Original Article

Evaluation of Temporomandibular Disorders and Comorbidities in Patients with Ehler-–Danlos: Clinical and Digital Findings

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Abstract

Objective: The objective of this study is to recognize representative cranio-cervico-mandibular features of patients with Ehler–Danlos syndrome and associated temporomandibular disorders (TMDs), to assess a targeted and integrated treatment plan.

Materials and Methods: After a diagnosis of disease, 38 individuals with Ehler–Danlos syndrome and temporomandibular symptomatology referred were evaluated. Gnathological evaluation, according to the Diagnostic Criteria for TMDs, and radiographic imaging was performed. In addition, digital evaluation of occlusal and muscular balance, using surface electromyography of jaw muscles, was conducted. Statistical software for data analysis - STATA (StataCorp, College station, Texas, USA) - was used.

Results: Most common temporomandibular dysfunctions were arthralgia, myalgia, disc displacement with reduction and subluxation. Headache and neck pain were the most frequent comorbidities. Somatization, depression, anxiety, and obsessive-compulsive behavior were the most recurrent psychological disorders. Electromyographic analysis showed out of normal range data.

Conclusion: Early diagnosis and interception are requested to avoid injuries and repeated traumatism. Multidisciplinary treatments are available to approach all the aspects of the syndrome.

Keywords: *Ehler–Danlos syndrome, electromyography, headache, neck pain temporomandibular disorders*

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Introduction

Oral and mandibular manifestations have been noticed in all types of Ehler–Danlos Syndromes. Collagen alterations compromise oral health affecting not only vascular system, bone, teeth, periodontium but also the neuromuscular and articular system.[1,2] These manifestations are often unknown and ignored by clinicians but are commonly reported by patients, with a substantial impact on the quality of life.[3]

Ehler–Danlos syndromes and temporomandibular disorders (TMD) have been linked in several studies.[4-11] In this kind of patients, temporomandibular joints (TMJ) are often hypermobile, subluxe and can dislocate.[1,12,13] TMJ dislocation is noted to occur more often in women than in the general population.[14] Recurrent subluxations and luxation of the TMJ could lead to the cartilaginous disc displacement resulting in pain, bone destruction, and in some severe cases, limited mobility. Jaw muscles can be overload and stressed, causing referred face, head and neck pain thus resulting in decreased functionality and quality of life.[15,16] Temporomandibular comorbidities such as cervical spine instability and headache are recognizable in patients with Ehler–Danlos syndrome.[17]

Psychological problems, such as depression and anxiety, are common and also caused by a deterioration of the quality of life for ineffective treatments. Sleep disorders are also associated.[18]

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Diagnostic guidelines are necessary for correct evaluation and treatment of patients with Ehler–Danlos and associated TMDs.

Materials and Methods

The study was approved by the Institutional Human Ethics Committee, Sapienza University of Rome, protocol no. 0001385.

Study design

In the first instance, individuals with Ehler–Danlos syndrome had to be recruited at the Department of Rare Diseases of Policlinico Umberto I, "Sapienza" University of Rome. In the second phase, patients had to be sent to the Department of Oral and Maxillo-facial Sciences of Policlinico Umberto I, "Sapienza" University of Rome, for the evaluation of the presence of TMDs.

Forty-five patients with Ehler–Danlos syndrome were visited between January 2017 and February 2018. Six patients did not report temporomandibular dysfunctions. Thirty-eight patients with cranio-cervico-mandibular symptomatology (30 females and eight males) with an average age of 34 years were selected. Whereas Ehler–Danlos syndromes are a group of rare diseases, the sample size was considered sufficiently representative.

Subjects eligible for the study had provided signed informed consent, according to the World Medical Association's Declaration of Helsinki.

Gnathological evaluation

The presence of TMDs was assessed, according to Diagnostic Criteria for Temporomandibular joint disorders (DC/TMD) Axis I.[19] DC/TMD includes pain disorders and joint Disorders. Twelve types of temporomandibular dysfunctions are mentioned: Arthralgia, myalgia, local myalgia, myofascial pain, myofascial pain with referral, four type of disc displacement disorders, degenerative joint disease, subluxation, and headache attributed to TMD.

The type of pain was evaluated, recording anatomical position, and intensity.

Pain intensity (cephalic, joint, muscle, and cervical pain) was quantified using the verbal numeric scale (VNS),[20] which has numeric values (0–100) to indicate pain intensity, with the division into five groups: 0 (no pain); 0–20 (slight and episodic pain); 20–50 (moderate pain); 50–80 (severe pain); and 80–100 (very severe pain).

Psychological problems and emotional strain were assessed with Symptom Check List revised 90. It is a brief self-report psychometric instrument (questionnaire) published by the Clinical Assessment division of the Pearson Assessment and Information group. It evaluates a wide range of psychological problems and symptoms. The SCL-90-R is normed on individuals 13 years and older. It consists of 90 items and takes 12–15 min to administer. The primary symptoms that are assessed are somatization, obsessive-compulsive behavior, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoia, and psychoticism. It is one of the most widely used measures of psychological distress in clinical practice and research.

Digital evaluation with surface electromyography

BTS JOINT device is a wireless surface Electromyography of masticatory muscles which analyzes the occlusal-muscular balance. Electromyography of the masseter muscles and the anterior bundle of the temporalis muscles was applied. The following indexes were considered:

POC (Percent Overlapping Coefficient) = index of standardized contraction symmetry within the same muscular couple (TA – temporalis anterior bundle; MM – masseter) (normal range % 83–100)

IMP = fatigue and parafunction index (normal range % 85–100)

ASIM = asymmetry index. Evaluation of balanced muscular activation between both sides (normal range % −10 and +10)

TORS = activation of couple of muscles who induces a mandibular rotation on the transversal plane (normal range % 90–100)

BAR = occlusal-muscular center of gravity (normal range % 90–100)

The same operator, previously calibrated, carried out all the clinical and instrumental evaluations. Another operator controlled all the data to verify their reliability.

All data were analyzed using descriptive percentages, average, and standard deviation systems. Results are shown in tabular and graphical forms.

Results

Given the great amount of data emerging from research, the results were divided into three sections: (a) results emerged from the gnathological evaluations (b) results emerged from the psychological evaluation, and (c) results emerged from the surface electromyography.

Gnathological evaluation results

Joint and pain disorders, according to DC/temporomandibular disorders

Most common joint disorders in patients with Ehler–Danlos syndrome are mono or bilateral disc displacements and mono or bilateral subluxation, as shown in Table 1.

Patients referred pain in correspondence of TMJs and masticatory muscles with high frequency and severe intensity, according to VNS, as shown in Table 2.

Headache

In our sample, 80% (30 patients) referred a moderate mono or bilateral pain in temporal region. VNS value was 7.59 ± 1.26. The type of pain was throbbing and dull with chronic frequency, also associated to episodes of migraine with aura and factors such as inclination head changes. Other frequent sites are the frontal and orbital portion of the skull and the occiput.

The comorbidity associated in all patients was cervical pain with high intensity.

Psychological evaluation

The SCL-90 reported a high percentage for somatization, obsessive-compulsive behavior, depression and anxiety, as showed in Figure 1 and Table 3.

Digital evaluation

Surface electromyography

In the sample, 95% (36 patients) had BAR (occlusal-muscular center of gravity) value x >100 and located in an anterior position. IMP (index of parafunction and muscular fatigue) value is x >100 in the 95% of patients and indicates the presence of parafunctions. Simmetry indexes were also alterated except for POC MM (index of standardized contraction symmetry within the couple of masseters) [Figure 2].

Table 1: Gnathological analysis according to diagnostic criteria for temporomandibular disorders. Percentage values of prevalence and absolute frequency (n) of each joint disorder

Joint disorders (mono or bilateral)	Percentage values of prevalence (%)	Absolute frequency (*n*)
Disc displacement with reduction	60%	23
Subluxation	100%	30
Degeneration joint disease	26%	8

Discussion

TMJs and related muscles are among the structures involved in patients with Ehler–Danlos syndrome. The complicated clinical picture requires a multilevel approach, to establish the most adequate treatment plan. The study was born with the necessity to define a specific diagnostic and therapeutic protocol for this type of patients. In the scientific literature, there is a representative study about definition of oral and mandibular manifestations of Ehler–Danlos syndrome,[21] to which we have done reference to define a more specific flowchart of diagnosis and therapy for each patient.

Furthermore, in addition to clinical and psychological evaluations, digital analysis of muscular balance on the basis of occlusal contacts was assessed for the first time in this kind of patients. This represents a starting point to evaluate the occlusal stability as support to articular and muscular balance and to find adequate conservative occlusal adjustments, with the help of the last generation device.

The sample group consisted of patients which had never undertaken rehabilitations and therapies and with a diagnosed TMD. Young patients were excluded for this last reason, in fact, they did not report any mandibular dysfunction. Anyway, they were included in a separate

Table 2: Gnathological analysis, according to diagnostic criteria for temporomandibular disorders. Percentage values of prevalence and absolute frequency (n) of each pain disorder

Pain disorders (mono or bilateral)	Percentage values (%)	Absolute frequency (*n*)	Verbal numeric scale (0-100) average±SD
Arthralgia	70%	27	6,52±1,03
Myalgia, local or myofascial	93%	35	7,97±0,85

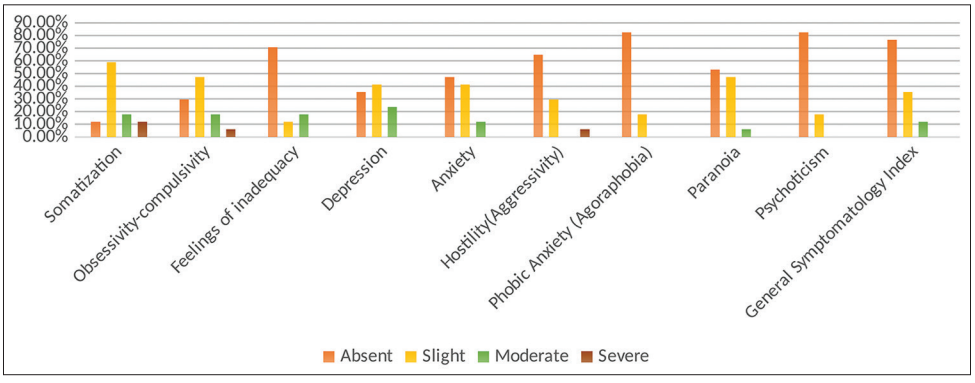

Figure 1: Percentage scores for each item of SCL-90

Table 3: Average and standard deviation for each item of symptom checklist revised 90. Psychopathological dimension: Absent ≤1; slight 1>×≥2; moderate 2>×≥3; and severe ≥3. After the calculation of the coefficient of variation (σ/μ), average values do not seem to be representative of the sample, except for some of these. Therefore, percentage values were taken into account for the conclusive considerations

Psychological disorders	Average and standard deviation
Somatization	1,808235294±0,820260898
Obsessivity-compulsivity	1,541176471±0,765717656
Feelings of inadequacy	0,882352941±0,714278739
Depression	1,271176471±0,623807686
Anxiety	1,052941176±0,702778101
Hostility	0,844117647±0,863025628
Phobic anxiety	0,437647059±0,498717473
Paranoia	0,861764706±0,600564685
Psychoticism	0,434117647±0,437650814
General symptomatology index	1,084705882±0,536459664

group to monitor the developments of disease to prevent and intercept any mandibular problem.

Clinical temporomandibular features

The scientific literature reports that patients with Ehler–Danlos syndrome had a history of hypermobility and a part of them referred the tendency to have mandibular luxation. Severe pain was reported in temporomandibular region and also noticeable in correspondence of masticatory muscles, probably due to the excessive joint excursion, ligamentous injuries, and parafunctions.[22] Bruxism is most common stress and when is combined with Ehler–Danlos syndrome, the effects are substantially amplified, particularly in patients with craniocervical instability.[23] In this research, most common pain was in correspondence of articulation points and temporalis, external pterygoideus muscles and masseters with a severe intensity and chronic frequency. Patients with hypermobile TMJ will often have increased maximal mouth opening range (40–55 mm)[1,9] with mandibular subluxation, expression of the lack of proprioception, and ligamentous laxity. This phenomenon leads to soft-tissue injuries, repeated microtraumatism and disc dislocations. Disc displacement with reduction (mono or bilateral, with or without pain) was a recurring feature in our sample and confirmed by the literature.[14] Disc displacements without reduction and limited mouth opening were not noticed, unlike what said in the literature.[15,16]

Headache is another common complaint of this kind of patients. JACOME[24] first described headache as a possible neurologic presentation of Ehler–danlos Syndrome. Clinical forms of headaches include migraine with aura, migraine without aura, tension headache,

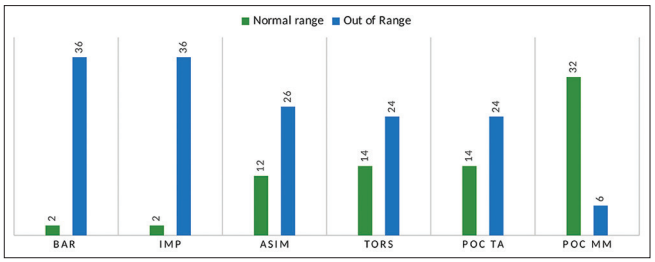

Figure 2: Results of surface electromyography. Absolute frequencies for each index

a combination of tension headache and migraine, and posttraumatic headache. This finding was repeatedly confirmed in the scientific literature[25-27] and also recognizable in this study. Cervical spine hypermobility is considered a common predisposing factor for this form of headache.[28] As confirmed in the literature,[29,30] in this sample, TMJ dysfunctions and neck pain are additional predisposing factors to multiple forms of craniofacial pain and among these, headache.

In this research, cervical spine instability and pain are the comorbidities recognizable in all patients with Ehler–Danlos syndrome and TMD.

Psychological features

It is observed a reduced quality of life because of the early onset time of pain, fatigue, sleep disturbance and because of ineffective treatments.[31] Patients belonging to this sample have psychological implications, deriving from chronic pain and disability, as confirmed by Symptom-Checklist revised 90 questionnaires.

The analysis of psychological aspect is necessary also for the evaluation of the limits of response to therapy. Perception of pain is influenced by psychological disturbances; therefore, the proposal of psychological intervention should be required.

Digital evaluation

Surface electromyography of jaw muscles was performed to assess the "occlusal-muscular" balance. This kind of electromyography does not allow to evaluate the muscular strength as an absolute value. It only relates muscular activity to occlusal findings since masticatory muscles cannot be "separate" from occlusal input. Therefore, the instrument could allow to identify and to intercept occlusal patterns that may disturb a formerly unstable articular/muscular condition.

Significant data emerged. The abnormal position of occlusal-muscular center of gravity shows the prevalent activity of temporalis muscles among masticatory muscles, due to prevalent anterior occlusal contacts (up to the first bicuspid). Anterior center of gravity is associated with dysfunctions because of the presence

of a retrusive condylar component and because of the increased articular load.[32] There is the presence in these patients of parafunctions such as bruxism and clenching which may worsen the painful symptomatology and the perception of muscular fatigue.

In addition, symmetry indexes reported out of normal range values. All these indexes are related to a balance that should be noticeable between right and left side in patients with an occlusal-muscular equilibrium. In our sample, they indicated that, in about two-thirds, there is an asymmetrical muscular activity between two sides, on the basis of the occlusal contacts. This could lead to an overload of the TMJs and masticatory muscles, to a retrusion of the condyle of the mandibular deviation side and wider balancing movements of the contralateral condyle. This can be worsen by the lack of proprioception and instability that cannot allow muscles to find a balance on the basis of occlusal contacts. To choice the most adequate treatment plan, it is necessary to verify if these EMG results are the expression of concomitant alterated occlusal patters or also due to the articular/muscular "instability" typical of this syndrome. For these patients, double-phase treatment should be assessed. The first phase is a gnathological treatment with functional-orthopedics issues; the second one is a conservative occlusal therapy to finalize goals achieved with the previous one.

Limitations of the study

- Learning curve of acquisition of skills for what concerning diagnosis and therapy, for dental practitioners
- Increased time to collect patients due to the rarity of the disease
- Difficulty to increase awareness of the importance of gnathologic diagnosis and therapy among the patients.

Advantages of the study

- Standardized protocol that allows to reach a correct diagnosis in view of individualized treatments
- Direct contact between the Department of Rare disease and the Department of Oral Sciences, as centers of reference for this disease, with the opportunity to visit almost the totality of patients with syndrome.

As stated above, the purpose of this study is to find clinical and digital features to improve temporomandibular and general symptomatology with specific treatments. The future research will concern the treatment flowchart for each joint/pain disorder (DC/TMD). The phase of articular repositioning with splints and proprioceptive education with myofunctional devices has started for all patients. Physical therapy in cranio-cervical district has been integrated in a therapeutic protocol. One-year follow-up is requested before collecting and analyze data for each patient.

Every patient also follows an integrated multidisciplinary approach which contributes to improve cranio-cervical symptomatology:

- Neurologic supervision to control the vascular aspect and types of headache
- Orthopedic and physiatric supervision to evaluate the level of bone mineralization and the entity of dysfunction in the cervical spine.

The sample size will be widened of year in year.

Conclusion

Ehler–Danlos syndromes are complex clinical conditions which need a multidisciplinary integrated approach to solve their several critical aspects. The involvement of TMJs and related structures in this syndrome and its impact on painful symptomatology and disability requires an expert examination. The aim is to prevent TMJ injuries, to intercept and treat incoming disorders, finding good articular stability. The detection of comorbidities and psychological aspects helps to improve as far as possible the results of therapy.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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