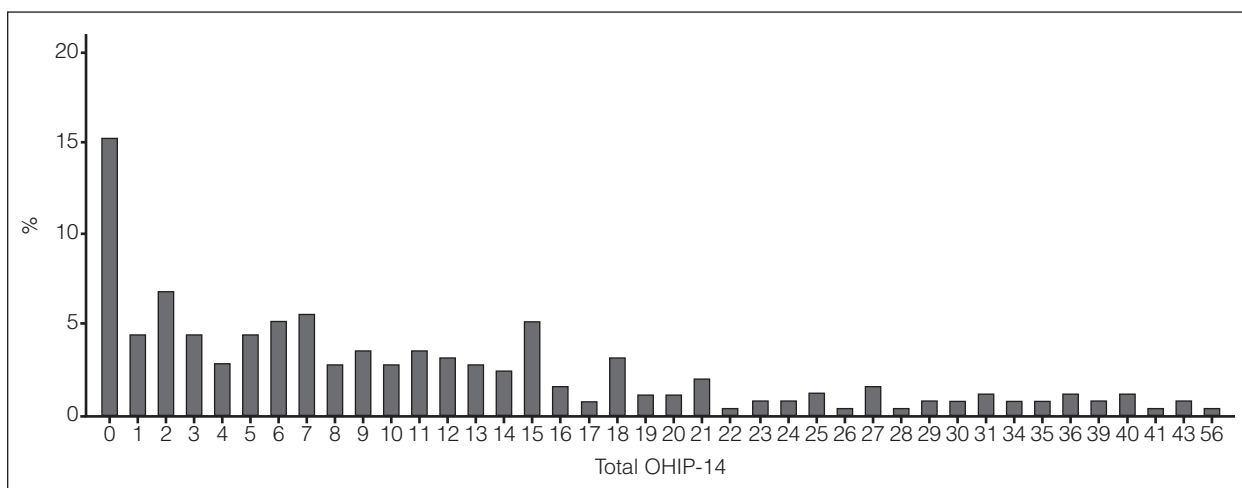


Fig 1 Frequency distribution (%) of individuals (n = 250) according to OHIP-14 scores. Note that empty bars are omitted.

manifestations of the Ehlers-Danlos syndrome, there is poor general knowledge that oral manifestations are a common feature of Ehlers-Danlos syndrome. In fact, oral health may be severely compromised by the syndrome.¹⁰ Most likely because of the presence of collagen fragility, oral and maxillofacial manifestations are frequently reported by individuals with Ehlers-Danlos syndrome. However, most reports of

oral manifestations are either case studies or small series.¹⁷

A lowered health-related quality of life in individuals with Ehlers-Danlos syndrome as a result of general fatigue and severe musculoskeletal complaints has previously been reported.¹⁸⁻²¹ Since oral manifestations are common in patients with Ehlers-Danlos syndrome, and a decline of psychologic

well-being in combination with oral and masticatory muscle problems has been described,¹² the authors wanted to investigate the oral health–related quality of life in individuals with Ehlers-Danlos syndrome.

The highest OHIP-14 scores were reported by women who stated they had a mixed type of Ehlers-Danlos syndrome, followed by those with the hypermobility form and the unknown type. Strictly speaking, the diagnosis of a mixed type of Ehlers-Danlos syndrome is not a nosological entity.^{4,8} Most of those individuals would likely fit into the diagnosis of a hypermobile type, which is the most common subtype of Ehlers-Danlos syndrome in clinical practice.

Men diagnosed with Ehlers-Danlos syndrome reported significantly fewer oral complaints than women with the diagnosis, and no difference was noted when men with Ehlers-Danlos syndrome were compared with men of the comparison group.¹³ The fact that only 9% of the subjects receiving the questionnaires were men does reflect the diagnostic setting in clinical genetics, where generally less than 10% of the diagnostic referrals for Ehlers-Danlos syndrome concern men (data not shown). The skewed distribution of men has also been found in previous studies of Ehlers-Danlos syndrome.^{6,7,12}

Women with Ehlers-Danlos syndrome between 26 and 65 years of age reported more oral complaints than the comparison group. No differences in OHIP-14 scores between women with Ehlers-Danlos syndrome and the comparison group above age 66 years were seen. In fact, the OHIP-14 scores in the Ehlers-Danlos syndrome group dropped to the same level as the comparison group, and there might be several reasons behind this finding. First and most importantly, there were few participants in Ehlers-Danlos syndrome group older than 66 years of age, which might have given a false low score. Second, given the fact that fatigue is a main manifestation of Ehlers-Danlos syndrome,¹⁸ the combination of age and fatigue might have impeded individuals with more severe forms to enroll in the national Swedish Ehlers-Danlos Syndrome Association, thus leading to a false negative result in this age group. Third, being older than the age of retirement with less working life stress might lead to a lower score than expected, which has been previously reported.¹³ Last, associated with an older population are oral problems such as missing teeth, dry mouth, and limitations in chewing ability¹⁷ that also might have leveled out the difference between the groups. As for the women with Ehlers-Danlos syndrome younger than 26 years of age, there was no difference in the mean OHIP-14 between the group

with Ehlers-Danlos syndrome and the comparison group. However, this was not calculated, due to the low number of participants in this age group. The fact that Ehlers-Danlos syndrome often is diagnosed later in life contributed to the small numbers in this group. A much larger cohort of individuals with Ehlers-Danlos syndrome younger than age 26 is thus needed to investigate their quality of life due to oral complaints.

Items of all dimensions of OHIP-14 except for social disability scored higher in the Ehlers-Danlos syndrome group. There were three dimensions in which both items were significant: physical pain, psychological discomfort, and handicap. It is not surprising that pain is commonly reported, since chronic pain of limb and joints is a minor diagnostic criterion for the hypermobility type of Ehlers-Danlos syndrome⁴ and is a common manifestation of Ehlers-Danlos syndrome.^{7,8,18} There might be several explanations as to why women with Ehlers-Danlos syndrome experience a lower oral health–related quality of life related to pain. Of major importance are the fragile tissues that cause bleeding gums, periodontal disease, spontaneous tooth fractures, and early dental loss.^{9,10} Another explanation is pain from the hypermobile temporomandibular joint.¹² The fact that local anesthesia often is ineffective during dental treatment¹² might have resulted in avoidance of dental care, which eventually may have led to a lower oral health-related quality of life. Insufficient effect of local analgesics in Ehlers-Danlos syndrome type was reported by Arendt-Nielsen et al,²² and furthermore, individuals with Ehlers-Danlos syndrome reported that a reason to avoid dental visits was ineffective anesthesia.⁶

Despite this, oral pain is often overlooked in patients with Ehlers-Danlos syndrome by health care professionals, and thus there is a need for greater awareness of this manifestation of the disorder.^{6,19} In a study by De Coster et al,¹⁰ problems with fragile oral mucosa induced by mastication and toothbrushing were found in 74% of the studied group. Tabolli et al²³ showed that oral mucosal diseases had a considerable impact on oral health–related quality of life. Thus, it is plausible that both oral and extra-oral manifestations of Ehlers-Danlos syndrome affected the oral health–related quality of life.

It is not surprising that individuals with Ehlers-Danlos syndrome reported high scores in the dimensions of psychologic discomfort and handicap. This finding is in line with the study by Rombaut et al²⁰ that reported that the hypermobility type of Ehlers-Danlos syndrome is characterized by severe musculoskeletal complaints with a detrimental effect on health-related quality of life in both physical

and psychosocial dimensions. Additionally, muscle weakness and pain severity have been found to be significant predictors for severe fatigue.¹⁹ It has also been reported that in Ehlers-Danlos syndrome, fatigue had a larger impact on daily functioning than pain.¹⁸ A further problem for individuals with Ehlers-Danlos syndrome is that the disorder is most often externally invisible, which can cause a low apprehension for suffering, which in turn can cause psychologic discomfort. To maintain a sense of control in their life, women with general chronic pain are empowered by quality encounters with health care professionals.²⁴

It is of interest to note that 92% of the women reported mucosal problems. Complaints from the mucosa of the eye or the oral or genital region were most common, and each of these was present in more than 60% of the women. A positive correlation was found between the number of mucosal sites involved and the OHIP-14 value. These results imply that a more severe phenotype with involvement of several mucosal sites can be present in women who experience a low oral health-related quality of life. It is therefore relevant to ask individuals with Ehlers-Danlos syndrome whether they experience mucosal problems in locations other than the mouth.

This study emphasizes that when a diagnosis of Ehlers-Danlos syndrome is considered, it is important to take oral symptoms into account as a part of the syndrome. To facilitate the oral medical history, the items of the OHIP-14 can be easily used. If individuals state they experience pain in their mouth (item 3), have discomfort when eating (item 4), and/or have been forced to interrupt meals (item 8), it should alert dentists that oral problems might be a major concern for affected individuals and that proper measures should be taken.

Study Limitations

A major limitation of this study is that it relied on self-reported questionnaires without physical examinations and that no information about medical history, medication, or dentures was obtained in the background form. The respondents were members of the Swedish Ehlers-Danlos Syndrome Association, and it is possible that these individuals represent a subgroup of Ehlers-Danlos syndrome with a more severe phenotype and therefore report more oral complaints than nonmembers with Ehlers-Danlos syndrome might. Also, the comparison group might have included persons with undiagnosed Ehlers-Danlos syndrome. Regardless, the respondents with Ehlers-Danlos syndrome reported a low oral health-related quality of life, which may be

connected to alterations in their mucosal condition and other oral problems.^{10,12} Medication causing hyposalivation may be a confounding factor, since the Ehlers-Danlos syndrome group may have used more medication than the comparison group. In fact, in a recent study, the use of antidepressants and sedatives, which are known to cause hyposalivation, was substantially reported by individuals with the hypermobility type of Ehlers-Danlos syndrome.²⁵ However, the aim of the present study was to investigate the oral health-related quality of life in this group, not the etiology of these problems.

Conclusions

This study is the first to reveal that women with Ehlers-Danlos syndrome report a low oral health-related quality of life as measured with the OHIP-14. Particularly relevant dimensions were physical pain, psychologic discomfort, and handicap. That Ehlers-Danlos syndrome has a considerable impact on the health-related quality of life is well known, and the present study contributes to this knowledge by demonstrating that also the oral health-related quality of life is impeded by the disorder.

Acknowledgments

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