# High prevalence of orofacial pain in juvenile fibromyalgia as detected by a novel tool specifically devised for children and adolescents

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## Abstract

### Objective

*To examine the prevalence of temporomandibular disorders (TMD) in patients with juvenile fibromyalgia syndrome (JFS) and identify TMD characteristics specifically associated to JFS.*

### Methods

*Signs and symptoms of TMD were assessed using a novel clinical tool specifically devised for children that consists of: 1. a self-report multiple-choice questionnaire; 2. a protocol for the clinical examination of the orofacial region. Multivariate logistic regression model was used to identify TMD features associated with JFS.*

### Results

*Thirty JFS patients (median age 15.5 years) and 45 healthy controls (median age 15.0 years) were included in this cross-sectional study. Orofacial pain was reported by 26 of 30 JFS patients (86.7%) and by 3 of 45 controls (6.7%; p<0.001). Pain on TMJ palpation was present in 18 of 30 JFS patients (60%) and in 5 of 45 controls (11.1%; p<0.001). Median values of maximum spontaneous mouth opening, voluntary active opening and assisted passive opening were significantly higher in JFS patients than in controls. On multiple regression analysis spontaneous orofacial pain (OR: 21.0; p=0.005), diffuse tenderness on palpation of the masticatory muscles (OR: 14.9; p=0.026) and TMJ hypermobility (OR 1.42; p=0.008) were independently associated with JFS.*

### Conclusion

*The high prevalence of TMD in JFS highlights the need for a broader interdisciplinary evaluation of JFS patients. TMJ hypermobility, in addition to orofacial and masticatory muscle pain, is an important clue for the diagnosis of TMD in adolescents with JFS. Elucidating the link between these disorders will advance individualised management and improve treatment efficacy.*

**Key words**

juvenile fibromyalgia syndrome, temporomandubular disorders, musculoskeletal pain, nociplastic pain

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## Introduction

Juvenile fibromyalgia syndrome (JFS) is a disabling condition characterised by diffuse musculo-skeletal pain, fatigue, non restorative sleep, and cognitive impairment that have a marked impact on the patients' functional ability and quality of life (1). Prevalence estimates for JFS range from 1.2 to 6.2% of the pediatric population, with female preponderance (3:1) (2, 3). The mean age of onset is approximately 11.4 to 13.7 years, ranging from 5 to 18 years (1).

Although studies of the pathogenesis of JFS are sparse, mounting evidence suggests that amplified processing and/or decreased inhibition of pain stimuli at multiple levels in the nervous system play a prominent role in the pathophysiology of this disorder, which is currently classified among the nociplastic pain syndromes (4-6). Prototypical nociplastic pain conditions include both widespread (*e.g.* JFS) and localised conditions such as chronic temporomandibular disorders (TMDs) (4).

The term TMD refers to a complex heterogeneous group of disorders characterised by chronic orofacial pain (7). In adults, TMDs are considered the first cause of orofacial non-odontogenic pain and the second most common chronic pain syndrome affecting the general population after back pain (7, 8). A recent systematic review of the literature reported that TMD prevalence in adolescent varies between 7% and 30% (9). According to the American Dental Association, the features of TMD include: 1) pain at masticatory muscles and/or temporomandibular joint (TMJ) and in the preauricular area; 2) limitations or interference in movement of the mandible (*i.e.* restricted ability to open the mouth), and 3) clicking or crepitation produced by TMJ joint during mandibular function (10, 11). Although the aetiology of TMDs is not fully elucidated, there is evidence that central dysregulation of the modulatory pathways of pain, rather than damage or inflammation of peripheral structures, plays a role in the development and maintenance of chronic orofacial pain (4, 12).

TMDs and JFS share common symptoms, such as muscle pain, sleep impairment, chronic fatigue, and mood disorders (*e.g.* anxiety, depression) (6, 13), which reflect a shared underlying pathophysiologic basis between these conditions, and led the US National Institutes of Health to coin the term chronic overlapping pain conditions (14).

Recent meta-analyses yielded a pooled prevalence rate for TMD in FM patients of 76.8% (69.5% to 83.3%), and almost a third of individuals (32.7%, 4.5% to 71.0%) with TMDs had comorbid FM (15). In addition, Harper DE et al. found that patients with TMD and FM phenotype experience a severe disease in terms of orofacial pain at rest, tenderness upon palpation, perceived jaw functional limitation and pain-related disability, suggesting that FM affects negatively TMD prognosis, with relevant consequences on therapeutic strategy (16).

In contrast to the plethora of studies performed in adults, coexisting nociplastic pain conditions have been very scarcely investigated in JFS. Furthemore, although orofacial pain is a well-known component of JFS clinical spectrum, the association between JFS and TMD has never been explored. The aim of the present study is to address this issue by examining the prevalence of TMDs in patients with JFS and by identifying TMD features specifically associated to JFS. An accurate assessment of chronic pain disorders that congregate with JFS is prerequisite to provide individualised management and improve treatment efficacy.

## Methods

Patients with JFS by the 2010 American College of Rheumatology (ACR) Adult Fibromyalgia Criteria (17, 18) were recruited at the Paediatric Rheumatology Department of the Gaslini Children's Hospital of Genova, Italy, between 2018 and 2019. Healthy children and adolescents undergoing routine oral hygiene at the Pediatric Dentistry and Orthodontics Unit of Gaslini Children's Hospital in the same period were included as control group. Signs and symptoms of TMD were evaluated using a clinical tool specifically designed for this study by adapting the adult version of TMD diagnostic criteria for use in children.

**SELF REPORTED QUESTIONARY**

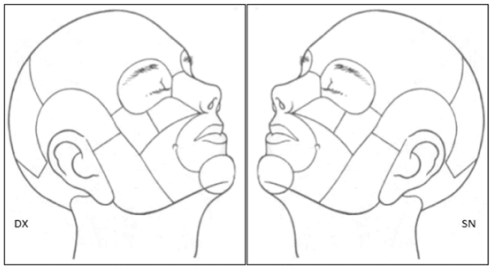
| | | |
|---|---|---|
| Date of Birth | | |
| Gender | Male | Female |

**RHEUMATOLOGICAL INFORMATION**

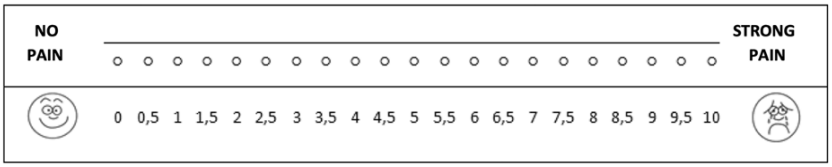
| | |
|---|---|
| Data onset symptoms | |
| Date of diagnosis of *juvenile* fibromyalgia | |
| Comorbidities | |

**Q.1)** *Does you face hurt?* *Yes* ☐ *No* ☐

**Q.2)** *Put a cross "X" where it hurts*




**Q.3)** *On a scale from 1 to 10 say how much it hurts on the places where you put the cross*




**Q.4)** *How long have you had this pain for?* ☐ *< 3 months* ☐ *3-12 months* ☐ *> 12 months*

**Q.5)** *Does this pain come by itself?* *Yes* ☐ *No* ☐

**Q.6)** *Does your face hurt when you eat, yawn or speak?* *Yes* ☐ *No* ☐

**Q.7)** *How difficult is it for you to do the following action?*

| | *No difficulty* | *A bit of difficulty* | *A lot of difficulty* | *Unable to do it* |
|---|---|---|---|---|
| *Open your mouth to bite a sandwich* | | | | |
| *Open your mouth when you wake up* | | | | |
| *Chew food* | | | | |
| *Speak* | | | | |
| *Open your mouth to yawn* | | | | |

**Q8)** *Are there other people in your family who have similar pain to yours or with your same problem?*

*Yes* ☐ *No* ☐

**Fig. 1.** Multiple-choice questionnaire completed by the patient and caregiver when needed.

It consists of two parts: 1. a multiple-choice questionnaire completed by the patient, with caregivers's support when needed (Fig. 1); 2. a clinical evaluation form completed by the dentist (Fig. 2). The self-report questionnaire includes questions related to the characteristics of orofacial pain (*e.g.* site, distribution, severity, etc). Participants were asked to rate their average level of pain in the orofacial region using a 21-numbered circle pain Numerical Rating Scale (NRS), that ranges from 0 (no pain) to 10 mm (pain as bad as it can be) (19). They were also asked to draw the location of their usual pain pattern on an anatomical map, including lateral, frontal, and occipital area of the face. In addition, the patient has to report pain duration and its associations with particular actions, such as chewing, talking, or yawning. Difficulty in opening the mouth upon waking, speaking, yawning, biting a sandwich and chewing was scored from 0 (no difficulty) to 3 (unable to do), resulting in a total functional disability score (FDS) ranging from 0 to 15.

The clinical evaluation form consists of a simplified protocol for the examination of the orofacial region based on the diagnostic criteria for TMD used in adults (20). It includes the evaluation of pain after two seconds of palpation with a pressure of one kilogram of the anterior, middle, and posterior temporal muscles and of the masseter muscle at its origin, body and insertion. Pain on palpation of the masticatory muscle was quantified by the dentists (GC, CC) using the a 21-numbered circle pain NRS. Tenderness upon TMJ palpation with a pressure of 0.5 kilogram and joint noises during three consecutive movements of maximum opening and closing of the mouth were quantified using the 21-numbered circle pain NRS. Maximum spontaneous mouth opening (MSO), maximum voluntary active opening (MVA), and maximum assisted passive opening (MAP) were measured in millimeters.

This study was approved by the Institutional Review Board for human subject's research (CER Liguria: OF-PJFS001). All participants and legal guardians provided an appropriate informed consent/assent for their inclusion in the study.

*Statistical methods*

Categorical data were reported in terms of absolute frequencies and percentages, whereas continuous quantitative data were reported as median and in-

**EXAMINATION FORM**

*1) MUSCLE PALPATION*

| | Pain on muscle palpation | |
|---|---|---|
| | R | L |
| Posterior portion of temporalis muscle | | |
| Medial portion of temporalis muscle | | |
| Anterior portion of temporalis muscle | | |
| Masseter muscle (origin) | | |
| Masseter muscle (body) | | |
| Masseter muscle (insertion) | | |

*2) MUSCLE TENDERNESS VAS*

NO PAIN ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ STRONG PAIN

0 0,5 1 1,5 2 2,5 3 3,5 4 4,5 5 5,5 6 6,5 7 7,5 8 8,5 9 9,5 10

*3) RANGE OF MOUTH OPENING ON VERTICAL SAGITTAL PLANE*

OverByte: ... mm SPONTANEOUS: ... mm VOLUNTARY: ...mm ASSISTED: ...mm

End-feel: ... mm ☐ inflexible ☐ flexible ☐ normal ☐ painful.

*4) ARTICULAR JOINT SOUND ON PALPATION DURING OPENING*

| | *R* | *L* |
|---|---|---|
| *No* | | |
| *Yes* | | |

*5) TMJ PAIN ON PALPATION* *Yes* ☐ *No* ☐

| | | | | | |
|---|---|---|---|---|---|
| TMJ RIGHT | Pressure lateral pole | | TMJ LEFT | Pressure lateral pole | |
| | Pressure posterior area | | | Pressure posterior area | |

*6) TMJ SORENESS VAS*

NO PAIN ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ STRONG PAIN

0 0,5 1 1,5 2 2,5 3 3,5 4 4,5 5 5,5 6 6,5 7 7,5 8 8,5 9 9,5 10

**Fig. 2.** Clinical evaluation form completed by the dentist.

terquartile range (IQR). Comparison between JFS and control group was made by means of Pearson's chi-square test or Fisher's Exact test for categorical data, while comparison of quantitative data was made by means of the non-parametric Mann-Whitney U test. Multivariate logistic regression model was used to identify TMD features independently associated with JFS. The diagnosis of JFS was considered as the dependent variable and the TMD signs and symptoms that were significantly associated with JFS in univariate analyses were included as explanatory variables. The selection of signs and symptoms to be included in the final model was carried out using a supervised stepwise backward algorithm, adopting a likelihood ratio test $p$-value >0.2 as cutoff to exclude factors. Because MSO, MVA and MAP were strongly closely correlated (Spearman rho≥0.8), a single multivariate model was used for each of those factors to account for collinearity.

Statistical significance was considered for two-tailed alpha error values <0.05. Given the exploratory nature of the study, no correction for multiple tests was applied. All statistical analyses were carried out using the software STATA v. 17.0 (StataCorp LP. College Station, TX, USA).

## Results

Thirty JFS patients (23 female; median age 15.5 years) and 45 healthy controls (26 female; median age 15.0 years), whose demographic and clinical features are reported in Table I, were included in the study. As shown in Table II, orofacial pain was reported by 26 of 30 JFS patients (86.7%) and by 3 of 45 controls (6.7%; $p$<0.001); it was bilateral in 25 of 26 JFS patients (96.2%) and in 2 of 3 controls (66.7%). The median intensity of orofacial pain was 4.0 (IQR 2.5-6.0) in JFS patients and 0.0 (IQR: 0.0-0.0; $p$<0.001) in the control group. Nineteen of 26 JFS patients (73.1%) reported orofacial pain on rest, whereas in 14 (53.8%) orofacial pain was elicited by TMJ movements. The median value of FDS, which reflects stomatognathic function impairment, was 1.5 (0.0-3.0) in JFS patients and 0.0 (0.0-0.0) in the control group ($p$<0.001). Twenty-eight of 30 JFS patients had a FDS ranging from 0.0 to 3.0 and only 2 patients had a FDS ranging between 4.0 and 7.0. A familiar history of orofacial pain was recorded in 50% of JFS patients, while it was not reported by any subject in the control group ($p$<0.001).

As reported in Table III, 24 of the 30 JFS patients (80%) had at least one

**Table I**. Demographic and clinical features of patients with juvenile fibromyalgia syndrome.

| | | JFS group (n=30) | Healthy controls (n=45) | *p* |
|---|---|---|---|---|
| Gender, n (%) | Male | 7 (23.3) | 19 (42.2) | 0.092* |
| | Female | 23 (76.7) | 26 (57.8) | |
| Age (years) | Median (IQR) | 15.5 (13.0-18.0) | 15.0 (14.0-17.0) | 0.802 † |
| Age at diagnosis (years) | Median (IQR) | 14.3 (12.1 -15.2) | | |
| Disease duration (years) | Median (IQR) | 1.2 (0.6-2.3) | | |
| Widespread pain index | Median (IQR) | 8 (4-11) | | |
| Symptoms Severity Scale | Median (IQR) | 6 (4-8) | | |
| Trigger points | Median (IQR) | 7 (4-10) | | |
| Pharmacological treatment | | | | |
| NSAIDs | n (%) | 4 (13.3%) | | |
| Pregabalin | n (%) | 3 (10%) | | |
| Amytriptiline | n (%) | 2 (6.7%) | | |

JFS: juvenile fibromyalgia syndrome. IQR: interquartile range; Std: Standard Deviation; NSAID: non-steroidal anti-inflammatory drugs.
* Pearson' Chi-square Test; † Mann-Whitney's ranksum test.

**Table II**. Self-report questionnaire: descriptive statistics (medians, 1st 3rd quartiles or absolute frequencies and %) for the JFS patients (n=30) and healthy controls (n=45).

| | | | JFS | Healthy controls | *p* |
|---|---|---|---|---|---|
| (Q.1) | Facial pain. | Yes | 26.0 (86.7) | 3.0 (6.7) | <0.001† |
| | n (%) | No | 4.0 (13.3) | 42.0 (93.3) | |
| (Q.2) | no. painful face area (Range 0-12) | Median (IQR) | 3.0 (2.0-4.0) | 0.0 (0.0-0.0) | <0.001† |
| | Localisation painful | Unilateral | 1.0 (3.8) | 1.0 (33.3) | 0.20‡ |
| | face area | Bilateral | 25.0 (96.2) | 2.0 (66.7) | |
| (Q.3) | Spontaneous orofacial pain intensity (10-mm pain NRS) | Median (IQR) | 4.0 (IQR 2.5-6.0) | 0.0 (0.0-0.0) | <0.001† |
| (Q.4) | Onset time of facial pain | < 3 months | 10.0 (38.4) | 2.0 (66.7) | 0.78‡ |
| | | 3-12 months | 10.0 (38.4) | 1.0 (33.3) | |
| | | >12 months | 6 (23.1) | 0.0 | |
| (Q.5) | Spontaneous onset | Yes | 19 (73.1) | 1 (33.3) | 0.22‡ |
| | facial pain | No | 7 (26.9) | 2 (66.7) | |
| (Q.6) | Induced onset facial pain | Yes | 14 (53.8) | 2 (66.7) | 0.99‡ |
| | | No | 12 (46.2) | 1 (33.3) | |
| (Q.7) | ∑ impairment in stomatognatic function (Range 0-15) | Median (IQR) | 1.5 (0.0-3.0) | 0.0 (0.0-0.0) | <0.001† |
| (Q.8) | Familiar history of | Yes | 15.0 (50.0) | 0.0 | <0.001* |
| | orofacial pain | No | 15.0 (50.0) | 45.0 (100) | |

NRS: numerical rating scale; IQR: interquartile range; Std: Standard Deviation.
* Pearson' Chi-square test; † Mann-Whitney's ranksum test; ‡ Fisher's exact test.

positive site on muscle palpation *versus* 5 of 45 controls (11.1%; $p<0.001$). The median number of muscular painful sites on palpation was 6.0 (IQR 4.0–12.0) in JFS and 0.0 (IQR 0.0–0.0; $p<0.001$) in the control group. The median value of pain intensity on masticatory muscle palpation was 6.0 (IQR 3.0–7.3) in the JFS patients and 0.0 (IQR 0.0–0.0; $p<0.001$) in controls. Seventeen of 24 (70.8%) JFS patients showed discordance between referred and detected pain on palpation of masticatory muscles. Pain on TMJ palpation was found in 18 of 30 JFS patients (60%) and in 5 of 45 controls (11.1%; $p<0.001$), with a median pain intensity of 3.5 (IQR 0.5–6.3) and 0.0 (IQR 0.0–0.0; $p<0.001$), respectively. TMJ noises were found in 7 of 30 JFS patients (23.3%) and in 6 of 45 controls (13.3%; $p=0.35$).

The median values of MSO, MVA and MAP were significantly higher in JFS patients than in controls (MSO 45.0 mm (IQR 43.0–47.0) *versus* 40.0 mm (IQR 38.0–41.0), $p<0.001$; MVA 47.0 mm (IQR 45.0–50.0) *versus* 41.0 mm (IQR 40.0–43.0), $p<0.001$; MAP 51.0 mm (IQR 47.0–54.0) *versus* 46.0 mm (IQR 45.0–48.0), $p<0.001$)).

Multivariable logistic regression model showed that spontaneous orofacial pain (odds ratio, OR: 21.0, 95% confidence interval (CI): 2.56–173.0, $p=0.005$), diffuse tenderness on palpation of masticatory muscles (OR: 14.9, 1.38-160.8, $p=0.026$) and increased maximum assisted passive mouth opening (OR: 1.42, 1.10–1.84, $p=0.008$) were independently associated with JFS (Table IV).

## Discussion

This study demonstrates that TMD symptoms are present in a relevant percentage of JFS patients, and highlights the need for a broader interdisciplinary approach to JFS, that should include involvement of a dentistry. To our knowledge, the involvement of stomatognathic system in JFS has never been investigated in detail.

Our findings are in line with the results of previous studies in adults, which reported sign and symptoms of TMD in 68-97% of FM patients (15, 21-23), and suggested a shared underlying pathophysiology related to generalised hyperexcitability in central nervous system (CNS) nociceptive pathways (4, 6, 24).

Literature data have shown that FM could be either an aetiologic or aggravating factor for TMDs (25-27). In fact, the coexistence of FM in patients with TMD has been associated with increased orofacial pain intensity and jaw disfunction (16). TMD patients with FM also had evidence of central sensitisation and allodynia (28-30), which may explain increased pain du-

**Table III.** Clinical examination: descriptive statistics (medians, 1st 3rd quartiles or absolute frequencies and %) for the JFS patients (n=30) and healthy controls (n=45).

| | | | JFS | Healthy controls | *p* |
|---|---|---|---|---|---|
| (E1) | Muscular painful site on palpation n (%) | Yes | 24.0 (80.0) | 5.0 (11.1) | <0.001* |
| | | No | 6.0 (20.0) | 40.0 (88.9) | |
| | Muscular painful site on palpation (range 0-12) | Median (IQR) | 6.0 (4.0-12.0) | 0.0 (0.0-0.0) | <0.001† |
| | Localisation of pain on palpation, n (%) | Unilateral | 4.0 (16.7) | 1.0 (20.0) | 0.99‡ |
| | | Bilateral | 20.0 (83.3) | 4.0 (80.0) | |
| (E2) | Concordance between referred and evocated pain on palpation, n (%) | Yes | 7 (29.2) | 3 (60.0) | 0.31* |
| | | No | 17 (70.8) | 2 (40.0) | |
| (E3) | Pain on palpation of the masticatory muscle (10-mm NRS) | Median (IQR) | 6.0 (3.0-7.3) | 0.0 (0.0-0.0) | <0.001† |
| (E4) | TMJ Tenderness on palpation, n (%) | Yes | 18.0 (60) | 5.0 (11.1) | <0.001 |
| | | No | 12.0 (40) | 40.0 (88.9) | |
| | Localisation TMJ tenderness on palpation, n (%) | Unilateral | 4.0 (22.2) | 1.0 (20.0) | 0.99‡ |
| | | Bilateral | 14.0 (77.8) | 4.0 (80.0) | |
| (E5) | Tenderness on TMJ palpation (10-mm NRS) | Median (IQR) | 3.5 (0.5-6.3) | 0.0 (0.0-0.0) | <0.001† |
| (E6) | TMJ Noise n (%) | Yes | 7.0 (23.3) | 6.0 (13.3) | 0.35* |
| | Localisation TMJ noise, n (%) | Unilateral | 5.0 (71.4) | 4.0 (66.7) | 0.99‡ |
| | | Bilateral | 2.0 (28.6) | 2.0 (33.3) | |
| (E7) | MSO (mm) | Median (IQR) | 45.0 (43.0-47.0) | 40.0 (38.0-41.0) | <0.001† |
| | MVA (mm) | Median (IQR) | 47.0 (45.0-50.0) | 41.0 (40.0-43.0) | <0.001† |
| | MAP (mm) | Median (IQR) | 51.0 (47.0-54.0) | 46.0 (45.0-48.0) | <0.001† |

TMJ: temporomandibular joint; MSO: maximum spontaneous opening; MVA: maximum voluntary active opening; MAP: maximum assisted passive opening; IQR: range interquartile.
* Pearson's chi-square test; † Mann-Whitney's ranksum test; ‡ Fisher's Exact test.

**Table IV.** Multivariable logistic model (n=75).

| | OR* | 95%CI | *p*-value |
|---|---|---|---|
| Spontaneous orofacial pain | 21.0 | 2.56-173.0 | 0.005 |
| Diffuse pain on muscle palpation | 14.9 | 1.38-160.8 | 0.026 |
| MAP (mm) | 1.42 | 1.10-1.84 | 0.008 |

OR: Odds Ratio; 95%CI: 95% Confidence Interval; MAP: maximum assisted passive opening.
Note: MAP in the model was considered as a continuous factor, thus OR represent the risk related to an increased MAP of 1 mm.

ration and intensity (31). Overall, these findings have a relevant impact on the management of TMD, as they suggest that targeting the CNS in patients with evidence of pain centralisation might improve pain and jaw dysfunction.

We investigated the prevalence of TMD signs and symptoms in patients and controls by devising a novel clinical tool, which adapts the gnatological examination used in adults to the developmental age. In keeping with studies in adults, JFS patients revealed enhanced and diffuse pain in masticatory muscles, especially in masseter muscles, compared to controls, along with more intense pain upon palpation of the TMJ. The concordance between patients reported and objectivetely detected orofacial pain during clinical examination was higher in the control group than in JFS patients. This result is not surprising because a discrepancy between self-reported subjective symptoms and results of physician's assessment, with a tendency toward symptom amplification in JFS patients, has been previously described (32-34).

Hence, our results emphasise the importance of including gnatologic examination in the routine assessment of JFS patients to integrate subjective symptoms with objective data.

The current ACR criteria for FM diagnosis do not mention TMD signs and symptoms (17, 18). Clinical examination of JFS patients is based on the evaluation of tenderness in 18 tender points, which do not comprise masticatory muscles. The high prevalence of TMD in patients with JFS found in our study, underscores the importance of including pain assessment in masticatory muscles in routine clinical evaluation of patients with JFS to early diagnose and treat timely TMD. Our protocol represents a suitable clinical tool to diagnose and quantify the severity of TMD signs and symptoms and to monitor their impact of JFS during the disease course.

Reduced mouth opening and restricted mandibular movements, which can cause difficulty in eating or speaking, are major symptoms in adults with FM and TMDs (21-23, 35-37). Noises in

the temporomandibular joints during jaw movement are also commonly observed (35, 37). In contrast with these findings, our JFS patients with TMD had modest functional impairment, with no or little difficulty in performing routine actions such as yawning, eating, and speaking.

In our study, JFS patients showed a paradoxiacally increased width of mouth opening compared to controls, suggesting a certain degree of TMJ hypermobility. This finding corroborates prior reports of frequent joint hypermobility in adolescent JFS patients, with a prevalence ranging from 40 to 81% (38, 39). It has been suggested that hypermobility could be a poor prognostic factor for JFS. In fact, Ting *et al*. found that JFS patients with hypermobility had enhanced pain sensitivity and increased tender point (TP) count compared to JFS patients without joint laxity (40). Although our patients have not been evaluated with the Beighton score (41), which does allow to establish whether TMJ hypermobility was a localised phenomenon or was part of a generalised joint laxity, an association between TMJ hypermobility and orofacial pain, similar to that observed in benign hypermobility syndrome, could be hypothesised. It might be assumed that TMJ hypermobility in JFS patients could increase pain sensitivity in the orofacial region, with relevant consequences on treatment strategy that should include tailored programmes focusing on joint protection and strengthening aimed to reduce mechanical stress and decrease pain tresholds.

Some limitations of our study should be acknowledged. Signs and symptoms of TMD were assessed by adapting the adult version of the TMD diagnostic criteria for use in children. Further validation studies are needed before this novel tool can be used as an outcome measure in interventional studies. Second, the statistical power is limited by the relatively small sample size. In addition, considering the high prevalence of females in JFS patients compared with controls, we cannot exclude that the difference in the prevalence of TMD may be overestimated, as this condition is more common in women. Third, we made a single time-point odontoiatric evaluation. Longitudinal studies are needed to define the chronicity of orofacial pain and to elucidate the temporal relationship between JFS and TMD, as well as the impact of TMD on the global burden of JFS disease. These findings may provide insight into the development of more comprehensive and targeted therapeutic approaches. Finally, the present study did not include imaging assessments. Although history and clinical examination are still the gold standards for diagnosis of TMD, imaging such as MRI, may support the diagnosis of TMD, particularly in patients in whom clinical examination suggests intra-articular disease (*i.e*. internal derangement, disc abnormalities, disc displacement, etc.), with relevant consequence on treatment strategy.

The development of a new tool that combines self-reported measurements and an odontoiatric examination protocol to assess TMD in children represents an added value of our study. Application of this tool in routine examination of JFS patients will allow identification of JFS subgroups with overlapping pain patterns, who require individualised management to halt the progression to jaw pain chronicity and related disability. Notably, studies in adults have highlighted that treatment for FM may be insufficient for the management of TMD, which requires multimodal approaches and targeted exercise programmes (*e.g*. physiotherapy, TMJ mobilisation, facial massage), and interventions (myocentric splint therapy, oral orthesis etc) to control pain and restore mandibular function (42-44). The application of our protocol in the routine evaluation of TMD patients may provide a new opportunity for early diagnosis of JFS before the progression towards a state of pain generalisation and a severe and difficult -to-treat condition.

In addition, because patients with TMD may not report co-existent pain occurring outside the face to their dental care providers, our tool offers to dentists a suitable instrument to screen TMD patients for the presence of JFS-associated TMD stomatologic features, especially TMJ hypermobility, that represent warning signs to prompt patient referral to the rheumatologist.

In summary, our study highlights the importance of an accurate evaluation of the stomatognathic system in JFS patients and introduces a novel clinical instrument for diagnosis and monitoring of TMDs signs and symptoms. Additional research is needed to elucidate the aetiological link between JFS and TMD and to develop more targeted and effective treatment strategies.

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