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Research Article

TMD IN EHLER-DANLOS SYNDROMES

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A B S T R A C T

Ehlers-Danlos syndromes are characterized by underdiagnosed heritable connective tissue disorders such as synovial joints hypermobility, hyperextensible skin and associated muscoskeletal, visceral, pelvic and neurologic dysfunctions. Temporomandibular joints and related structures are also involved with pain, dysfunctions and presence of associated comorbidities**. Aim of the study.** To focus typical cranio-cervico-mandibular features of EDS patients and psychological implications of the syndrome in order to assess a targeted and integrated treatment plan. **Material and methods.** 30 patients with Ehler-Danlos Syndromes and TMD were examined. Psychological tests, gnatological evaluation, according to Diagnostic Criteria for Temporomandibular disorders and surface electromyography with BTS JOINT device were submitted to patients. **Results.** *Psychological tests*. Significative percentage values of the sample were found out for what concerning somatization, depression, anxiety and obsessive-compulsive behavior. *Gnatological evaluation.* Most common disorders were headache associated to TMD, arthralgia, myalgia, disc displacement with reduction and subluxation. *Electromyographic evaluation.* Almost all patients had BAR (occluso-muscular centre of gravity) and IMP (fatigue index and parafunction) out of normal. Simmetry indexes were also alterated. **Conclusion.** Early diagnosis and interception are needed in order to prevent TMJ injuries. Multidisciplinary treatments are available to approach all the aspects of the syndrome.

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INTRODUCTION

The Ehlers-Danlos syndromes (EDS) are a clinically and genetically heterogeneous cluster of heritable connective tissue disorders characterized by joint hypermobility, skin hyperextensibility, and tissue fragility. The Villefranche Nosology, which delineated six subtypes on a biochemical and molecular basis, has been widely used as the standard for clinical diagnosis of EDS (Beighton P. 1998), up until two years.

The 2017 International classification for the Ehler - Danlos Syndrome recognized 13 subtypes on the basis of a genetic validation with identification of (a) causative variant(s) in the corresponding gene. In fact there is a vast genetic heterogeneity and phenotypic variability of the EDS subtypes, and a clinical overlap between many of these subtypes (Fransiska M *et al*. 2017).

Oral and mandibular manifestations have been noticed in all types of EDS patients. Collagen alterations compromise oral health affecting vascular system, bone, teeth, periodontium, but also the stomatognatic neuromuscular and articular system (Abel MD 2006; Norton LA 1997). These oromandibular manifestations in EDS are often unknown and ignored by clinicians but are commonly reported by patients with a substantial impact on the quality of life (Conti PCR, 2012).

Temporo-mandibular joints (TMJ) hypermobility and Temporo-mandibular disorders (TMD) have been linked to systemic joint hypermobility in several studies (Buckingham RB, 1991; De Coster PJ, 2005 a; Harinstein D 1988; Hirsch C, 2008; Kavuncu V, 2006; Westling L, 1991; Westling L. 1992; Diep D, 2016). In EDS patients, the TMJ often is hypermobile, subluxes and can dislocate (Norton LA 1997; Pasinato F, 2011; Wincour E, 2000). TMJ dislocation is noted to occur more often in women in the general population (Nosouhian S., 2015). Recurrent subluxations and luxation of the TMJ could lead to the cartilaginous disc displacement resulting in pain, bony destruction, and in some severe cases a limited mobility. The muscles of mastication can be overused, spasm, and cause referred face, head, and neck pain thus resulting in decrease functionality and quality of life (Berglund B, 2012; Hagberg C, 2004). In EDS patients the typical co-morbidities of TMD are present such as cervical spine instability and headache (Castori M , 2014).

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Excessive translation of the mandible may be associated with pharyngeal collapse which could be related to sleep-disordered breathing in EDS patients and responsible of daytime fatigue (Guilleminault C, 2013). Psychological problems, such as depression and anxiety, are common and also caused by a deterioration of quality of life for ineffective treatments.

Diagnostic guidelines are necessary for correct evaluation and treatment of the EDS patients with temporo-mandibular joints disorders.

MATERIAL AND METHODS

The study was approved by the Institutional Human Ethics Committee.

Thirty patients with Ehler -Danlos syndromes and temporo-mandibular symptomatology referred, sent from the Department of Rare Diseases, Umberto I hospital, and come under our observation, in the Department of Oral and Maxillo-facial sciences, Umberto I Hospital, were recruited between January 2017 and January 2018. Patients' age is between 18 and 50 yrs old, 20 % male (6) and 80% female (24). After the sampling phase, every patient was submitted to:

1. Psychological questionnaires (Toronto Alexitimia Scale and Symptom Check List revised 90).
2. Gnatological evaluation of temporo-mandibular disorders, according to Diagnostic Criteria for Temporomandibular joint disorders (Shiffman *et al*, 2014) and evaluation of perceived pain with VAS (Visual Analogic Scale).
3. Electromyographic evaluation with BTS JOINT device in order to assess the occlusal-muscular balance.

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

The TAS is a 20-item instrument that is one of the most commonly used measures of alexithymia. Alexithymia refers to people who have trouble identifying and describing emotions and who tend to minimize emotional experience and focus attention externally. This instrument examines three main domains: ability to identify and to describe feelings, and to distinguish feelings of bodily sensations, ability to daydream and preference for focusing on external events rather than inner experiences. The score indicated by the instrument ranges from 26 to 130. Values lower than 62 do not indicate symptoms of alexithymia, and values higher than 62 indicate the presence of symptoms.

The Symptom Checklist-90-R (SCL-90-R) 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 minutes to administer. The primary symptoms that are assessed are somatization, obsessive-compulsive behavior, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoia, psychoticism.. It is one of the most widely used measures of psychological distress in clinical practice and research.

Diagnostic Criteria for Temporomandibular Joint Disorders

	History		Examination	
Disorder	*Criteria*	*SQ*	*Criteria*	*Examination Form*
Pain Disorders				
Myalgia (ICD-9 729.1) • Sens 0.90 • Spec 0.95	Pain in a masticatory structure	SQ3	Confirmation of pain in masticatory muscle(s)	E1a
	Pain modified by jaw movement, function, or parafunction	SQ4	Familiar pain in masticatory muscle(s) with either muscle palpation or maximum opening	E4b, E4c, or E9: familiar pain in temporalis or masseter, or in other masticatory muscles if also relevant; **or** E10: familiar pain in supplemental muscles, if E10 included
Myalgia Subtypes				
Local Myalgia (ICD-9 729.1) Sens and Spec not established	[same as for Myalgia]	[SQ3 & SQ4]	Confirmation of pain in masticatory muscle(s)	E1a
			Familiar pain with muscle palpation	E9: familiar pain in masseter or temporalis; **or** E10: familiar pain in supplemental muscles, if E10 included
			Pain remains local to the area of stimulation	E9: negative referred and spreading pain; **and** E10: negative referred and spreading pain, if E10 included
Myofascial Pain (ICD-9 729.1) Sens and Spec not established	[same as for Myalgia]	[SQ3 & SQ4]	Confirmation of pain in masticatory muscle(s)	E1a
			Familiar pain with muscle palpation	E9: familiar pain in masseter or temporalis; **or** E10: familiar pain in supplemental muscles, if E10 included
			Spreading (but not referred) pain with muscle palpation	E9: spreading pain; **or** E10: spreading pain, if E10 included; **AND** E9: negative referred pain; **and** E10: negative referred pain, if E10 included

	History		Examination	
Disorder	*Criteria*	*SQ*	*Criteria*	*Examination Form*
Myofascial Pain with Referral (ICD-9 729.1) • Sens 0.86 • Spec 0.98	[same as for Myalgia]	[SQ3 & SQ4]	Confirmation of pain in masticatory muscle(s)	E1a
			Familiar pain with muscle palpation	E9: familiar pain in masseter or temporalis; **or** E10: familiar pain in supplemental muscles, if E10 included
			Referred pain with muscle palpation	E9: positive referred pain; **or** E10: positive referred pain, if E10 included
Arthralgia (ICD-9 524.62) • Sens 0.89 • Spec 0.98	Pain in a masticatory structure	SQ3	Confirmation of pain in TMJ(s)	E1a
	Pain modified by jaw movement, function, or parafunction	SQ4	Familiar pain with TMJ palpation or range of motion	E4b, E4c, E5a-c, or E9: familiar pain in TMJ
Headache Attributed to TMD (ICD-9 339.89 [other specified headache syndrome], or ICD-9 784.0 [headache]) • Sens 0.89 • Spec 0.87 Note that for a secondary headache diagnosis, a primary diagnosis of either myalgia or arthralgia is required.	Headache of any type in temporal region	SQ5	Confirmation of headache in temporalis muscle	E1b
	Headache affected by jaw movement, function, or parafunction	SQ7	Report of familiar headache in temporalis area from either: a. Palpation of the temporalis muscle **or** b. Range of motion of jaw	E4b, E4c, E5a-c, or E9: familiar headache pain in the temporalis muscle

	History		Examination	
Disorder	*Criteria*	*SQ*	*Criteria*	*Examination Form*
Joint Disorders				
Disc Displacement with Reduction (ICD-9 524.63) • Sens 0.34 • Spec 0.92	Current TMJ noises by history, **OR**	SQ8	Click(s) with opening and closing, **OR**	E6: (open & close) click, **OR**
	Patient reports noise during the examination	E6 or E7: noise reported by patient	Both (a) click with opening or closing, **and** (b) click with lateral or protrusive movements	E6: (open or close) click, **and** E7: click
Disc Displacement with Reduction, with Intermittent Locking (ICD-9 524.63) • Sens 0.38 • Spec 0.98	[same as disc displacement with reduction]	[same as DD with red]	[same as disc displacement with reduction]	[same as DD with red]
	Current intermittent locking with limited opening	SQ11=yes SQ12=no	When disorder present in clinic: maneuver required to open mouth	E8 (optional)
Disc Displacement without Reduction, with Limited Opening (ICD-9 524.63) • Sens 0.80 • Spec 0.97	Current* TMJ lock with limited opening	SQ9	Passive stretch (maximum assisted opening) < 40mm	E4c < 40mm including vertical incisal overlap
	Limitation severe enough to interfere with ability to eat	SQ10		
Disc Displacement without Reduction, without Limited Opening (ICD-9 524.63) • Sens 0.54 • Spec 0.79	Prior* TMJ lock with limited opening	SQ9	Passive stretch (maximum assisted opening) ≥ 40mm	E4c ≥ 40mm including vertical incisal overlap
	Limitation severe enough to interfere with ability to eat	SQ10		
Degenerative Joint Disease (ICD-9 715.18) • Sens 0.55 • Spec 0.61	Current TMJ noises by history, **OR**	SQ8	Crepitus during jaw movement	E6 or E7: crepitus detected by examiner
	Patient reports noise during the examination	E6 or E7: noise reported by patient		
Subluxation (ICD-9 830.0) • Sens 0.98 • Spec 1.00	TMJ locking or catching in wide open jaw position	SQ13	When disorder present in clinic: maneuver required to close mouth	E8 (optional)
	Unable to close mouth without specific maneuver	SQ14		

Electromyography of the masseter muscles and the anterior bundle of the temporal muscles with BTS TMJOINT 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 index and parafunction (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 = occluso-muscular center of gravity

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

RESULTS

In view of the great amount of data emerging from research, the results were divided into three sections, a) results emerged from the psychological evaluation, b) results emerged from the gnatological examinations c) results emerged from the surface electromyographic.

Psychological questionnaire

Reference values

TAS-20	**Normal data**
PsychoBiological regulation of Emotions	
Difficulty in identifying feelings	≤20,60
Difficulty in describing feelings	≤17,90
Thinking oriented to the outside	≤22,00
Total Difficulty in Emotional regulation	≥61 high level

SCL-90-R	**Normal data**			
Psychopatological Dimension	**absent**	**slight**	**moderate**	**Severe**
Somatization	≤ 1	da 1 a 2	da 2 a 3	≥ 3
Obsessivity-Compulsivity	≤ 1	da 1 a 2	da 2 a 3	≥ 3
Feelings of inadequacy	≤ 1	da 1 a 2	da 2 a 3	≥ 3
Depression	≤ 1	da 1 a 2	da 2 a 3	≥ 3
Anxiety	≤ 1	da 1 a 2	da 2 a 3	≥ 3
Hostility (Aggressivity)	≤ 1	da 1 a 2	da 2 a 3	≥ 3
Phobic Anxiety (Agorafobia)	≤ 1	da 1 a 2	da 2 a 3	≥ 3
Paranoia	≤ 1	da 1 a 2	da 2 a 3	≥ 3
Psychoticism	≤ 1	da 1 a 2	da 2 a 3	≥ 3
General Sintomatology Index	≤ 2	da 1 a 3	da 2 a 4	≥ 4

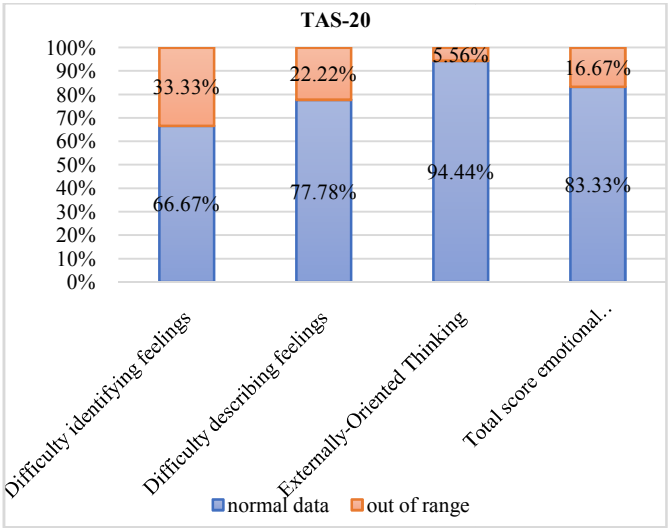


Table 1 Percentage scores for each item of TAS-20.

Table 2 Average and standard deviation for each item of TAS-20.

	Average and SD
Difficulty identifying feelings	18,05555556 ± 8,249579114
Difficulty describing feelings	12,11111111 ± 5,613941563
Externally-Oriented Thinking	15,72222222 ± 3,409425612
Total score emotional management difficulty	45,88888889 ± 14,69249063

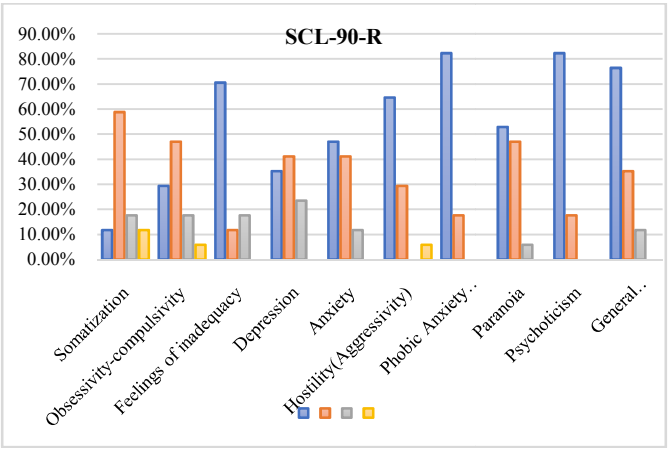


Table 3 Percentage scores for each item of SCL-90.

Table 4 Average and Standard deviation for each item of SCL-90-R.

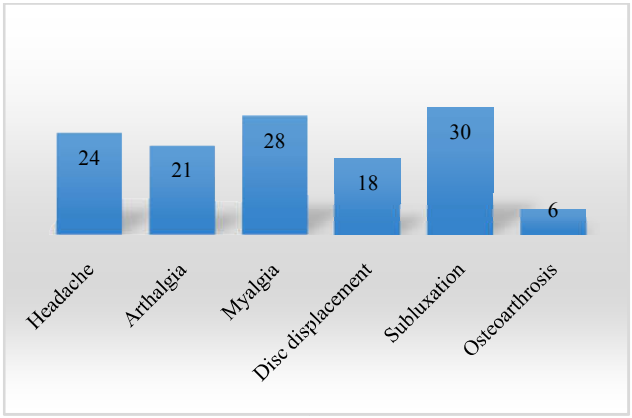
	Average and Standard Deviation
Somatization	1,808235294 ± 0,820260898
Obsessivity-Compulsivity	1,541176471 ± 0,765717656
Feelings of inadequacy	0,882352941 ± 0,714278739
Depression	1,271176471 ± 0,623807686
Anxiety	1,052941176 ± 0,702778101
Hostility	0,844117647 ± 0,863025628
Phobic Anxiety	0,437647059 ± 0,498717473
Paranoia	0,861764706 ± 0,600564685
Psychoticism	0,434117647 ± 0,437650814
General Symptomatology Index	1,084705882 ± 0,536459664

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.

Table 5 Gnatological analysis, according to Diagnostic Criteria for temporomandibular disorders.

Pain disorder	
Headache attributed to TMD	- 80% of patients - Intensity 6,7 (Visual analogic scale) - Chronic - with eventual migraine episodes
Arthralgia	-70% of patients in TMD region -Intensity 6,5 -93% of patients
Myalgia	- muscles involved: temporalis m., masseters, external pterygoideus
Joint disorder	
Disc displacement with reduction	-60% of patients, mono o bilateral
Subluxation	-100% of patients
Degeneration joint disease	-26% of patients

Table 6 Absolute frequencies for each pain and joint disorders.

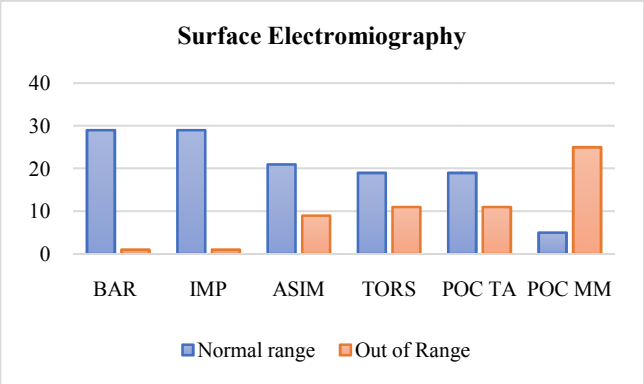


The comorbidity associated in all patients is cervical pain with high intensity.

Table 7 Results of Surface Electromiography. Absolute frequencies for each index.

	Percentage scores out of normal range
BAR	96%
IMP	96%
ASIM	70%
TORS	63%
POC TA	63%
POC MM	16%

Table 8 Significative percentage scores (out of normal range) for each index.



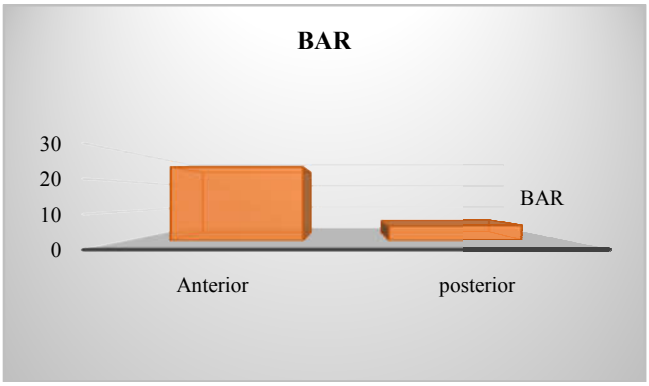


Table 9 Position of centre of gravity.

Bar Anterior 83%

DISCUSSION

EDS are characterized by recurrent articular subluxations and dislocations. Temporo-mandibular joint hypermobility leads to soft tissue injuries and repeated micro-traumatism. These patients often suffer from early onset chronic debilitating musculoskeletal pain and headache (Voermans N.C, 2010). It is observed a reduced quality of life due to pain, fatigue, sleep disturbance and not totally effective treatment (Rombaut L, 2011). In this study, from what emerging from the evaluation of alexitimia (TAS questionnaire), patients' values were within the normal range. On the contrary, the SCL-90 reported high percentage frequencies of out of normal range values for somatization (88,24%- 58,84% slight - 17,64% moderate - 11,76% severe), obsessive-compulsive behavior (70,06%- 47,07%slight -17,64%moderate-5,89%severe), depression (64,71%- 41,18% slight - 23,53% moderate) and anxiety (52,94%-41,18% slight -11,76% moderate). Confirming what said in the scientific literature, ED syndromes have psychological implications, deriving from chronic pain and disability. Alexitimia does not seem to be related, in our sample, to the syndrome. This probably occurs because EDS patients have not difficulty in recognizing their own emotions in association with more complaints and implications of the syndrome such as increased pain, fatigue and abnormal functionality.

Clinical evaluation. Clinical evaluation includes the analysis of joint and pain disorders, as defined by DC criteria, and associated comorbidities.

Headache. In our sample, patients referred a moderate mono or bilateral pain in temporal region (confirmed with the palpation and affected by parafunction), throbbing and dull with chronic frequency, aggravated by 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. Jacome (1999) first described headache as a possible neurologic presentation of EDS. Clinical forms of headaches include migraine with aura, migraine without aura, tension headache, a combination of tension headache and migraine, and post-traumatic headache. This finding was repeatedly confirmed by Bendik EM, 2011; Castori *et al*.,2011; Rombaut *et al*., 2010). Cervical spine hypermobility is considered a common predisposing factor for this form of headache (Rozen TD,2006). As confirmed in the literature, in this sample temporomandibular joint dysfunctions and cervicalgia (cervical pain) are additional predisposing factors to multiple forms of craniofacial pain and, among these, this "form" of headache (Castori M, 2010b; De Coster PJ, 2005 b).

Temporomandibular joint dysfunctions. Temporomandibular joints and related muscles are among the structures involved in EDS. Patients had an history of hypermobility and about 20% of them referred the tendency to have opening mouth locking. Moderate pain was referred in temporo-mandibular region and also recognizable in correspondence of masticatory muscles, probably due to excessive joint excursion, ligamentous injury and parafunctions. Bruxism is most common stress and when is combined with EDS, the effects are substantially amplified, particularly in patients with craniocervical intability (Ines M, 2008). Patients with hypermobile TMJ will often show increased maximal mouth opening often well beyond the normal range of 40-55 mm (Hirsch C, 2008; Norton LA, 1997) with mandibular subluxation, expression of the lack of proprioception and ligamentous laxity. Disc displacement with reduction (mono or bilateral, with or without pain) was a recurring feature in our sample and confirmed by the literature (Nosouhian S, 2015). Disc displacements without reduction and limited mouth opening were not noticed, unlike what said in the literature (Berglund B, 2012; Hagberg C, 2004;).

Cervical spine instability and pain are the comorbidities recognizable in all TMD/EDS patients.

Surface Electromyography

This type of evaluation was performed in order to evaluate the "occluso-muscular" assessment. This kind of EMG doesn't allow to investigate the muscular strenght as absolute value. It only relates muscular activity to occlusal findings, since in the stomatognatic system, muscles cannot be "separate" from occlusal input. Therefore EMG could allow to identify and to intercept occlusal features that may disturb a formerly unstable articular/muscular condition.

Significant data emerged. Almost all patients had BAR value out of normal range and located in an anterior position. This highlights the prevalent activity of temporalis muscles among masticatory muscles, due to prevalent anterior occlusal contacts (up to the first bicuspid). Anterior centre of gravity is associated with dysfunctions because of the presence of a retrusive condylar component and because of the increased articular load (De Felício CM, 2013). IMP value is out of normal range in the 96% of patients and indicates the presence of parafunctions such as bruxism and clenching. The presence of night- diurnal parafunctions, as confirmed by IMP values, worsens the painful sintomatology and the perception of muscular fatigue.

Also ASIM, TORS and POC TA 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 occluso-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 temporomandibular joints and masticatory muscles, to a retrusion of the condyle of the mandibular deviation side and the wider balancing movements of the contralateral condyle. This can be worsen by the lack of proprioception and instability that can't allow muscles to find a balance on the basis of occlusal contacts. In order 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 gnatologic treatment with functional-orthopedics issues; the second one is a conservative occlusal therapy to finalize goals achieved with the previous one.

CONCLUSIONS

EDS are complex clinical conditions which need a multidisciplinar integrated approach to solve their several critical aspects. The involvement of temporo-mandibular joints 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 a good articular stability. The detection of comorbidities and psychological aspects helps to improve as far as possibile the results of therapy.

Statement of Interests

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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References

1. Abel MD, Carrasco LR. 2006. Ehlers-Danlos syndrome: Classifications, oral manifestations, and dental considerations. *Oral Surg Oral Patol Oral Radiol Endod* 102:582-590.
2. Beighton P., De Paepe A., Steinmann B., Tsipouras P., And Wenstrup R. J. 1998. Ehlers-Danlos Syndromes: Revised Nosology, Villefranche, 1997. Ehlers-Danlos National Foundation (Usa) And Ehlers-Danlos Support Group (Uk). *Am. J. Med. Genet.* Part A 77:31-37
3. Bendik EM, Tinkle BT, Al-shuik E, Levin L, Martin A, Thaler R, Atzinger CL, Rueger J, Martin VT. 2011. Joint hypermobility syndrome: A common clinical disorder associated with migraine in women. *Cephalalgia* 31:603-613
4. Berglund B, Bjorck E. 2012.Women with Ehlers-Danlos syndrome experience low oral health-related quality of life. *J Orofac Pain* 26:307-314
5. Buckingham RB, Braun T, Harinstein DA, Oral K, Bauman D, Bartynski W, Killian PJ, Bidula LP. 1991. Temporomandibular joint dysfunction syndrome: A close association with systemic joint laxity (the hypermobile joint syndrome*). Oral Surg Oral Med Oral Pathol* 72:514-519.
6. Castori M, Camerota F, Celletti C, Danese C, Santilli V, Saraceni VM, Grammatico P. 2010b. Natural history and manifestations of the hypermobility type Ehlers-Danlos syndrome:Apilot study on 21 patients. *AmJ Med Genet* Part A 152A:556-564
7. Castori M, Sperduti I, Celletti C, Camerota F, Grammatico P. 2011a. Symptom and Joint Mobility Progression in the Joint Hypermobility Syndrome (Ehlers-Danlos Syndrome, Hypermobility Type). *Clin Exp Rheumatol* 29:998-1005
8. Castori M, Voermans NC. 2014. Neurological manifestations of Ehlers-Danlos syndrome- (s): A review. *Iran J Neurol* 13:190-208
9. Conti PCR, Pinto-Fiamengui LMS, Cunha CO, Conti AC. 2012. Orofacial pain and temporomandibular disorders: The impact on oral health and quality of life. *Braz Oral Res* 26:120-123
10. De Coster PJ, Van den Berghe LI, Martens LC. 2005 a. Generalized joint hypermobility and temporomandibular disorders: Inherited connective tissue disease as a model with maximum expression. *J Orofac Pain* 19:47-57
11. De Coster PJ, Martens LC, De Paepe A. 2005 b. Oral health in prevalent types of Ehlers-Danlos syndromes. *J Oral Pathol Med* 34:298-307
12. De Felício CM1, Mapelli A, Sidequersky FV, Tartaglia GM, Sforza C. 2013 Mandibular kinematics and masticatory muscles EMG in patients with short lasting TMD of mild-moderate severity. *J Electromyogr Kinesiol*. 23; 627-633.
13. Diep D, Fau V, Wdowik S, Bienvenu B, Benateau H, Veyssiere A. 2016. Temporomandibular disorders in Ehlers-Danlos syndrome, hypermobility type. A case-control study. *Rev Stomatol Chir Maxillofac Chir Orale* 117:228-233.
14. Fransiska Malfait, Clair Francomano, Peter Byers, John Belmont, Britta Berglund *Et Al*. 2017. The International Classification of the Ehler-Danlos Syndromes.

American Journal of Medical Genetics Part C (Seminars in Medical Genetics) 175C:8-26
15. Guilleminault C, Primeau M, Chiu HY, Yuen KM, Leger D, Metlaine A. 2013. Sleepdisordered breathing in Ehlers-Danlos syndrome: A genetic model of OSA. *Chest* 144:1503-1511
16. Hagberg C, Berglund B, Korpe L, Andersson- Norinder J. 2004. Ehlers-Danlos syndrome (EDS) focusing on oral symptoms: A questionnaire study. *Orthodont Craniofac Res* 7:178-185.
17. Harinstein D, Buckingham RB, Braun T, Oral K, Bauman DH, Killian PJ, Bidula LP. 1988. Systemic joint laxity (the hypermobile joint syndrome) is associated with temporomandibular joint dysfunction. *Arthritis Rheum* 31:1259-1264
18. Hirsch C, John MT, Stang A. 2008. Association between generalized joint hypermobility and signs and diagnoses of temporomandibular disorders. *Eur J Oral Sci* 116: 525-530.
19. Ines M, Ferao B, Traebert J. 2008. Prevalence of temporomandibular dysfunction in patients with cervical pain under physiotherapy treatment. *Fisioter* Mov 21:63-70.
20. Jacome DE. 1999. Headache in Ehlers-Danlos syndrome. *Cephalalgia* 19:791-796
21. Kavuncu V, Sahin S, Kamanli A, Karan A, Aksoy C. 2006. The role of systemic hypermobility and condylar hypermobility in temporomandibular joint dysfunction syndrome. *Rheumatol Int* 26:257-260
22. Norton LA, Assael LA. 1997. Orthodontic and temporomandibular joint considerations in treatment of patients with Ehlers-Danlos syndrome. *Am J Orthod Dentofacial Orthop* 111:75-84.
23. Nosouhian S, Haghighat A, Mohammadi I, Shadmehr E, Davoudi A, Badrian H. 2015. Temporomandibular joint hypermobility manifestation based on clinical observations. *J Int Oral Health* 7:1-4.
24. Pasinato F, Souza JA, Corre ECR, Silva AMT. 2011. Temporomandibular disorder and generalized joint hypermobility: Application of diagnostic criteria. *Braz J Otorhinolaryngol* 77:418-425
25. Rombaut L, Malfait F, Cools A, De Paepe A, Calders P. 2010. Musculoskeletal complaints, physical activity and health-related quality of life among patients with the Ehlers-Danlos syndrome hypermobility type. *Disabil Rehabil* 32:1339-1345.
26. Rombaut, L., Malfait, F., De Paepe, A., Rimbaut, S., Verbruggen, G., De Wandele, I., and Calders, P. Impairment and impact of pain in female patients with Ehlers-Danlos syndrome: a comparative study with fibromyalgia and rheumatoid arthritis. *Arthritis Rheum*. 2011; 63: 1979-1987
27. Rozen TD, Roth JM, Denenberg N. 2006. Cervical spine joint hypermobility: A possible predisposing factor for new daily persistent headache. *Cephalalgia* 26:1182-1185
28. Shiffman E, Ohrbach R, Truelove E, Look J, Anderson J. 2014. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: recommendations of the International RDC/TMD Consortium Network* and Orofacial Pain Special Interest Group. *Journal of Oral and Facial Pain and Headache* 28(1):6-27
29. Voermans N.C., Knoop H., Bleijenberg G., and van Engelen B.G. 2010. Pain in ehlers-danlos syndrome is common, severe, and associated with functional impairment. *J. Pain Symptom Manage*.; 40: 370-378
30. Westling L, Mattiasson A. 1991. Background factors in craniomandibular disorders: Reported symptoms in adolescents with special reference to joint hypermobility and oral parafunctions. *Scand J Dent Res* 99:48-54
31. Westling L. 1992. Temporomandibular joint dysfunction and systemic joint laxity. *Swed Dent J Suppl* 81:1-79.
32. Wincour E, Gavish A, Halachmi M, Bloom A, Gazit E. 2000. Generalized joint laxity and its relation with oral habits and temporomandibular disorders in adolescent girls. *J Oral Rehabil* 27:614-622.

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