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# Association between Comorbidities and Subtypes of Temporomandibular Dysfunction: An Observational Study

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# Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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# ABSTRACT

**Aims:** Temporomandibular disorder (TMD) has an important relationship with a compromised general health status, which is why the present study evaluated the presence of comorbidities in individuals diagnosed with TMD, identifying the TMD subtype, whether muscle and/or joint, and verifying the most frequent comorbidities related to TMD subtypes, relating them to human body systems.

**Materials and Methods:** We selected 270 individuals in the city of Fortaleza/CE, aged between 18 and 70 years old. The individuals were evaluated using the DC/TMD instrument. In addition, a questionnaire to quantify comorbidities was applied.

**Results:** Regarding the subtype of TMD in the sample under study, it was observed that the most prevalent was muscle/joint (53.3%; n = 144), followed by muscle (46.3%; n = 125) and last to articulate (0.4%; n = 1). No important correlations were identified (p > 0.05) when we compared TMD subtypes with gender and age variables. When asked about the presence of diseases, it was shown that the nervous system (n = 89; 33%) and sensory (n = 84; 31.1%) were the ones with the highest prevalence among comorbidities.

**Conclusion:** all TMD subtypes were found in the sample, predominantly mixed TMD. Several comorbidities were found, especially in the nervous and sensory systems. No correlations were found between the presence of comorbidities and gender or age.

Keywords: Comorbidity; diagnosis; temporomandibular joint disorders.

## **1. INTRODUCTION**

Temporomandibular Disorders (TMDs) include various neuromuscular and musculoskeletal conditions of the Temporomandibular Joint (TMJ) and associated structures. According to the American Academy of Orofacial Pain (AAOP), the current definition is a collective term that encompasses a range of clinical problems involving the muscles of mastication, TMJ, and associated structures [1].

TMD affects 5-12% of the general population and is the second most frequent cause of pain and musculoskeletal limitation, preceded only by low back pain [2]. It is often associated with symptoms of other chronic pain disorders and comorbidities. Individuals with TMD are more likely to have other joint pain compared to those without TMD [3].

Comorbidity is considered when two diseases have correlation and temporal continuity, with the possibility of them appearing simultaneously, or one preceding the other with an association that is more than casual. There is a positive association between the number of comorbidities and the intensity/duration of TMD pain. The influence occurs mutually and leads to direct effects on the signs and symptoms reported by the patient [4,5].

The identification of comorbidities in patients being treated for TMD has direct implications for the elaboration of the treatment to be proposed, and must be done since the initial examination in the patient's anamnesis and reported separately. There are situations in which only when both conditions, TMD and comorbidity, are treated, the patient improves [4-6].

Treatment success and TMD control will therefore not be obtained in isolation, making further studies necessary to correlate this disorder with the present comorbidities. This research evaluated the presence of comorbidities in individuals diagnosed with TMD, of subtypes of temporomandibular disorders (TMD), classified by DC/TMD, and verified the association between comorbidities and TMD subtypes.

#### 2. MATERIALS AND METHODS

## 2.1 Study Population, Sampling Plan, and Sample Calculation

This is a cross-sectional, observational research of quantitative nature. The sample consisted of individuals of both sexes, aged between 18 and 70 years of age, who attended the TMD clinic of the Specialized Dental Center of the State of Ceará (CEO-CENTRO), located in Fortaleza -CE- Brazil for treatment. We considered all patients attended on this specialized clinic at the moment of the study.

The inclusion criteria were patients of both sexes aged between 18 and 70 years of age,

diagnosed with TMD, and who signed the Free and Informed Consent Form. Exclusion criteria were patients with any inability to complete forms and answer questions asked during the interview, as well as patients who refused to participate in the survey.

### 2.2 Methodology for Data Collection

Initially, the participants treated at CEO received the Free and Informed Consent Form. Then, the examiner assessed the patient according to the DC/TMD (Axis 1); diagnosing the present TMD subtype(s). Soon after, the patient was asked about the existence of other pathologies, which were allocated in a questionnaire, according to the corresponding human body system.

Participants were assessed using the DC/TMD instrument (Axis I) to diagnose the presence and define subtypes of TMD. After the application of the DC/TMD (Axis I), the patients were asked to report other present diseases. The examiner recorded the reported diseases in the corresponding system: cardiovascular, respiratory, digestive, nervous, sensory, endocrine, excretory, urinary, reproductive, musculoskeletal, immunological, lymphatic, and integumentary. Next, data were tabulated regarding the diagnosis of TMD subtypes and the system corresponding to the comorbidity, collected in the anamnesis, for comparative purposes and verification of which system would be more related to the presence of TMD.

## 2.3 Analysis of Results

The results obtained were tabulated and submitted to a descriptive statistical analysis to assess the prevalence of TMD subtypes and the most frequent comorbidities reported by the patient. The comorbidities found were related to the TMD subtypes, as well as the distribution between sexes and between age groups, with data tabulated by decades. Data were tabulated in Microsoft Office Excel® software and exported to SigmaPlot software version 11.0. Clinicaldemographic data were expressed in absolute frequency and percentage, and quantitative data as mean and standard deviation. Spearman correlation and the Chi-square test were used, where the value of p < 0.05 was adopted as statistically significant.

## 3. RESULTS

A total of 270 patients were selected, of which 88.5% (n = 239) were female and 11.5% (n = 31)

were male (Table 1), with an age mean of  $43 \pm 12.9$  years (p = 0.48; Kolmogorov-Smirnov test).

After dividing the range by decades, the most prevalent age was between 39 and 48 years old (27%; n = 73), followed by 49 to 58 years old (24.4%; n = 66) and 29 to 38 years old (18, 9%; n = 51) (Table 1). A significant difference was found (p < 0.05; Chi-square test) when comparing age by age group.

Regarding the subtype of TMD in the study sample, it was observed that the most prevalent was joint/muscular (53.3%; n = 144), followed by muscular (46.3%; n = 125) and finally joint (0.4%; n = 1) (Table 2).

Table 3 represents the correlation between sex (r = -0.11) and age (r = 0.03) variables with TMD subtype. No important correlations were identified (p > 0.05) when comparing TMD subtypes with sex and age variables.

When questioned about the presence of diseases, it was shown that the nervous (n = 89; 33%) and sensory (n = 84; 31.1%) systems were the ones with the highest prevalence among comorbidities; however, disorders in the lymphatic (n = 1; 0.4%), excretory (n = 4; 1.5%), and urinary (n = 4; 1.5%) systems were rarely reported by the study sample (Table 4).

Table 5 highlights the correlation between comorbidities and TMD subtype, showing that joint/muscular TMD was the most prevalent, followed by muscular, both in the nervous and sensory systems.

No important correlations (moderate or strong) were observed when comparing comorbidities regarding sex (Table 6). In females, the most prevalent comorbidities were in the nervous (n = 82; 30.4%) and sensory (n = 76; 28.1%) systems, and in males, in the cardiovascular (n = 9; 3.3%) and sensory systems (n = 8; 3%).

Table 1. Sample age group

Variables	
Age	%
Up to 28 years	16.3%
29 – 38 years	18.9%
39 – 48 years	27.0%
49 – 58 years	24.4%
59 – 68 years	11.1%
69 – 78 years	01.1%

Caption: p < 0.05 (Chi-square test).

\*Age group that showed the biggest difference when compared to other age groups.

Subtypes	%
Joint and Muscular	53.3%
Articulate	0.4%
Muscular	46.3%

#### Table 2. Data distribution in relation to TMD subtype

Caption: p < 0.05 (Chi-square test)

	TMD			r	Р
Variables	Muscular	Joint	Joint/ Muscular		
Sex					
Female	106 (39.3%)	1 (0.4%)	132 (48.9%)	-0.11	0.08
Male	19 (7%)	0	12 (4.4%)		
Age					
Up to 28 years	24 (9%)	0	20 (7.5%)	0.03	0.61
29 – 38 years	22 (8.2%)	0	29 (10.9%)		
39 – 48 years	32 (12%)	1 (0.4%)	40 (15%)		
49 – 58 years	29 (10.9%)	0`´´	37 (13.9%)		
59 – 68 years	14 (5.2%)	0	16 (6%)		
69 – 78 years	2 (0.7%)	0	1 (0.4%)		

#### Table 3. Correlation between sex, age and TMD subtype

Caption : TMD = temporomandibular disorder. Number of subjects followed by relative frequency in percentage (%); r = Spearman correlation, P = Chi-square.

Table 7 demonstrates the correlation between v age and comorbidities, noting that there were no r important correlations (moderate or strong) in the ( study sample. The only exception was the a cardiovascular system, which showed a weak s correlation (r = 0.37). The ages at which the v comorbidities had the greatest influence were v from 39 to 48 years old and from 49 to 58 years

old in the nervous and sensory systems.

#### 4. DISCUSSION

This study aimed to evaluate the prevalence of comorbidities in individuals with TMD, identifying the human body system and relating it to the subtype of TMD, be it muscle and/or joint. The research was composed of individuals of both sexes, aged between 18 and 70 years, who were diagnosed with TMD. In the sample, a total of 88.5% (n = 239) were female and 11.5% (n = 31) male, with a mean age of  $43 \pm 12.9$  years, thus predominating the age group between 39 and 48 years, different from the results found in other studies [5,6], in which women in the 20-40 years age group have more TMD symptoms, the present study may have differed due to the disparity between the number of men and women collected.

Regarding the subtype of TMD in the study sample, it was observed that the most prevalent

was muscular/joint (53.3%; n = 144), followed by muscular (46.3%; n = 125), and lastly ioint (0.4%; n = 1). In this research, instruments such as the DC/TMD questionnaire and a form for surveying comorbidities were used. Other studies with similar outcomes are found by Progrante [7], which in 1643 found symptoms of pain in 36.2% of the sample, with 29.5% muscle pain, and 6.5% joint pain. Ismail [8] observed in a sample composed of 92 individuals a prevalence of 30.4% of muscular TMD, 67.4% joint/muscular, and 2.2% of joint. In the review carried out by Reis [9], patients with muscle TMD are more anxious and depressed than patients with other TMD subtypes, showing that the high prevalence of muscle problems can either influence or be influenced by comorbidities of a psychosomatic nature. In the study by Lei [10], he adds that sleep and quality of life related to oral health are associated also with painful subtypes. having a considerable influence on these symptoms.

The various comorbidities and conditions of bodily pain in TMD have been associated with generalized alterations in pain processing. In the present study, the main comorbidities found were related to the nervous (n = 89; 33%) and sensory (n = 84; 31.1%) systems, which were the ones with the highest prevalence among comorbidities, while disorders in the lymphatic ( n = 1: 0.4%), excretory (n = 4: 1.5%) and urinary (n = 4: 1.5%) systems were rarely reported by the sample under study, with no significant correlations between age or sex and comorbidities. Individuals with TMD reported multiple pain comorbidities, especially those of muscular origin, coexisting with other clinical conditions, a situation pointed out by several studies [11,12]. In the study by Gonçalves [10] TMD subtypes were related to frequently reported situations, such as headache, with myofascial and joint/muscular TMD being

strongly associated with these episodes, a situation not found in joint TMD. In order to have a more accurate correlation, Klasser [13] did not consider joint/muscular TMD, observing a greater number of comorbidities in muscular TMD, with psychological and neurological conditions being the most frequent ones. In the present study, all TMD subtypes were found in the sample, predominantly joint/muscular TMD, as previously mentioned. which were compared to comorbidities related to human body systems and not to specific situations.

Comorbidities	n	Fr	Р
Cardiovascular			
Yes	61	22.6%	<0.05
No	209	77.4%	
Respiratory			
Yes	32	11.9%	<0.05
No	238	88.1%	
Digestive			
Yes	55	20.4%	<0.05
No	215	79.6%	
Nervous			
Yes	89	33%	<0.05
No	181	67%	
Sensory		<u>.</u> .,.	
Yes	84	31.1%	<0.05
No	186	68.9%	<0.00
Endocrine	100	00.070	
Yes	29	10.7%	<0.05
No	241	89.3%	<0.03
Excretory	271	00.070	
Sim	4	1.5%	<0.05
Não	266	98.5%	<0.05
Urinary	200	30.370	
Yes	4	1.5%	<0.05
No	4 266	98.5%	<0.05
Reproductive	200	90.070	
Yes	0	3%	-0.05
No	8 262	3% 97%	<0.05
Skeletal Muscle	202	97%	
	40	44.00/	0.05
Yes	40	14.8%	<0.05
No	230	85.2%	
Immunological	10	45.00/	0.05
Yes	43	15.9%	<0.05
No	227	84.1%	
Lymphatic		0.404	
Yes	1	0.4%	<0.05
No	269	99.6%	
Integumentary			
Yes	5	1.9%	<0.05
No	265 subjects: Er – relative fre	98.1%	

#### Table 4. Reported comorbidities

Caption : n = n umber of subjects; Fr = relative frequency in percentage; <math>P = p-value, Binomial Test.

	TMD			r	Р
Variables	Muscular	Articulate	Muscular/ Articulate		
Cardiovascular					
Yes	34 (12.6%)	0	27 (10%)	-0.10	0.10
No	91 (33.7%)́	1 (0.4%)	117 (43.3%)		
Respiratory			, <i>,</i> ,		
Yes	17 (6.3%)	0	15 (5.6%)	-0.05	0.42
No	108 (7%)	1 (0.4%)	129 (47.8 <sup>°</sup> %)		
Digestive			· · · · · · · · · · · · · · · · · · ·		
Yes	27 (10%)	0	28 (10.4%)	-0.03	0.67
No	98 (36.3%)	1 (0.4%)	116 (43%)		
Nervous				0,04	0,54
Yes	39 (14,4%)	0	50 (18,5%)	- , -	- / -
No	86 (7%)	1 (0,4%)	94 (34,8%)		
Sensory		(0,170)			
Yes	38 (14.1%)	0	46 (17%)	0.02	0.78
No	87 (32.2%)	1 (0.4%)	98 (36.3%)	0.02	011 0
Endocrine	01 (021270)	1 (01170)			
Yes	16 (5.9%)	0	13 (4.8%)	-0.06	0.32
No	109 (40.4%)	1 (0.4%)	131 (48.5%)	0.00	0.02
Excretory		. (0.170)			
Yes	2 (0.7%)	0	2 (0.7%)	-0.01	0.89
No	123 (45.6%)	1 (0.4%)	142 (52.6%)	0101	0100
Urinary	120 (101070)	1 (01170)	112 (021070)		
Yes	2 (0.7%)	0	2 (0.7%)	-0.01	0.89
No	123 (45.6%)	1 (0.4%)	142 (52.6%)	0.01	0.00
Reproductive	120 (10.070)	1 (0.170)	112 (02.070)		
Yes	6 (2.2%)	0	2 (0.7%)	-0.10	0.10
No	119 (44.1%)	1 (0.4%)	142 (52.6%)	0.10	0.10
Skeletal Muscle	110 (11.170)	1 (0.170)	112 (02:070)		
Yes	17 (6.3%)	0	23 (8.5%)	0.04	0.58
No	108 (40%)	1 (0.4%)	121 (44.8%)	0.04	0.00
Immunological	100 (4070)	1 (0.470)	121 (44.070)	7-0.02	
Yes	21 (7.8%)	0	22 (8.1%)	1 0.02	0.74
No	104 (38.5%)	1 (0.4%)	122 (45.2%)		0.7 4
Lymphatic		· (0. + /0)	122 (-TU.270)		
Yes	0	0	1 (0.4%)	0.05	0.35
No	0 125 (46.3%)	1 (0.4%)	143 (53%)	0.00	0.00
Integumentary	120 (40.070)	1 (0.+70)	1-5 (5570)		
Yes	3 (1.1%)	0	2 (0.7%)	-0.04	0.54
				-0.04	0.04
No	122 (45.2%)	1 (0.4%)	142 (52.6%)		

#### Table 5. Correlation between comorbidities and TMD subtype

Caption : TMD = temporomandibular disorder. Number of subjects followed by relative frequency in percentage (%); r = Spearman correlation, P = Chi-square.

Source: Own authorship

Several other pieces of evidence point to the relationship between comorbidities and TMD, especially regarding the muscular subtype, indicating that this subtype is more associated with comorbidities, as is the case in this study. They also report that there is a bigger relationship between muscular TMD and situations of anxiety, depression and suicidal ideation, promoting an increased risk of chronic facial pain [8,9,14-16].

It is a consensus that TMD is a condition more associated with the female sex. In the present study, most individuals were of this sex, however it has not influenced the correlations [6,17]. Other studies that evaluated comorbidities and TMD also used the DC as an instrument, as well as the present study, and observed that painful comorbidities, such as migraine, chronic fatigue syndrome, irritable bowel syndrome and intestinal cystitis, had a positive association with presence of TMD. Moreover, a strong relationship with the presence of chronic depression is described as a risk factor for the TMD onset, especially in elderly and female patients [4,8,17-19]. Individuals with TMD are up to 5 times more likely to develop other joint pain. Other comorbidities have a close relationship with the symptoms worsening and should be monitored, such as: sinus disease, tinnitus, headache, eye disorders, fatigue, dizziness, genitourinary disorders, fibromyalgia, and xerostomia. Low back pain conditions and chronic pelvic pain are also often associated with TMD [3,4,7,12,20-26].

	TMD		r	Ρ
Variables	Female	Male		
Cardiovascular				
Yes	52 (19.3%)	9 (3.3%)	0.06	0.36
No	187 (69.3%)	22 (8.1%)		
Respiratory				
Yes	29 (10.7%)	3 (1.1%)	-0.02	0.69
No	210 (77.8%)	28 (10.4%)		
Digestive				
Yes	49 (18.1%)	6 (2.2%)	-0.01	0.88
No	190 (70.4%)	25 (9.3%)		
Nervous				
Yes	82 (30.4%)	7 (2.6%)	-0.08	0.19
No	157 (58.1%)	24 (8.9%)		
Sensory				
Yes	76 (28.1%)	8 (3%)	-0.04	0.50
No	163 (60.4%)	23 (8.5%)		
Endocrine				
Yes	26 (9.6%)	3 (1.1%)	-0.01	0.84
No	213 (78.9%)	28 (10.4%)		
Excretory				
Yes	4 (1.7%)	0	-0.05	0.47
No	235 (87%)	31 (11.5%)		
Urinary				
Yes	4 (1.5%)	0	-0.05	0.47
No	235 (87%)	31 (11.5%)		
Reproductive				
Yes	8 (3%)	0	-0.06	0.30
No	231 (85.6%)	31 (11.5%)		
Skeletal Muscle				
Yes	38 (14.1%)	2 (0.7%)	-0.08	0.16
No	201 (74.4%)	29 (10.7%)		
Immunological	· · ·	•		
Yes	38 (14.1%)	5 (1.9%)	0.00	0.97
No	201 (74.4%)	26 (9.6%)		
Lymphatic	· · ·	· · · ·		
Yes	0	1 (0.4%)	0.17	<0.05
No	239 (88.5%)	30 (11.1%)		
Integumentary	× 7	, , , , , , , , , , , , , , , , , , ,		
Sim	5 (1.9%)	0	-0.05	0.42
No	234 (86.7%)	31 (11.5%)		

#### Table 6. Correlation between comorbidities and sex

Caption : number of subjects accompanied by the relative frequency in percentage (%); r = Spearman correlation, P = Chi-square.

	Age (Years)					r	Р	
Variables	Up to 28	29 – 38	39 – 48	49 – 58	59 - 68	69 - 78		
Cardiovascular	-							
Yes	1 (0.4%)	3 (1.1%)	18 (6.7%)	21 (7.9%)	14 (5.2%)	3 (1.1%)	0.37	0.00
No	43(16.1%)	48 (18%)	55 (20.6%)	45 (16.9%)	16(6%)	0		
Respiratory								
Yes	6 (2.2%)	10 (3.7%)	6 (2.2%)	8 (3%)	2 (0.7%)	0	-0.08	0.17
No	38 (14.2%)	41 (15.4%)	67(25.1%)	58 (21.7%)	28 (10.5%)	3 (1.1%)		
Digestive	· · ·							
Yes	7 (2.6%)	9 (3.4%)	15 (5.6%)	16(6%)	6 (2.2%)	1 (0.4%)	0.06	2.29
No	37 (13.9%)	42 (15.7%)	58 (21.7%)	50 (18.7%)	24 (9%)	2 (0.7%)		
Nervous				. ,				
Yes	9 (3.4%)	18 (6.7%)	29 (10.9%)	25 (9.4%)	6 (2.2%)	2 (0.7%)	0.05	0.46
No	35 (13.1%)	33 (12.4%)	44 (16.5%)	41 (15.4%)	24 (9%)	1 (0.4%)		
Sensory								
Yes	13 (4.9%)	15(5.6%)	30 (11.2%)	18 (6.7%)	7 (2.6%)	1 (0.4%)	-0.03	0.58
No	31 (11.6%)	36 (13.5%)	43 (16.1%)	48 (18%)	23 (8.6%)	2 (0.7%)		
Endocrine								
Yes	1 (0.4%)	1 (0.4%)	6 (2.2%)	11 (4.1%)	7 (2.6%)	2 (0.7%)	0.26	0.00
No	43 (16.1%)	50 (18.7%)	67 (25.1%)	55 (20.6%)	23 (8.6%)	1 (0.4%)		
Excretory								
Yes	0	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0.13	0.04
No	-44 (16.5%)	-51 (19.1%)	72 (27%)	65 (24.3%)	29(10.9%)	2 (0.7%)		
Urinary								
Yes	0	1 (0.4%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	0	0.05	0.43
No	-44(16.5%)	50 (18.7%)	72 (27%)	65 (24.3%)	29(10.9%)	-3 (1.1%)		
Reproductive								
Yes	1 (0.4%)	3 (1.1%)	3 (1.1%)	1(0.4%)	0	0	-0.07	0.25
No	43 (16.1%)	48 (18%)	70 (26.2%)	65 (24.3%)	-30 (11.2%)	-3 (1.1%)		
Skeletal Muscle								
Yes	0	5 (1.9%)	10 (3.7%)	16 (6%)	8 (3%)	1 (0.4%)	0.25	0.00
No	-44 (16.5%)	46 (17.2%)	63 (23.6%)	50 (18.7%)	22 (8.2%)	2 (0.7%)		

# Table 7. Correlation between comorbidities and age

	Age (Years)					r	Р	
Variables	Up to 28	29 – 38	39 – 48	49 – 58	59 - 68	69 - 78		
Immunological								
Yes	8(3%)	8(3%)	11 (4.1%)	12 (4.5%)	2 (0.7%)	2 (0.7%)	-0.02	0.79
No	36(13.5%)	43 (16.1%)	62 (23.2%)	54 (20.2%)	28 (10.5%)	1 (0.4%)		
Lymphatic								
Yes	0	0	1 (0.4%)	0	0	0	-0.00	0.98
No	-44 (16.5%)	-51 (19.1%)	72 (27%)	-66 (24.7%)	-30 (11.2%)	-3 (1.1%)		
Integumentary								
Yes	1 (0.4%)	2 (0,7%)	1 (0.4%)	1 (0.4%)	0	0	-0.06	0.30
No	43 (16.1%)	49 (18.4%)	72 (27%)	65 (24.3%)	-30 (11.2%)	-3 (1.1%)		

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Caption : number of subjects accompanied by the relative frequency in percentage (%); r = Spearman correlation, P = Chi-square.

Although most studies indicate a relationship between TMD and some comorbidity [20-26.27]. as well as in the present study, when relating these comorbidities by systems and not by conditions, specific found no association between the incidence of TMD and pathologies of the endocrine, cardiovascular system or hematological systems, sleep apnea and history of hospitalization for surgery or serious illnesses, despite suggesting that some specific comorbidities have a greater influence on the appearance and perpetuation of TMD symptoms, such as poor sleep, there is no differentiation between the systems, suggesting that the overall compromised health status, regardless of the system, may be more relevant in the process. However, more studies must be carried out for better conclusions.

The results of this study indicate and reinforce that TMD symptoms are related to comorbidities. Finally, knowledge of the presence of other conditions is fundamental in order to achieve better targeting and better results in the treatment of this disorder, with the ideal medical diagnosis of comorbidities to identify these conditions.

## 5. CONCLUSION

In the present study, all TMD subtypes were found in the sample, with a predominance of joint/muscle TMD. Several comorbidities were found, mainly related to the nervous and sensorial systems, being necessary more studies to evaluate the influence that each comorbidity has in relation to the appearance or perpetuation of TMD symptoms. Although in the literature there is a predominance of symptoms in women aged between 20 and 40 years, studies paired by gender and number should be carried out.

# CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

# ETHICAL APPROVAL

The procedures for carrying out this research respected the guidelines and norms that regulate research involving human beings approved by resolution 466/12, of the National Health Council (CNS) of the Brazilian Ministry of Health. It was submitted to the Ethics Committee in Research (CEP) involving human beings of the São Leopoldo Mandic Dental Research Center, Campinas-São Paulo- Brazil. 2.431.538.

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# **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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