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Temporomandibular joint problems and self-registration of mandibular opening capacity among adults with Ehlers-Danlos syndrome. A questionnaire study

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Structured Abstract

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Objectives – To study maximal mandibular opening capacity and the prevalence of temporomandibular joint (TMJ) problems reported among a larger group of adults with Ehlers-Danlos syndrome (EDS). Furthermore, to compare proportions of disorders with those in a cohort of randomized population-based controls.

Design – A questionnaire study with self-registration of maximal mandibular opening capacity.

Setting and Sample Population – One hundred and fourteen persons with EDS and 114 controls in a randomized population-based cohort.

Experimental variables – Self-registered maximal mandibular opening capacity values that were calculated from the markings of maximal interincisal distance on spatulas and the assessments of overbite with the aid of photos. Questions concerning EDS, TMJ problems and other related questions.

Outcome Measure – Mean values of maximal mandibular opening capacity compared between groups. Proportions of affirmative answers about TMJ problems compared between persons with EDS and controls who did not have the syndrome.

Results – The EDS persons who reported problems with poor mouth opening capacity when biting into thick pieces of food had a lower mean maximal mandibular opening value compared with the other EDS persons ($p < 0.05$). The proportions of affirmative answers concerning mobile joints during mouth opening, present TMJ problems, poor mouth

opening capacity when biting into thick food, clicking, crepitations and permanent locking were greater compared with the controls ($p < 0.05$).

Conclusion – These data corroborate the reports in literature that persons with EDS are naturally predisposed to TMJ problems. The self-registration of maximal mandibular opening capacity was a useful diagnostic tool to provide an objective clinical measure of movement capacity of the TMJ. The clinical measure was in line with the affirmative answers on having problems with poor mouth opening capacity among the EDS persons.

Key words: Ehlers-Danlos; mandibular opening; masticatory muscle pain; temporomandibular disorders; temporomandibular joints

Introduction

Ehlers-Danlos syndrome (EDS) is mostly an inherited connective tissue disorder. The syndrome is manifested by articular hypermobility, skin extensibility and tissue fragility (1, 2). The syndrome is rare and most often unknown among dentists. The prevalence of all types of EDS is 1/5000 (2). Most clinical reports found concerning EDS and odontological issues, are case reports that describe recurrent subluxations of the joints (3–5). No previous studies could be found on the prevalence of TMJ symptoms among a larger group of persons with EDS. This was the purpose of the present study, but it was also desired to use an objective diagnostic tool for the evaluation of mandibular function. A recently developed method for self-registration of mandibular opening capacity was therefore included (6).

According to Fridrich et al., the TMJ often demonstrates profound laxity in conjunction with generalized joint mobility and dislocation (7). Still, it was reported by Harinstein et al. that among 40 patients admitted for surgery, only a few out of those seeking treatment for hypermobility of the TMJ were found to have EDS (8, 9). General joints instability seems to decrease with age (10). The abnormal collagen synthesis also affects the blood vessels and internal organs (11). Some common problems are easy bruising and skin ruptures that heal poorly with scaring (2, 12, 13). More severe cardiovascular complications are seen especially in the vascular type of EDS. One type, the periodontal, has the criteria of fast developing, aggravating periodontal disease (14–16).

Two main classification systems are used in Sweden to describe the varying types of EDS that can be seen (17, 18). The classical types (EDS I gravis, EDS II mitis) and the hypermobile type (EDS III) are found in 90% of the cases. The previously mentioned vascular type (EDS IV) is found in 3–10% and the periodontal type (EDS VIII) is rare (2, 17, 19, 20). Odontological hard tissue defects of the teeth have also been reported for persons with EDS (7, 16, 21). In dental practice, it is more common to register missing tooth enamel, fractures of enamel from the underlying dentine, different tooth anatomy and fragile mucous membranes than milder TMJ problems. Untreated TMJ problems could potentially develop into severe problems.

The aim of this study was to study the prevalence of TMJ problems reported among a larger group of adults with Ehlers-Danlos syndrome (EDS). The recently developed method for self-registration of maximal mandibular opening capacity was included in the questionnaire as a complementary diagnostic tool for a clinical measure of mandibular function in terms of the present movement capacity of the TMJ. Furthermore, we wanted to compare proportions of disorders with those in a cohort of randomized population-based controls.

Material and methods

In January 2002 there were 265 accessible members of the Swedish Ehlers-Danlos syndrome (EDS) Association living in Sweden. They received a questionnaire

and a spatula for self-registration of maximal inter-incisal distance (6). The response rate was 66% ($n = 174$). One reminder had been sent out. Exclusion criteria were: age below 18 years ($n = 11$), support membership and membership with suspected but not medically confirmed EDS ($n = 19$) and declination to participate ($n = 13$). Altogether 43 persons were excluded. The study base then consisted of 131 adults with diagnosed EDS. Altogether 121 of 131 eligible spatulas were returned (92%). Seven spatulas were excluded (four persons had full prosthetic dentures, one spatula was marked upside down, one person had an open bite and another missed frontal upper teeth). The EDS group then comprised 114 persons.

Among a group of 750 randomly chosen adult persons from the Swedish population, the first 114 answers with a marked inter-incisal distance on the spatula were used as controls. The randomization was weighted for gender and age group according to the distribution of these variables among the members of the Swedish EDS Association. Exclusion criteria were: diagnosed EDS, full prosthetic dentures and open bite. The first 124 questionnaires were considered for the control group in order to create a control group of 114 persons. None was excluded because of the criteria set but 10 persons had not returned the spatulas.

Method for registration of maximal mandibular opening capacity

The method has previously been tested and described (6). The questionnaire included written instructions and a photo showing the procedure to open up the jaws as much as possible and mark the distance between the jaws, 'the maximal inter-incisal distance', with a pencil on the enclosed spatula (Fig. 1). In order to obtain a value for maximal mandibular opening capacity, a value for the vertical overlap between upper and lower frontal teeth was also needed. Each participant was therefore asked to assess the amount of vertical overbite between his or her upper and lower frontal teeth. This was carried out by looking in a mirror and comparing the frontal overbite in the intercuspal position with included photos. The intercuspal position is the jaw position seen when the upper and lower teeth are maximally closed together. In a deep bite, the upper incisors then overlap most of the lower incisors and in a normal bite only a small part of the upper and lower frontal teeth overlap. A standard value of 2 mm for a normal and 5 mm for a deep frontal over bite has in a previous methodological study been found to give an acceptable approximation of the true value (6). The appropriate value according to the participant's assessment of the type of overbite was added to the marked distance measured on the spatula in order to obtain the value for maximal mandibular opening capacity. This value reflects the total opening movement of the temporomandibular joints. Open bites are seen when the upper and lower teeth do not meet in the intercuspal position. They are rare in adults and were not to be included in this study.

Fig. 1. The maximal inter-incisal distance marked with a pencil on the spatula that was enclosed with the questionnaire.

One investigator (CH) measured all spatulas with a ruler graduated in millimeters. For later calculation of the measurement error the first 50 were remeasured blindly to whether TMJ problems were present and the previous values.

The questionnaire

The questionnaire was first sent as a pilot test to 10 persons with EDS. Out of these, seven wanted to participate and were interviewed by telephone concerning the design of the questionnaire. None reported difficulties with the questions. The questions presented

Table 1. **95% CI for the difference between proportions of affirmative answers in the EDS group and the control group. (*n* = total number of answers in the EDS group and the control group respectively)**

Questions concerning:	EDS proportion yes answers	Controls proportion yes answers	Difference between proportions	95% CI for the difference between proportions
Present problems from joints	0.44 ($n = 114$)	0.06 ($n = 113$)	0.38	0.27–0.47
Pain in masticatory muscles	0.47 ($n = 110$)	0.04 ($n = 114$)	0.43	0.32–0.53
Experience of hypermobile joints during mouth opening	0.65 ($n = 111$)	0.04 ($n = 114$)	0.61	0.50–0.69
Present pain in body joints except for TMJ	0.89 ($n = 111$)	0.23 ($n = 111$)	0.66	0.56–0.75
Awareness of hypermobile hand/ wrist	0.83 ($n = 114$)	0.07 ($n = 114$)	0.76	0.65–0.82
Permanent locking of TMJ	0.46 ($n = 113$)	0.04 ($n = 113$)	0.42	0.31–0.51
Poor mouth opening capacity when biting into thick food	0.28 ($n = 112$)	0.05 ($n = 113$)	0.23	0.14–0.32
TMJ clicking during the last month	0.67 ($n = 114$)	0.19 ($n = 112$)	0.48	0.36–0.58
TMJ crepitation during the last month	0.57 ($n = 114$)	0.15 ($n = 113$)	0.42	0.30–0.52
Awareness of present clenching of the teeth	0.56 ($n = 112$)	0.32 ($n = 114$)	0.24	0.12–0.37
Awareness of present grinding of the teeth	0.35 ($n = 112$)	0.16 ($n = 113$)	0.19	0.08–0.30
Present use of an occlusal splint	0.18 ($n = 111$)	0.08 ($n = 114$)	0.10	0.01–0.19
Hypnotic medication	0.18 ($n = 113$)	0.04 ($n = 113$)	0.14	0.05–0.22
Analgesic medication	0.75 ($n = 113$)	0.25 ($n = 110$)	0.50	0.37–0.60

in this study mainly concern problems related to the temporomandibular joints (Table 1). Other odontological aspects and quality of life aspects will be presented later. The study was approved by the Ethics Committee of the Medical Faculty of Göteborg University.

Statistics

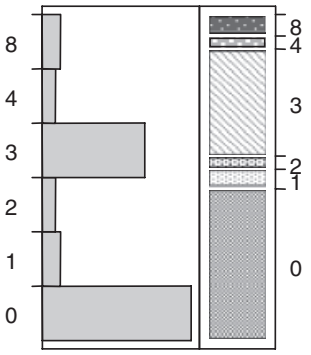
The measurement error was calculated for the first 50 spatulas as the repeatability value (22). The within-subject standard deviation, s_w, was first calculated using the formula $s_w^2 = 1/2n \sum d_i^2$ where d_i is the difference between the two observations for subject i and n is the number of subjects. The repeatability was then calculated according to the formula $\sqrt{2} \times 1.96 s_w$ ($2.77\ s_w$) (22).

The affirmative answers were when graded 'yes always', 'yes sometimes' or 'yes both sides' added for a compressed presentation. A few questions also included the answer 'do not know' as a 'no' answer. The 95% confidence interval for the difference between proportions was calculated by using the Wilson method (23). A significant difference is assumed when the interval does not include zero. JMP and JMP IN® software (SAS Institute Inc., Cary, NC, USA) was used for descriptive data analyses (24).

Results

The age distribution was similar between groups. The mean age was 43 years (95% CI 41–45 years) for the EDS group and 42 years (95% CI 40–45 years) for the controls. There were 101 women and 13 men in the EDS group. The control group comprised 94 women and 20 men. The measurement error, s_w, was 0.4 mm and the repeatability for the two measurements of the first 50 spatulas was 1.1 mm. Sixty-one persons knew their EDS type of the disease while 53 did not know. The most common group among the known EDS types was type III, the hypermobility type (Fig. 2).

Mean maximal mandibular opening capacity values for the EDS and the control groups were similar, 54 mm (range 28–78 mm) and 53 mm (range 38–77 mm) respectively (Fig. 3). The mean values were also similar for the different EDS types. The largest group of persons with diagnosed EDS was type III (hypermobile) group (Fig. 2). The mean value for this group of 37 women was 53 mm (Fig. 3). In the EDS group, 55 persons chose a photo of a normal overbite to match their bite in the intercuspal position and 59 persons chose a deep overbite. The control group reported 60 normal overbites and 54 deep ones.



EDS type	Berlin nosology	Number observations	Proportion
Unknown		53	0.46
Type I	Gravis	7	0.06
Type II	Mitis	5	0.04
Type III	Hypermobile	37	0.32
Type IV	Arterial-eccymotic	5	0.04
Type VIII	Periodontal	7	0.06
Total		114	1.00

Fig. 2. Histogram bars for the distributions of different types of EDS (24).

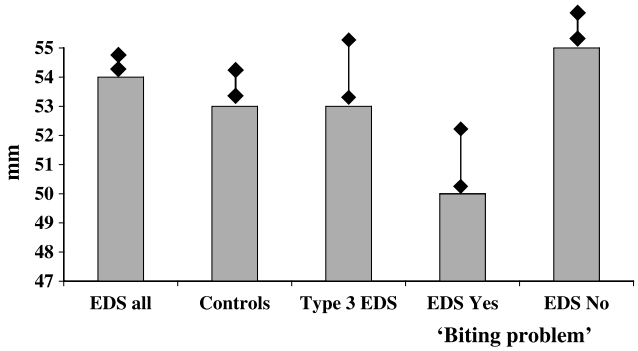


Fig. 3. Mean maximal mandibular opening values in millimeter for all EDS persons ($n = 114$) all controls ($n = 114$) and the EDS persons with diagnosed EDS type III (hypermobile) ($n = 37$). The last two bars concern opening values for those who answered 'Yes' ($n = 31$) and 'No' ($n = 81$) respectively to the question about 'mouth opening problems when biting into thick pieces of food'. The standard error is given on top of each bar.

Forty-four per cent of the EDS persons had present problems from the temporomandibular joints and almost half reported pain in masticatory muscles. They experienced hypermobility of their joints during wide mouth opening (65%). The increased mobility of the joints had caused permanent locking in almost half the cases. Among the controls, only a few persons (4%) had experienced permanent lockings (Table 1).

Among the EDS persons who reported hypermobility of the joints, the mean maximal mandibular bite opening value did not differ significantly from the mean value for those who did not give affirmative answers ($p > 0.05$). In contrast, the bite opening capacity was reduced when biting into thick pieces of food such as a hamburger in one third of the EDS group. The EDS persons who reported problems with poor mouth opening capacity when biting into thick pieces of food had a lower mean maximal mandibular opening value (50 mm) compared with the other EDS persons (55 mm) ($p < 0.05$). The difference between sample means was 5.8 mm (95% CI 2.4–9.2 mm) (Fig. 3).

Clicking and crepitations in the joints were very common among EDS persons. Clenching of the teeth was reported as more common than grinding and was increased compared with controls. Only 18% of the EDS persons and 8% of the controls currently used a splint. The EDS persons more often used analgesic and hypnotic medication than the controls did (Table 1).

The proportion of affirmative answers for the EDS persons was very high concerning pain in general body joints (89%) and the hand and wrist mobility was experienced as hypermobile (83%) (Table 1). The frequency of affirmative answers for all questions above was significantly increased among EDS persons comparing the 95% confidence intervals for the proportions with the randomized control group (Table 1).

Discussion

The clearly increased proportions of temporomandibular joint and/or masticatory muscle disorders (TMD) among EDS persons are considered important findings warranting extra awareness in dental treatment of persons with EDS. A careful clinical examination of the masticatory system is recommended. The present study mainly concerns women as only 13 men were eligible among the members of the Swedish EDS Association. A higher prevalence of reported TMD symptoms in women than in men has been found (25, 26). In a study by Magnusson et al., differences between the sexes concerning clinical signs were limited to TMJ sounds and masticatory muscle tenderness (25). The control group was weighted for women and only comprised 20 men in order to avoid gender being a confounding factor when comparing EDS persons and controls.

Almost half the persons (46%) with EDS did not know their EDS diagnosis type. The most frequent known

diagnosis was type III (32%), also called the hypermobility type. In all types of EDS, general joint hypermobility is included as stigmata of the disease. As hypermobility of the joints is a general problem, the answers are suggested to reflect joint problems and related issues overall among EDS persons although not being specifically related to any particular type of EDS.

In the above-mentioned study by Magnusson et al., 135 randomly selected persons had originally been followed from 15 to 35 years of age. At 35 years of age, only three of 100 clinically examined persons were found to have severe or moderate clinical signs of TMD (25). This is in line with the low frequencies of TMD reported for the controls in the present questionnaire study.

The maximal mandibular opening measures were used to study the movement capacity of the joints (temporomandibular joints). The mean values did not differ when they were compared between EDS persons and controls. Many of the subjects reported that they experienced increased jaw mobility when they were younger and that it decreased with age. The mean age was close to 40 years and the age factor could explain the lack of differences in movement capacity of the joints. Beighton observed recurrent, easily reducible dislocations of the joints in two patients that disappeared as the 'joints grew older with age' (5). It is also possible that the EDS persons were so aware of their tissue fragility that they habitually avoided extreme mandibular movements. Permanent lockings of the joints were reported by almost half the EDS persons and could be handled by the person him or herself. Only three persons with EDS had to visit the hospital for repositioning. Among controls, the described situation was rare. The permanent lockings and the increased proportions of reported clicking and crepitations of the joints among EDS persons still point towards an imbalance and/or degenerative changes in the joints. An interesting finding is that the EDS persons who reported problems when biting into thick pieces of food had significantly lower maximal mandibular opening capacity compared with the EDS persons who did not report this problem.

In the epidemiologic longitudinal study by Magnusson et al. (25), the maximal mouth opening at four different examinations (ages 15, 20, 25 and 35 years) showed equal mean values (range 55.5–56.9 mm). However, the interindividual range at a specific age was large. For example, at age 35 a range between 43 and 74 mm was found. The range found in the present study was even larger for both EDS persons (28–78 mm) and control persons (38–77 mm). It is therefore suggested for future studies on mandibular opening capacity to focus longitudinally on intra-individual changes in mandibular opening capacity, either clinically or self-registered, and to individually correlate these findings to signs or symptoms of TMD.

Less than half of the persons with present problems from the joints reported that they used an occlusal splint. This is despite the fact that women are reported to seek treatment for craniomandibular disorders more frequently (26, 27) and were therefore assumed to have been suggested TMD treatment, which commonly includes occlusal splint therapy. Current therapy also includes, for example, anti-inflammatory agents, muscle relaxants and physical therapy (7). Avoidance of surgery in certain variants of EDS is recommended (7). In this questionnaire study, it is not possible to distinguish between a dominance of muscular and/or joint structure pain. In a case control study by Hagberg (28), TMD patients showed increased relative risks of having general musculoskeletal pain, especially in the upper neck, the shoulder and lower neck region, the shoulder joint and the thoracic back. For the moment, it is not possible to evaluate the impact severe TMD disorders would have on a person with EDS who already has musculoskeletal and/or joint pain because of the connective tissue disorder *per se*. Sacheti et al. interviewed 51 individuals with EDS and they were found to report chronic pain of early onset. Most frequently affected were the shoulders, hands and knees (29). In the present study, many EDS persons were frequently using analgesics and hypnotic medication because of their general pain. The medication could have implied an underestimation of the TMD problems. Sleep complaints have previously been reported as not rare in Marfan and EDS patients (30).

Limitations of the present study are that a questionnaire study only gives subjective information and that the questions could have been misinterpreted. However, it is not likely that the EDS persons would understand the questions differently compared with the controls. This source of error is then likely to have the same impact on both groups. The EDS persons who had chosen to become members of the Swedish EDS Association could represent a group of EDS persons with more severe problems than usual, resulting in the

need of support from an organization. Even so the knowledge of increased risks for TMJ problems among persons with EDS is important diagnostic and prognostic information in clinical dental practice. In conclusion, the data from this study support the literature that persons with EDS are naturally predisposed to TMJ problems. The self-registration of maximal mandibular opening capacity is a useful diagnostic tool in giving an objective clinical measure of movement capacity of the joints. The clinical measure was in line with the affirmative answers on having problems with poor mouth opening capacity when biting into thick pieces of food among the EDS persons.

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References

1. Beighton P. Articular manifestations of the EDS. *Semin Arthritis Rheum* 1971;**1**:246–301.
2. Steinmann B, Royce PM, Superti-Furga A. The Ehlers-Danlos syndrome. In: Royce PM, Steinmann B, editors. *Connective Tissue and its Heritable Disorders: Molecular, Genetic and Medical Aspects*. New York: Wiley-Liss; 1993. pp. 351–407.
3. Goodman RM, Allison ML. Chronic temporomandibular joint subluxation in Ehlers-Danlos syndrome: report of a case. *J Oral Surg* 1969;**27**:659–61.
4. Thexton A. A case of the Ehlers-Danlos syndrome presenting with recurrent dislocation of the temporomandibular joint. *Br J Oral Surg* 1965;**2**:190–3.
5. Beighton P. *The Ehlers-Danlos syndrome*. London and Colchester: Spottiswoode, Ballantyne and Company; 1970:88.
6. Hagberg C. Self-registration of mandibular opening capacity and vertical overbite. A method study. *J Orofac Pain* 2003;**17**:341–6.
7. Fridrich KL, Fridrich HH, Kempf KK, Moline DO. Dental implications in Ehlers-Danlos syndrome. A case report. *Oral Surg Oral Med Oral Pathol* 1990;**69**:431–5.
8. Harinstein D, Buckingham RB, Braun T, Oral K, Bauman DH, Killian PJ et al. Systemic joint laxity (the hypermobile joint syndrome) is associated with temporomandibular joint dysfunction. *Arthritis Rheum* 1988;**31**:1259–64.
9. Buckingham RB, Braun T, Harinstein DA, Oral K, Bauman D, Bartynski W et al. Temporomandibular joint dysfunction syndrome: A close association with systemic joint laxity (the hypermobile joint syndrome). *Oral Surg Oral Med Oral Pathol* 1991;**72**:514–9.
10. Hagen K. Understanding Ehlers-Danlos syndrome. *Dermatology Nursing* 1993;**5**:431–4.
11. Caillet R. *Soft Tissue Pain and Disability*. 3rd edn. F.A. Davis Company: Pain Series; 1996.
12. Beighton P. The Ehlers-Danlos syndromes. In: Beighton P, editor. *McKusick's Heritable Disorders of Connective Tissue*, 5th edn. St Louis: Mosby; 1993. pp. 189–257.
13. Stanitski DF, Nadjarian R, Stanitski et al. Orthopaedic manifestations of Ehlers-Danlos syndrome. *Clin Orthop* 2000;**376**:213–21.
14. Wilton JM, Griffiths GS, Curtis MA et al. Detection of high-risk groups and individuals for periodontal diseases. Systemic predisposition and markers of general health. *J Clin Periodontol* 1988;**15**:339–46.
15. Bond PJ, Friend GW, Meridith MW. Ehlers-Danlos syndrome identified from periodontal findings: case report. *Pediatr Dent* 1993;**15**:212–3.
16. Perez LA, Al-Shammari KF, Gianmobile WV, Lay Wang, H-L. Treatment of periodontal disease in a patient with Ehlers-Danlos syndrome. A case report and literature review. *J Periodontol* 2002;**73**:564–70.
17. Beighton PH, De Paepe A, Danks D et al. International nosology of heritable disorders of connective tissue. Berlin 1986. *Am J Med Genet* 1988;**29**:581–94.
18. Beighton P, De Paepe A, Steinmann B et al. Ehlers-Danlos syndromes: revised nosology, villefranche, 1997. *Am J Med Genet* 1998;**77**:31–7.
19. Beighton PH. Ehlers-Danlos syndrome. In: David TJ, editor. *Recent Advances in Paediatrics II*. Edinburgh: Churchill Livingstone; 1993. pp. 133–46.
20. Bergqvist D. Ehlers-Danlos Type IV syndrome. A review from a vascular surgical point of view. *Europ J Surg* 1996;**162**:163–70.
21. Barabas GM, Barabas AP. The Ehlers-Danlos syndrome. A report of the oral and haematological findings in nine cases. *Br Dent J* 1967;**123**:473–9.
22. Bland JM, Altman DG. Measurement error. *BMJ* 1996;**313**:744–53.
23. Newcombe RG, Altman DG. Proportions and their differences. In: Altman DG, Machin D, Bryant TN, Gardner MJ, editors. *Statistics With Confidence*, 2nd edn. Bristol: BMJ books, JW Arrowsmith Ltd; 2000. pp. 45–56.
24. Sall J, Lehman A. JMP Start statistics. A guide to statistics and data analysing using JMP and JMP IN R software. In: Stan Loll (software development ed), SAS Institute Inc. USA: Duxbury Press; 1996. pp. 1–495.
25. Magnusson T, Egermark I, Carlsson GE. A longitudinal epidemiologic study of signs and symptoms of temporomandibular disorders from 15 to 35 years of age. *J Orofac Pain* 2000;**14**:310–9.
26. Carlsson GE. Epidemiology and treatment need for temporomandibular disorders. *J Orofac Pain* 1999;**13**:232–7.
27. Hagberg C, Hagberg M and Kopp S. Musculoskeletal symptoms and psychosocial factors among patients with craniomandibular disorders. *Acta odontol Scand* 1994;**52**:170–7.
28. Hagberg C. General musculoskeletal complaints in a group of patients with craniomandibular disorders (CMD). A case control study. *Swed Dent J* 1991;**15**:179–85.
29. Sacheti A, Szemere J, Bernstein B, Tafas T, Schechter N, Tsipouras P. Chronic pain is a manifestation of the Ehlers-Danlos syndrome. *J Pain Symptom Manage* 1997;**14**:88–93.
30. Verbraecken J, Declerck A, Van de Heyning P, De Backer W, Wouters EFM. Evaluation for sleep apnea in patients with Ehlers-Danlos syndrome and Marfan: a questionnaire study. *Clin Genet* 2001;**60**:360–5.