

Volume 8, n 1, 2020

Articles

The effects on Oral Related Quality of Life induced by periodontitis in patients with juvenile idiopathic arthritis

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Abstract

The objective of study was to evaluate the impact of periodontitis on the health-related quality of life (HRQoL) in patients affected by juvenile idiopathic arthritis (JIA). Sixty consecutive patients with JIA with or without periodontitis and 33 healthy control subjects were enrolled in the study. The demographic data, disease activity and clinical characteristics were obtained from all patients. HRQoL and disability was assessed by two questionnaires, the Italian version of the Childhood Health Assessment Questionnaire (C-HAQ) and the Child Perception Questionnaire (CPQ₁₁₋₁₄). Possible determining factors of periodontitis comprised demographic and disease characteristics and HRQoL scores that were assessed by uni- and multivariable logistic regression analysis. Compared to patients without periodontitis, JIA patients with periodontitis presented higher disability and lower HRQoL scores. The multivariable logistic regression analysis highlighted that female subjects (OR 1.4) or a JIA duration over 4.1 years (OR 2.6), higher C-HAQ and CPQ₁₁₋₁₄ scores (OR 2.8 – 2.9) were the greatest determining factors for periodontitis. JIA patients with periodontitis presented lower HRQoL compared to JIA patients without periodontitis. Periodontitis was strongly associated with JIA duration and activity and negatively influenced the HRQoL of JIA patients.

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Keywords:

Juvenile idiopathic arthritis; Periodontitis; Disability; Articular joint; Quality of life.

Received: 2 March 2020

Accepted: 23 March 2020

Published: 20 April 2020

Citation: Polizzi, A., Santonocito, S., Di Stefano, M., Ferlito, S., Indelicato, F., Palazzo, G. (2020). The effects on Oral Related Quality of Life induced by periodontitis in patients with juvenile idiopathic arthritis. *Mediterranean Journal of Clinical Psychology* 8(1). Doi: <https://doi.org/10.6092/2282-1619/mjcp-2426>



1. Introduction

Juvenile idiopathic arthritis (JIA) is a chronic disease of unknown etiology, with an estimated incidence of 16 to 150 cases per 100,000 children worldwide, characterized by chronic synovitis in one or many joints that represents an important cause of disability in childhood (Manners & Bower, 2002). Periodontitis is a common consequence of the systemic disease in worldwide (Isola et al., 2019b, 2020a, h; Matarese et al., 2013) associated with diabetes (Isola et al., 2019d, 2020b; Settineri, Frisone, Merlo, Geraci, & Martino, 2019), cardiovascular disease (Isola, Polizzi,

Alibrandi, Indelicato, & Ferlito 2020; Isola, Polizzi, Muraglie, Leonardi, & Lo Giudice 2019; Piancino et al., 2017) and with some others systemic disorders (Caputo 2013; Engstrom, Wanman, Johansson, Keshishian, & Forsberg, 2007; Settineri, Frisone, Alibrandi, & Merlo, 2019). Previous reports have shown that up to 93% of patients with JIA may present early inflammatory findings in mouth (Bruns, Hilario, Jennings, Silva, & Natour, 2008). The impairment due to periodontitis, may lead to difficulties in many daily activities, such as eating, smiling and performing oral hygiene (Leksell, Ernberg, Magnusson, & Hedenberg-Magnusson, 2012) and tooth impaction (Ahola et al., 2015; Isola, Matarese, Ramaglia, Cicciù, & Matarese, 2019; Isola et al., 2019a; Isola et al., 2019c; Matarese et al., 2016b). Periodontitis, such as temporomandibular joint (TMJ) arthritis was shown to perhaps also determine, if not properly treated, a reduced and asymmetric craniofacial and mandibular growth with the appearance of a skeletal malocclusion and micrognathia (Hainarosie et al, 2019; Isola et al., 2017b). Moreover, the appearance of stomatognathic disorders during childhood has been demonstrated to determine disabilities and dysfunctions during adulthood (Fjeld et al., 2010). Indeed, some reports have highlighted that the appearance of mouth problems during childhood determines a high percentage of orofacial impairments even still after 26 years of the appearance of JIA (Bakke, Zak, Jensen, Pedersen, & Kreiborg, 2001).

The diagnosis of periodontitis in JIA patients during the active phases of the disease is a challenging task, because sometimes the signs and symptoms may be misleading or misdiagnosed. In fact, previous reports showed that pain, that is one of the main factors associated with periodontitis and TMJ arthritis is very unreliable because it is reported in only a quarter of JIA patients with manifest radiological signs of mouth disorders (Fjeld et al., 2010).

However, the presence of periodontitis during JIA has been demonstrated to influence the quality of life of the JIA patients (Tollisen, 2017) and to be a significant burden on patient caregivers (Merlo 2019a, b; Motofei & Rowland 2015, 2018; Oliveira et al., 2007; Settineri et al., 2018; Settineri & Merlo, 2019; Settineri, Frisone, Alibrandi, & Merlo, 2019). Orofacial pain due to the involvement of periodontal disease and TMJs is a frequent finding in patients affected by JIA and is reported to severely influence daily life in almost 25% of patients (Ardeleanu et al., 2020; Rowland & Motofei, 2017; Tollisen et al, 2017).

For many years, several health-related quality of life (HRQoL) questionnaires have been used to detect the impact of the disease on the daily quality of life and the patient-relevant burden of daily disease in patients affected by JIA (Tollisen et al., 2017). However, a new generation of questionnaires has been developed to more appropriately assess the oral health quality of life during childhood, such as the Childhood Health Assessment Questionnaire (C-HAQ) and the

Child Perception Questionnaire (CPQ₁₁₋₁₄), both of them translated into many different languages (Ruperto et al., 2001; Settineri et al., 2019). Moreover, this new generation of questionnaires has been confirmed as a useful tool to well assess the impact of JIA in the quality of life of JIA patients (Frid et al., 2017).

As a negative impact of arthritis of periodontitis during JIA, there is an increasing interest concerning the influences that periodontitis exerts on the HRQoL in JIA patients. In light of these findings, the aim of this study was to assess the differences in clinical characteristics, HRQoL, oral alterations and disability induced by periodontitis in a cohort of patients affected by JIA with or without periodontitis compared to healthy subjects and to assess which factors had influences and effects on periodontitis. The null hypothesis to invalidate was that patients with and without periodontitis presented no differences in clinical characteristics, disability and HRQoL.

2. Materials and methods

2.1 Study design

Patients with a diagnosis of JIA performed in accordance with ILAR criteria, with and without periodontitis were enrolled in the present case-control study between February 2012 and September 2017. The local ethical committee approved the protocol of the study (#918-10, 5 February 2010). The written informed consent was acquired from the parents of each patient who were informed about the study type and characteristics, in accordance with the Declaration of Helsinki in 1975, revised in 2000.

The inclusion criteria were: (1) diagnosis of JIA (only in JIA groups) (2) no injections of any steroid during the last 12 months. The exclusion criteria were: (1) previous orthodontic treatment, (2) previous maxillofacial surgery, and (3) genetic or congenital syndromes or any concurrent medical condition that could influence the results of the study.

Seventy-four consecutive patients with a diagnosis of JIA, aged between 8-17 years (40 female and 34 males, mean age of 11.4 ± 1.8 years) were initially enrolled as the study group.

Thirty-three healthy subjects, matched for age and sex (16 female and 17 males, mean age of 11.7 ± 2.3 years), were enrolled as the control group, between subjects attending dental clinics for routine oral visits. The healthy subjects did not present any history of rheumatic, congenital or systemic diseases or TMJ disorders, with a good occlusion and maxillary relationship.

After the first screening, 14 patients with JIA were excluded because they did not fully meet the inclusion criteria ($n=6$), declined to participate ($n=4$), or missed the clinical examination ($n=4$). Thus, the final number of patients assessed for eligibility as JIA group was 60.

2.2 Data collection

The clinical characteristics data and subtype of JIA was obtained from the hospital chart of each patient and was documented by a paediatric rheumatologist (Table 1) divided by the square of the patient's height, i.e., kilogram per square meter (kg/m^2).

The periodontal evaluation comprised probing depth (PD), clinical attachment loss (CAL), bleeding on probing (BOP), and plaque score (PI), and the presence of bleeding was recorded up to 30 s after probing. CAL was recorded as PD plus recession, with the cemento-enamel junction as a reference for CAL measurements. All clinical periodontal parameters were recorded, in all patients, at six sites per tooth on all teeth present, excluding third molars, by two independent calibrated examiners.

The study involved 3 groups (Table 1): Group 1, JIA patients with periodontitis (JIA + periodontitis group); Group 2, JIA patients without periodontitis (JIA group); Group 3, Healthy subjects (control group).

During the calibration sessions and after the clinical evaluation, intra-examiner repeatability and reproducibility was evaluated to obtain duplicate measurements of clinical parameters from patients randomly selected from the sample. One examiner evaluated the parameters of the two JIA groups and a second examiner evaluated the control group.

The intra-examiner agreement, which was 0.823 (95% CI 0.71 – 0.9), was obtained by calculating Cohen's κ coefficient from all outcomes deriving from the two HRQoL questionnaires, predicted a good degree of reliability.

2.3 Sample size

The sample size was established considering the mean prevalence of JIA in the population equal to 0.08% (1), the study group incidence of 2.8% (as the prevalence of JIA in our database), alpha level of 0.05 and a power of 80%. A minimum sample of 51 JIA patients was determined to ensure a good sample size. Sixty patients affected by JIA and 33 healthy subjects in the control group were finally enrolled.

2.4 HRQoL and functional disability measurement

HRQoL was assessed by two questionnaires, the Italian version of the C-HAQ (18) and the Child Perception Questionnaire (CPQ) (Ruperto et al., 2001). The C-HAQ consisted of several domains aimed at evaluating the impact of the frequency of the quality of care related to daily life activities and the ability of the patient to achieve distinct functions. The C-HAQ version chosen for this study was composed of seven different domains regarding daily activities like walking, eating, arising, dressing, hygiene, gripping and reaching/activity calculated by a range

from 0 (no or minimal physical disability) to 3 (very severe physical disability). A visual analog scale (PRgloVAS) (0-10-cm, ranged from 0, very health and 10 the poorest) was chosen to measure the parent's global assessment of the general health of the child's in the last 10 days.

The Child Perception Questionnaire (CPQ₁₁₋₁₄) was chosen to measure the oral health related quality of life (OHRQoL) for the enrolled patients. The version of CPQ₁₁₋₁₄ chosen for this study comprised four health domains (oral symptoms, functional limitations, social well-being, emotional well-being) aimed at measuring the impact of oral disease and the extent to which the patient's condition affected his/her overall global well-being in the previous three months. In the CPQ₁₁₋₁₄ the answers options were "never=0"; "once or twice =1"; "sometimes =2"; "often =3"; "every day or almost every day =4." The summary score following the sum of these domains ranged from 0 to 140. A low total summary score predicted a good OHRQoL, while a high summary score predicted a low OHRQoL. Both questionnaires were filled out by the patient aged >9 years old, or by one of the caregivers.

2.5 Statistical analysis

All statistical analyses were executed using a software program (SPSS version 17.0 for Windows, Chicago, IL). The parametric approach was used because the data are normally distributed, such as verified by Kolmogorov Smirnov test. The chi-square test and the *t*-test were used to compare the categorical and the continuous variables, respectively. A univariable logistic regression analysis was used to assess the influence of quality of life measurements on periodontitis. The same analysis was performed in order to recognize factors distinguishing JIA patients with the presence/absence of periodontitis by using the C-HAQ and CPQ₁₁₋₁₄ domains as exploratory measures. To recognize factors independently associated with periodontitis, a multivariable logistic regression was performed. $P < 0.05$ was considered to be statistically significant.

3. Results

The demographic data, age and gender distribution, JIA types, drug therapy and the serological values of the sample are presented in Table 1. A total of 92 patients participated in the study; 30 patients in JIA+periodontitis group, 30 patients in JIA group and 32 patients in control group. The examined groups were matched for age and gender. Regarding the JIA patients, JIA was diagnosed at 8.6 ± 2.9 (SD) years of age. 36.6% of the JIA patients presented JIA of up to 2 years of duration, 28.4% between 2 and 5 years of duration and 35% more than 5 years' duration. Ten patients in group JIA+periodontitis (33.3%) and 8 (26.7%) in group JIA presented rheumatoid factor–negative polyarthritis (Table 1). Eighteen patients (60%) in group JIA+periodontitis and 13 patients (43.3%) in group JIA underwent DMARD at least once while

17 patients (56.7%) in group JIA+periodontitis and 14 patients (46.7%) in group JIA underwent biological drugs (Table 1).

Table 1: Sociodemographic and clinical characteristics of the study population. Values are expressed with mean (\pm SD).

Characteristics	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=33)
Age, mean \pm SD	11.7 \pm 2.1	12.2 \pm 2.1	11.7 \pm 2.1
Female sex, N°	16	14	15
BMI, mean, \pm SD kg/m ²	20.5 \pm 6.5	21.4 \pm 5.8	20.4 \pm 5.2
<i>JIA subtype, no. (%)</i>			
Systemic JIA, N°	11 (34.4)	10 (33.3)	-
RF-negative polyarthritis, N°	9 (28.1)	7 (23.3)	-
RF-positive polyarthritis, N°	4 (12.5)	5 (16.6)	-
Enthesitis-related arthritis, N°	1 (3.1)	-	-
Psoriatic arthritis, N°	2 (6.2)	1 (3.3)	-
Extended oligoarthritis, N°	5 (15.6)	6 (20)	-
Undifferentiated arthritis, N°	-	1 (3.3)	-
<i>Biological drugs</i>			
Age at disease onset, mean \pm years	8.7 \pm 3.4	8.5 \pm 2.8	-
No. of JIA patients with active joint, N°	18	17	-
No. of active Joint in JIA patients (median)	8.2 \pm 3.6	3.0 \pm 3.1	-
No. of joints with pain (median)	6.0 \pm 2.1	3.0 \pm 1.9	-
Current morning stiffness >15 min, N°	9	7	-
CRP level, mean \pm SD mg/dl	11.6 \pm 11.2	12.7 \pm 13.4	5.7 \pm 9.4
ESR, median	31.0 \pm 6.4	21.0 \pm 7.2	10.0 \pm 6.5
Positive ANA test at baseline, N°	10	13	-
Positive HLA-B27 test, N°	7	9	-
Any comorbidity, N°	14	12	-
History of uveitis, N°	7	6	-
<i>DMARD treatment</i>			
Etanercept, N°	16	10	-
Adalimumab, N°	4	5	-
<i>Periodontal characteristics</i>			
Methotrexate, N°	13	11	-
chloroquine/hydroxychloroquine, no. (%)	3	2	-
azathioprine, no. (%)	2	2	-
Cyclosporin A, no. (%)	-	1	-
Probing depth (PD), mm \pm SD	4.5 \pm 5.2	2.1 \pm 1.9	2 \pm 1.5
Clinical Attachment level (CAL), mm \pm SD	4.6 \pm 3.9	2.2 \pm 1.6	1.9 \pm 1.1
Bleeding on Probing (BOP), mm \pm SD	56.9 \pm 12.3	22.5 \pm 12.7	20.2 \pm 5.1

Regarding the C-HAQ and the CPQ₁₁₋₁₄, patients in group JIA+periodontitis showed statistically significant differences in the disability score compared to patients in group JIA and control group (Figure 1 and 2).

As reported in Figure 1, patients in group JIA+periodontitis presented a mean score of more than twice C-HAQ with respect to the domains related to eating, hygiene and reaching activities, and of the PRgloVAS score, both that were significantly higher compared to patients of the

other groups. Moreover, compared to control group, patients in JIA group presented higher, but not significant values of dressing, eating and reaching activities.

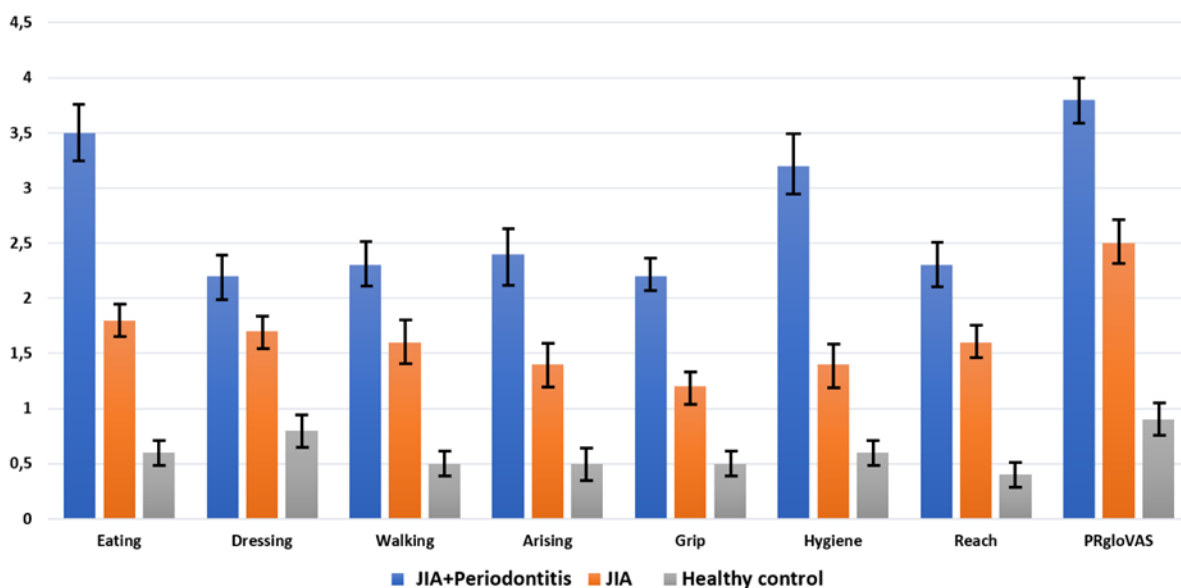


Figure 1: National version of the childhood health assessment questionnaire (C-HAQ) scores of the patient sample. Results are presented as mean and confidence intervals (CI).

Regarding the CPQ₁₁₋₁₄, the patients in group JIA+periodontitis presented lower scores regarding the domains of functional limitations and well-being, while they presented higher scores in domains of oral symptoms compared to the others two groups (Figure 2).

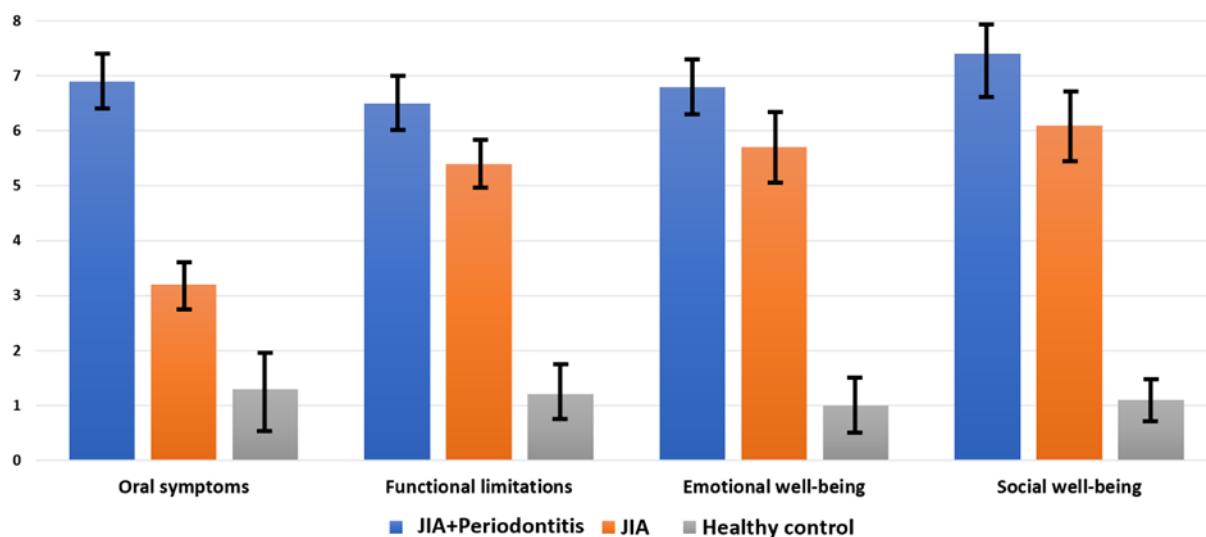


Figure 2: Child Perception Questionnaire (CPQ₁₁₋₁₄) scores of the patient sample. Results are presented as mean and confidence intervals (CI).

Moreover, as reported in Table 2, the univariate analyses (odds ratios [ORs] with 95% confidence intervals), which assessed the association of JIA activity/disability and quality of life with periodontitis, showed that, in group JIA+periodontitis, a significant association of periodontitis was found with the C-HAQ and CPQ₁₁₋₁₄ domains. Disease activity and disability were higher in the patients in group JIA+periodontitis which presented higher values especially for the eating (OR 5.7) and hygiene (OR.3.3) scores, such as the PRgloVAS score (OR 3.5). Regarding the CPQ₁₁₋₁₄ domains, group JIA+periodontitis presented higher scores compared with the others two groups regarding oral symptoms and functional limitations (OR 2.3 and OR 3.7, respectively).

Table 2: Univariable logistic regression analysis of the quality of life measurements of the patient sample. Values expressed OR (95% CI).

Parameters	Periodontitis OR (95% CI)
<i>C-HAQ</i>	
Eating	5.7 (2.4 – 6.4)
Dressing	3.1 (2.3 – 4.5)
Walking	2.5 (1.5 – 3.9)
Arising	3.2 (2.4 – 5.6)
Grip	3.1 (2.6 – 4.9)
Hygiene	3.3 (2.1 – 4.6)
Reach	3.6 (1.8 – 5.5)
PRgloVAS	3.5 (2.3 – 5.5)
<i>CPQ₁₁₋₁₄</i>	
Oral symptoms	2.3 (1.6 – 4.2)
Functional limitations	3.7 (2.1 – 4.8)
Emotional well-being	2.2 (1.4 – 3.1)
Social well-being	2.3 (1.3 – 2.9)

In the final regression model, all variables significantly related to periodontitis at the univariate analysis based on OR such as gender, JIA duration, RF, number of active joints, ESR, C-HAQ and CPQ₁₁₋₁₄ global scores were selected. In order to validate also for the level of disease activity, in the final model the score results were adjusted with the OR for the RF values and for the number of active joints. The multivariable analysis demonstrated that variables such as the female gender (OR 1.4), with a JIA duration over 4.1 years (OR 2.6), and with higher C-HAQ and CPQ₁₁₋₁₄ scores (OR 2.8–2.9) were the greatest determining factors for periodontitis (Table 3).

Table 3: Multivariable logistic regression analysis of quality of life measures, disease activity and clinical and demographic characteristics associated with periodontitis.

Parameters	Crude OR (95% CI)	Adjusted OR (95% CI)
C-HAQ total score > 1.3	3.8 (1.5 – 5.8)	2.8 (2.3 – 5.1)
CPQ ₁₁₋₁₄ total score > 1.4	2.8 (1.3 – 4.8)	2.9 (2.4 – 6.9)
Disease duration >4.1 years	2.1 (1.9 - 2.9)	2.6 (2.3 – 4.4)
Female sex	1.4 (1.2 – 1.7)	1.4 (1.3 – 3.5)
PRgloVAS > 2.1	3.6 (2.3 – 5.5)	1.7 (1.3 – 3.7)

4. Discussion

This study evaluated the impact of periodontitis in the OHRQoL and its determining factors that influence the quality of life in patients affected by JIA.

The present study showed an association between high disease duration and JIA activity with periodontitis in patients affected by JIA. In our cohort, JIA patients with periodontitis presented a lower OHRQoL (measured by C-HAQ and CPQ₁₁₋₁₄ scores) compared to JIA patients without periodontitis and healthy subjects. Moreover, there was an independent association between periodontitis and presence of JIA over 4.1 years of duration and the presence of a higher number of active joints.

According to previous studies (Frid et al., 2017; Koos et al., 2014), in our sample there was a high proportion of JIA patients with periodontitis; the diagnosis was performed by a clinical evaluation that allowed to specifically assess the presence of periodontitis in the analyzed sample. Moreover, also the associations between periodontitis and JIA disease characteristics found in our sample (70% in total) were in agreement with previous clinical and radiological studies that reported signs of TMJ arthritis and periodontitis in almost of JIA patients or with patients with different psychological mood (Cannizzaro, Schroeder, Muller, Kellenberger, & Saurenmann, 2011; Kirkhus et al., 2016; Isola et al., 2017a; Settineri, Frisone, & Merlo, 2019; Settineri, Frisone, Alibrandi, & Merlo, 2019).

Periodontitis and TMJ involvement comprise a group of different signs and symptoms of dysfunctions at TMJs, including facial and muscular pain, click, periodontal disease and tooth impaction (Briguglio, Briguglio, Briguglio, Cafiero, & Isola, 2013; Cannavale, Matarese, Isola, Grassia, & Perillo et al., 2013; Isola et al., 2018, 2019g; Sheppard & Sheppard, 1965). However, even if it was reported as a frequent finding in JIA patients, it was demonstrated that periodontitis and mouth disorder, although present, is almost always asymptomatic, especially at a young age and can influence negatively the psychological status (Koos et al., 2014).

Moreover, this study showed also that JIA patients with periodontitis presented, in a univariate and multivariate analysis, a strong association with disability and daily difficulties such as eating, hygiene, functional limitations and well-being compared to JIA patients without periodontitis and to healthy subjects. In accordance with our results, a previous report showed that periodontitis involvement negatively influenced the quality of life in JIA patients and that JIA active disease is strongly associated with a lower quality of life (Frid et al., 2017; Isola et al., 2017a; Perillo et al., 2012).

Our study demonstrated an association between periodontitis and reduced HRQOL (measured with C-HAQ scores) and OHRQoL (measured with CPQ₁₁₋₁₄ scores).

One of the reasons for this association may be explained by the role that is played by periodontium that is a joint such as TMJs in the orofacial district. Indeed, it was shown that the health of periodontium is fundamental for many daily life activities such as chewing, talking, eating, and oral health well-being in general during JIA (Cavuoti et al., 2016; Cutroneo et al., 2012; Ferlazzo et al., 2017; Hsieh et al., 2020; Isola et al., 2019f; Schroeder, Muller, Kellenberger, & Saurenmann, 2011). In our sample, JIA patients with periodontitis reported eating difficulties, in accordance with previous reports that demonstrated chewing and masticatory performance impairment during JIA (Isola et al., 2019h; Lo Giudice et al., 2015; Matarese, 2012; Matarese et al., 2015). Eating difficulties and, in general, mouth disabilities during JIA were associated with a lower level of oral hygiene, gingivitis and a high percentage of tooth decay (Currò et al., 2014; Matarese et al., 2016a; Ostile, Johansson, Aasland, Flato, & Moller, 2010). All of these impairments, associated with periodontitis, are determining factors that negatively influenced the quality of life in JIA patients (Isola et al., 2015, 2019e; Frid et al., 2017).

In conclusion, this study indicated an association between periodontitis and a lower global quality of life in JIA patients. Periodontitis was strongly associated with high JIA duration and activity and influenced some daily activities, such as eating, hygiene, emotional and social well-being, especially in female subjects.

This initial study is promising and demands further studies on a larger sample to better understand the role and impact of periodontitis on the quality of life in patients affected by JIA.

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DOI: 10.6092/2282-1619/mjcp-2426