

Oral Health-Related Quality of life and its association with malocclusion and self-perception of dental aesthetics in Adolescents**Qualidade de vida relacionada à saúde bucal e sua associação com má oclusão e autopercepção da estética dentária em adolescentes**

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Fabírcia Soares Rodrigues

Mestre em Hebiatria

Instituição: Universidade de Pernambuco

Endereço: Av. General Newton Cavalcanti, 1650, CEP: 54753-220, Camaragibe – PE

E-mail: fabricia.rodrigues@hotmail.com

Sérgio Soares da Silva

Mestrando em Hebiatria

Instituição: Universidade de Pernambuco

Endereço: Av. General Newton Cavalcanti, 1650, CEP: 54753-220, Camaragibe – PE

E-mail: sergio_oi007@yahoo.com.br

Aline Cavalcanti da Silva

Mestre em Hebiatria

Instituição: Universidade de Pernambuco

Endereço: Av. General Newton Cavalcanti, 1650, CEP: 54753-220, Camaragibe – PE

E-mail: aline.casilv@gmail.com

Maria Carlla Aroucha Lyra

Mestre em Odontopediatria

Instituição: Universidade de Pernambuco

Endereço: Av. General Newton Cavalcanti, 1650, CEP: 54753-220, Camaragibe – PE

E-mail: mcarllalyra@gmail.com

Mariana Araújo Coutinho da Silveira

Mestranda em Hebiatria

Instituição: Universidade de Pernambuco

Endereço: Av. General Newton Cavalcanti, 1650, CEP: 54753-220, Camaragibe – PE

E-mail: marianaaraujocs@gmail.com

Aronita Rosenblatt

Doutora em Odontopediatria

Instituição: Universidade de Pernambuco

Endereço: Av. General Newton Cavalcanti, 1650, CEP: 54753-220, Camaragibe – PE

E-mail: aronitarosenblatt@gmail.com

Nicola Patrícia Thérésè Innes

Doutora em Odontologia

Instituição: University of Dundee

Endereço: Park Place, Dundee, DD1 4HR, UK

E-mail: innes@dundee.ac.uk

Monica Vilela Heimer

Doutora em Odontopediatria

Instituição: Universidade de Pernambuco

Endereço: Av. General Newton Cavalcanti, 1650, CEP: 54753-220, Camaragibe – PE

E-mail: monica.vilelaheimer@gmail.com

ABSTRACT

Introduction: Studies have shown that malocclusions can have a negative impact on the quality of life and self-esteem of adolescents. This study aimed to verify the association between Oral Health-Related Quality of Life, malocclusion and self-perceived dental aesthetics in Brazilian adolescents. **Methods:** A cross-sectional study was conducted with a sample of 580 students between 12 and 15 years old. The oral health-related quality of life (OHRQoL) was evaluated using Child OIDP, malocclusion was determined by DAI, self-perceived dental aesthetics was evaluated using the OASIS, and IOTN-AC assessed the self-perceived orthodontic treatment need. The statistical analysis involved descriptive and inferential methods, such as Pearson's chi-square test or Fisher's exact test and multiple logistic regressions, with significance level of 5%. **Results:** The prevalence of oral impact was high (73.4%), 49.1% presented malocclusion and 25.0% had a highly desirable orthodontic treatment need. Negative self-perception of dental aesthetics was observed in 50.0% of adolescents and 13.1% thought they needed orthodontic treatment. The impact on quality of life was associated to gender, self-perceived dental aesthetic ($p < 0.001$), malocclusion + self-perceived dental aesthetic ($p < 0.001$) and self-perceived orthodontic treatment need ($p = 0.045$). The logistic regression results indicated that being female and having negative self-perception of dental aesthetics are directly involved in the quality of life of adolescents. **Conclusion:** Being female and having a negative self-perception of one's dental aesthetics are risk factors for impacting negatively on oral health related quality of life.

Keywords: Self-perception, dental aesthetics, adolescents, orthodontics.

RESUMO

Introdução: Estudos têm demonstrado que as más oclusões podem impactar negativamente na qualidade de vida e na autoestima de adolescentes. Este estudo teve como objetivo verificar a associação entre Qualidade de Vida Relacionada à Saúde Bucal, maloclusão e autopercepção da estética dentária em adolescentes brasileiros. **Métodos:** Foi realizado um estudo transversal com amostra de 580 alunos entre 12 e 15 anos. A qualidade de vida relacionada à saúde bucal (OHRQoL) foi avaliada pelo Child OIDP, a má oclusão foi determinada pelo DAI, a estética dentária autopercebida foi avaliada pelo OASIS e o IOTN-AC avaliou a autopercepção da necessidade de tratamento ortodôntico. A análise estatística envolveu métodos descritivos e inferenciais, como teste qui-quadrado de Pearson ou teste exato de Fisher e regressões logísticas múltiplas, com nível de significância de 5%. **Resultados:** A prevalência de impacto oral foi elevada (73,4%), 49,1% apresentavam má oclusão e 25,0% tinham necessidade de tratamento ortodôntico altamente desejável. Autopercepção negativa da estética dentária foi observada em 50,0% dos adolescentes e 13,1% consideraram necessitar de tratamento ortodôntico. O impacto na qualidade de vida foi associado ao gênero, autopercepção da estética dentária ($p < 0,001$), má oclusão + autopercepção da

estética dentária ($p < 0,001$) e autopercepção da necessidade de tratamento ortodôntico ($p = 0,045$). Os resultados da regressão logística indicaram que ser do sexo feminino e ter autopercepção negativa da estética dentária estão diretamente envolvidos na qualidade de vida dos adolescentes. Conclusão: Ser do sexo feminino e ter uma autopercepção negativa da própria estética dentária são fatores de risco para impactar negativamente na qualidade de vida relacionada à saúde bucal.

Palavras-chave: Autopercepção, estética dentária, adolescentes, ortodontia.

1 INTRODUCTION

Indication for orthodontic treatment has, traditionally, been based only on perceptions of professionals related to normative aspects of the diagnosis. These aspects take into account mainly the anteroposterior, vertical relationships and transverse disharmony.¹ However, the presence of malocclusions affects the lives of young people beyond the regulatory aspects and function. The aesthetic impairment caused by the malocclusion results from changes in the smile. In addition, it is worth mentioning that there are some types of malocclusions that have a greater influence on satisfaction with dental appearance.^{1,2} Studies have shown that malocclusions can have a negative impact on the quality of life^{3,4,5} and self-esteem⁶ of adolescents.

A systematic review⁷ provide evidence for a clear inverse association of malocclusion with oral health-related quality of life (OHRQOL) and verified that the impact on OHRQOL was 1.7 times higher in children with malocclusion than in children without malocclusions. Another systematic review⁸ found scientific evidence considered strong since four studies with high level of quality reported that malocclusions have negative effects on OHRQOL, predominantly in the dimensions of emotional and social wellbeing.

Other important factor that influences orthodontic treatment is self-perception of dental appearance.⁹ There are children complaining about minor aesthetic orthodontic problems, while others with severe malocclusions are not even aware of it.¹⁰ The negative self-perception of smile can be the result of feelings provoked by dissatisfaction associated with social, cultural, psychological and environmental factors.¹¹

Understanding the factors involved in the demand for orthodontic treatment in a given population allows for better planning of resources and a better assessment of needs and priorities of treatment.⁴ In this context, the assessment of quality of life has attracted the attention of health researchers, encouraging researches on the impact of oral health problems on people's wellbeing.^{1,3,4}

In order to assess the impact of oral health on quality of life in children and adolescents, some indices, generically called socio-dental indicators, have been developed¹² and they are considered as fundamental complements to clinical indicators.¹³

Therefore, this study aimed to evaluate the association between malocclusion, Oral Health-Related Quality of Life and self-perceived dental aesthetics in Brazilian adolescents.

2 METHODS

2.1 ETHICS APPROVAL AND CONSENT TO PARTICIPATE

A cross-sectional study was conducted with students between 12 and 15 years old of both sexes, enrolled in primary school of municipal chain schools of the city of Recife-PE. This study was approved by the Research Ethics Committee of the University of Pernambuco (protocol number 3.242.121). Informed consent was obtained for all adolescents and one of their parents.

2.2 SAMPLE SELECTION

Prevalence of malocclusion in the Northeast (41.5%) according to the latest national oral health survey¹⁴ was used for sampling calculation. It was based on a universe of 13,750 students, according to the list provided by the Municipal Department of Education, confidence interval of 95%, standard error of 5% and a design effect (DEFF) DE of 1.5. Thus, the required minimum sample size was 543 students. However, 20% of sampling was added to compensate possible losses during the survey, resulting in 625 adolescents. A two-stage sampling method allowed the representativeness of the sample. The first stage was the randomization of public schools in each administrative district. In the second stage of random selection, the subjects were chosen from the list of names from each school. Incomplete questionnaires were considered losses and represented 7.2% of the sample, resulting in a final sample of 580 students. Adolescents undergoing orthodontic treatment, or with mixed dentition and those with neuropsychomotor deficiencies (referenced by teachers), which could compromise the application of the instruments, were excluded.

2.3 DATA COLLECTION

Data collection was performed by questionnaires directed to adolescents and oral clinical examination. Socioeconomic Classification questionnaire, according to criteria of Brazilian Association of Companies and Research (ABEP) was applied. These criteria include a series of questions related to the possession of household items and categorize families by socioeconomic class. In this study the families were classified as being in a high (classes A or B), intermediate

(class C) or low socioeconomic class (classes D or E). Schooling of the household head was assessed by number of years of study and categorized as <8 or ≥ 8 years of study.

2.4 ORAL HEALTH-RELATED QUALITY OF LIFE (OHRQOL)

The OHRQoL was evaluated by the Child Oral Impacts on Daily Performances (Child-OIDP) index.^{15,16} The objective of this index is to measure the impacts of oral health problems on daily activities commonly performed by children. It comprises dimensions not tapped by clinical measures, such as functional, psychological and social limitations. The adolescents were asked to record all oral health related problems they have experienced in the past three months. In the event that a child reported an impact on their performance of these eight daily performances: eating, speaking, cleaning mouth, sleeping, emotional status, smiling, studying, and social contact, the child responded to questions about the severity and frequency of the specific impact. When no impact had been reported, the child received a score of zero (without impact) and when the impact reported was 1 or greater than 1, there was impact.

2.5 SELF-PERCEIVED DENTAL AESTHETICS

Evaluation of self-perception in relation to dental aesthetics was performed using the questionnaire "Oral Aesthetic Subjective Impact Scale" (OASIS).^{17,18} This instrument generates a score that can range from 5 to 35 and the higher the score, the worse the perception that the individual has of his/her smile. The median of the score of the total sample was set as the cut-off point in this study and adolescents scored above or equal to the median were considered to have a negative perception while adolescents scored below the median were considered to have a positive perception¹⁹.

2.6 SELF-PERCEIVED ORTHODONTIC TREATMENT NEED

The adolescents also assessed their own occlusion using the Aesthetic Component of the Index of Orthodontic Treatment Need (IOTN-AC).²⁰ This index takes into account the aesthetic perception that the patient has its own malocclusion. It is a scale used for the evaluation of dental aesthetics illustrated by 10 numbered color photographs. This scale has a continuous, decreasing degree of dental aesthetics (photo 1 show the most aesthetically pleasing tooth arrangement and photo 10 shows the least pleasing tooth arrangement). The participants were instructed to choose a photograph that best represented their own dentition. In the present study, the scale was divided into two categories: 1 (scores 1 to 4) the adolescent had a positive self-perception of occlusion and

perceived little or no orthodontic treatment need, and 2 (scores 5 to 10) the adolescent had a negative self-perception of occlusion and perceived need of orthodontic treatment (1= no orthodontic treatment need; 2= orthodontic treatment need).

2.7 CLINICAL MEASURES

Clinical examination was performed by a calibrated orthodontist ($k= 0.74$), aided by an annotator. Adolescents were examined at school seated under natural light in front of the examiner. Periodontal probes of type CPI (*Community Periodontal Index*) and tongue depressors, gloves, and masks were used in compliance with the precepts of infection control.

Data on malocclusion was collected through the Dental Aesthetic Index (DAI)²¹ according to World Health Organization (WHO) criteria²². DAI assessment includes ten parameters of dentofacial structure relating to tooth positioning and the relationship between maxillary and mandibular arches. Four grades of malocclusion are given, with priorities and orthodontic treatment recommendations assigned to each grade: grade 1 indicates normal or minor malocclusion/ no treatment need or slight need ($DAI \leq 25$); grade 2, definite malocclusion/treatment is elective ($26 \leq DAI \leq 30$); grade 3, severe malocclusion/treatment is highly desirable ($31 \leq DAI \leq 35$); and grade 4, very severe malocclusion/treatment is mandatory ($DAI \geq 36$). In this study, according to severity, the adolescents were classified as little or no orthodontic treatment need (score ≤ 25 points), elective orthodontic treatment need (score 26 to 30 points) and highly desirable or mandatory orthodontic treatment need (score ≥ 31).⁹ In addition, the scores were dichotomized into without malocclusion (score ≤ 25 points) and malocclusion (score > 25).⁴

2.8 STATISTICAL ANALYSIS

Independent variables assessed were self-perceived dental aesthetic (OASIS), self-perceived orthodontic treatment need (IOTN-AC), Dental aesthetic index (DAI) and sociodemographic characteristics. Dependent variable was Impact on Daily Performance (Child-OIDP). Descriptive statistics included computation of frequencies and absolute percentages for the categorical variables. Bivariate analysis involved Pearson's chi-square and Fisher exact tests to determine associations among the categorical variables.

A logistic regression model with the variables that showed a significant association up to 20% ($p < 0.20$) in the bivariate study was used to verify which variables influenced the presence of the impact on daily performance.

The logistic regression models were adjusted estimating the Odds Ratios (OR), their 95% confidence intervals (CI) and significance levels. All statistical analyses were conducted using SPSS version 23 (Statistical Package for Social Science), with 5% of margin of error.

3 RESULTS

It is important specify that, out of the initial number of the sample (625), 580 adolescents to complete the entire questionnaire, which accounts for a 92.8% response rate. Among these students, 63.1% were female, most were 12-13 years old (67.1%) and belonged to intermediate socioeconomic level (71.7%). A similar distribution was found in relation to the schooling of the head of the family (49.5% x 50.5%) and impact on quality of life was reported by 73.4% of the students. Statistical associations were found between gender and impact on quality of life ($p < 0.001$), with the girls presenting 2.54 more likely to have an impact than boys (TABLE 1).

Table 1. Impact on Daily Performance (n=580)

Variable	Number of children n (%)	Impact on Daily Performance ^a				P value	OR (IC à 95%)
		Yes		No			
		n	%	n	%		
Total group	580 (100,0)	426	73,4	154	26,6		
Age						$p^{(1)} = 0,253$	
12 a 13	389 (67,1)	280	72,0	109	28,0		1,00
14 a 15	191 (32,9)	146	76,4	45	23,6		1,26 (0,85 a 1,89)
Gender						$p^{(1)} < 0,001^*$	
Male	214 (36,9)	132	61,7	82	38,3		1,00
Female	366 (63,1)	294	80,3	72	19,7		2,54 (1,74 a 3,70)
Head of household's schooling						$p^{(1)} = 0,243$	
< 8 years	287 (49,5)	217	75,6	70	24,4		1,25 (0,86 a 1,80)
≥ years	293 (50,5)	209	71,3	84	28,7		1,00
Socioeconomic level						$p^{(1)} = 0,601$	
High	104 (17,9)	74	71,2	30	28,8		1,00
Intermediate	416 (71,7)	305	73,3	111	26,7		1,11 (0,69 a 1,79)
Low	60 (10,3)	47	78,3	13	21,7		1,47 (0,69 a 3,09)

(*) $P < .05$ considered statistically significant

(1) Pearson's chi-square test.

(a) yes ≥ 1 / no = 0

The prevalence of malocclusion among adolescents was 49.1% and 25.0% of these had a highly desirable need, however, no association was found between impact on daily performance and malocclusion, severity of malocclusion and types of malocclusion. Regarding self-perception of dental aesthetics, half (50.0%) of adolescents demonstrated a negative perception and 13.1% thought they needed orthodontic treatment (TABLE 2).

Table 2. Bivariate analysis of association between the Impact on Daily Performance with malocclusion (DAI), Self-perceived dental aesthetic (OASIS) and Self-perceived orthodontic treatment need (IOTN-AC) (n=580)

Variable	Amostra Total n (%)	Impact on Daily Performance				P value	OR (95% CI)
		Yes		No			
		n	%	n	%		
Total groupe	580 (100,0)	426	73,4	154	26,6		
Missing tooth						p ⁽¹⁾ = 0,474	
One or more	33 (5,7)	26	78,8	7	21,2		1,37 (0,58 a 3,21)
None	547 (94,3)	400	73,1	147	26,9		1,00
Incisal crowding						p ⁽¹⁾ = 0,636	
Present	352 (60,7)	261	74,1	91	25,9		1,10 (0,75 a 1,59)
Absent	228 (39,3)	165	72,4	63	27,6		1,00
Anterior segment spacing						p ⁽¹⁾ = 0,982	
One or two segments	218 (37,6)	160	73,4	58	26,6		1,00
None	362 (62,4)	266	73,5	96	26,5		1,00 (0,69 a 1,47)
Maxillary overjet						p ⁽¹⁾ = 0,376	
> 4 mm	76 (13,1)	59	77,6	17	22,4		1,30 (0,73 a 2,30)
≤ 4 mm	504 (86,9)	367	72,8	137	27,2		1,00
Maxillary misalignment						p ⁽¹⁾ = 0,881	
≥ 2 mm	176 (30,3)	130	73,9	46	26,1		1,03 (0,69 a 1,54)
< 2 mm	404 (69,7)	296	73,3	108	26,7		1,00
Mandibular overjet						p ⁽¹⁾ = 0,341	
Present	44 (7,6)	35	79,5	9	20,5		1,00
Absent	536 (92,4)	391	72,9	145	27,1		1,44 (0,68 a 3,07)
Mandibular misalignment						p ⁽¹⁾ = 0,283	
≥ 2 mm	95 (16,4)	74	77,9	21	22,1		1,33 (0,79 a 2,25)
< 2 mm	485 (83,6)	352	72,6	133	27,4		1,00
Anterior open bite						p ⁽¹⁾ = 0,661	
> 2 mm	30 (5,2)	21	70,0	9	30,0		1,00
≤ 2 mm	550 (94,8)	405	73,6	145	26,4		1,20 (0,54 a 2,67)
Molar relationship						p ⁽¹⁾ = 0,083	
Normal	259 (44,6)	180	69,5	79	30,5		1,00
Half cusp desviation	236 (40,7)	177	75,0	59	25,0		1,32 (0,89 a 1,96)
Full cusp desviation	85 (14,7)	69	81,2	16	18,8		1,89 (1,03 a 3,47)
Median diastema						p ⁽¹⁾ = 0,611	
≥ 2 mm	43 (7,4)	33	76,7	10	23,3		1,21 (0,58 a 2,52)
< 2 mm	537 (92,6)	393	73,2	144	26,8		1,00
Malocclusion (DAI)						p ⁽¹⁾ = 0,103	
Present	285 (49,1)	218	76,5	67	23,5		1,36 (0,94 a 1,97)
Absent	295 (50,9)	208	70,5	87	29,5		1,00
Severity os malocclusion						p ⁽¹⁾ = 0,253	
No need	295 (50,9)	208	70,5	87	29,5		1,00
Elective	140 (24,1)	106	75,7	34	24,3		1,30 (0,82 a 2,07)
Highly desirable	145 (25,0)	112	77,2	33	22,8		1,42 (0,89 a 2,25)
Self-perceived dental aesthetic (OASIS)						p ⁽¹⁾ < 0,001*	
Positive	290 (50,0)	185	63,8	105	36,2		1,00
Negative	290 (50,0)	241	83,1	49	16,9		2,79 (1,89 a 4,12)
Malocclusion / Self-perceived dental aesthetic						p ⁽¹⁾ < 0,001*	
Malocclusion / negative self-perception	165 (28,4)	136	82,4	29	17,6		3,05 (1,84 a 5,06)
Malocclusion / positive self-perception	120 (20,7)	82	68,3	38	31,7		1,40 (0,86 a 2,30)
Without malocclusion / negative self-perception	125 (21,6)	105	84,0	20	16,0		3,42 (1,93 a 6,03)
Without malocclusion / positive self-perception	170 (29,3)	103	60,6	67	39,4		1,00
Self-perceived orthodontic treatment need (OTN-AC)						p ⁽¹⁾ = 0,045*	
Need (Negative)	76 (13,1)	63	82,9	13	17,1		1,88 (1,00 a 3,53)
No need (Positive)	504 (86,9)	363	72,0	141	28,0		1,00

(*) P < .05 considered statistically significant

(1) Pearson's chi-square test

(2) Fisher exact test.

(a) yes≥1 / no=0

The findings indicate that the impact on quality of life was associated to self-perceived dental aesthetic ($p < 0.001$), malocclusion + self-perceived dental aesthetic ($p < 0.001$) and self-perceived orthodontic treatment need ($p = 0.045$). Adolescents with and without malocclusion, but with negative self-perception of dental aesthetics, presented 3.05 and 3.42, respectively, more likely to have impact on quality of life. When the occlusion was assessed through photos (IOTN-AC), the adolescents who believed they needed orthodontic treatment presented almost twice as likely to have impact (OR 1.88) (TABLE 2).

Table 3 presents the results of the logistic regression where the variables with $p < 0.20$, as gender, molar relationship, malocclusion, self-perceived dental aesthetic (OASIS) and self-perceived orthodontic treatment need (OTN-AC) were included in the analysis. The results indicated that being female and have a negative self-perception of dental aesthetic are risk factors for causing impact on quality of life of adolescents.

Table 3 Logistic regression analysis considering associations between Impact on Daily Performance and gender, molar relationship, malocclusion, OASIS and OTN-AC

Variável	Bivariate		Ajusted	
	OR e IC de 95.0%	P value	OR e IC de 95.0%	P value
Gender		< 0,001*		< 0,001*
Male	1,00		1,00	
Female	2,54 (1,74 a 3,70)		2,51 (1,70 a 3,71)	
Molar relationship		0,083		0,460
Normal	1,00		1,00	
Half cusp desviation	1,32 (0,89 a 1,96)		1,18 (0,75 a 1,84)	0,474
Full cusp desviation	1,89 (1,03 a 3,47)		1,55 (0,79 a 3,13)	0,221
Malocclusion (DAI)		0,103		0,915
Present	1,36 (0,94 a 1,97)		1,03 (0,65 a 1,61)	
Absent	1,00		1,00	
Self-perceived dental aesthetic (OASIS)		< 0,001*		< 0,001*
Positive	1,00		1,00	
Negative	2,79 (1,89 a 4,12)		2,58 (1,72 a 3,86)	
Self-perceived orthodontic treatment need (OTN-AC)		0,045*		0,188
Need	1,88 (1,00 a 3,53)		0,64 (0,33 a 1,24)	
No need	1,00		1,00	

(*): $P < .05$ considered statistically significant

4 DISCUSSION

Since oral health related problems can interfere with a person's daily activities, influencing their general quality of life,²³ and the malocclusions have a significant impact on the quality of life of children and adolescents,^{7,8} this research aimed to assess the quality of life related to oral health of adolescents and its association with self-perception of dental aesthetics, self-perceived orthodontic treatment need and malocclusion. For this purpose used the Child-Oidp index, which is a Socio-dental indicators, specific for children and adolescents, which was validated in Brazil by

Castro *et al.*¹⁵ and demonstrated to be a measure of oral health-related quality of life that can be applied to Brazilian children.

There was no association between socioeconomic variables and variables related to individual perception, which suggests that any individual, regardless of their social and economic position, can be equally affected by the need for self-perceived treatment and satisfaction with aesthetics. Other studies have also confirmed that the concern of an individual with good appearance is generalized in any society.^{24,25}

Consistent with previous studies,^{26,27} statistical associations were found between gender and impact on quality of life, with the girls presenting 2.54 times more chances of having an impact than boys. Girls, usually, are more sensitive to the perception of their own appearance than boys,^{26,28} present more attention, perception and appreciation of with own oral health.²⁶ However, it should be noted that in some researches this association was not found.^{4,29}

Disagreeing of previous surveys,^{3,5} in the present study found no association between impact on daily performance and malocclusion, severity of malocclusion, or types of malocclusion. These divergences can be justified due to different diagnostic criteria used to assess malocclusion and/or quality of life, age range, in addition to cultural differences between countries or regions that may influence the perception of aesthetics in each society.³⁰

Despite the high prevalence of malocclusion in this sample, the bivariate analysis showed that the determinant factor to have impact on quality of life was the self-perception of adolescent. Adolescents with and without malocclusion, but with negative self-perception of dental aesthetics, presented 3.05 and 3.42, respectively, more chances of having impact on quality of life. When the adolescents assessed their occlusion through photos, those who believed who need orthodontic treatment had almost twice as chances to have impact (OR 1.88). These results are in line with a previous study carried out in the Brazil,³ where the authors verified that adolescents with unfavorable self-perceived aesthetic were 11.7 times more likely to have oral health impacts than those with favorable perceived aesthetics.

After adjusting of the logistic regression of the variables that showed a association up to 20% ($p < 0.20$) in the bivariate study, the only ones that maintained the association were the gender and self-perception of dental aesthetics, indicating that they are risk factor for oral health related with quality of life. These findings indicate that a malocclusion can be perceived differently by the affected person, and a person's degree of awareness of their malocclusion might not be related to its severity.²⁴ Some people with a severe malocclusion are satisfied with or indifferent to their dental

aesthetics, because it does not cause negative impact on daily living, whereas others are concerned about minor occlusal alteration.^{3,10}

Some authors have demonstrated the importance of psychosocial factors as predictor for oral health related with quality of life. Baets *et al.*¹⁰ verified that higher the self-esteem, the better the OHRQoL. The Sense of Coherence has also been shown to be a predictor for establishing healthy behaviors and positive self-perceptions of oral health.

The data of this study demonstrate that clinical indicators for the assessment of oral health are important, but its limitation should be taking into account, and the multi-dimensional assessment of the oral health condition involving clinical and subjective indicators must be considered. One factor to be emphasized is that the sample of this study was composed of adolescents and this is a period of intense biological, physical, psychological and social changes and the understanding of the quality of life view of adolescents emphasizes the importance of focusing on their psychosocial health to promote and maintain their quality of life.³⁰

The results of the present study revealed that being female and having a negative self-perception of one's dental aesthetics are risk factors for impacting negatively on oral health related quality of life.

5 CONCLUSION

Being female and having a negative self-perception of one's dental aesthetics are risk factors for impacting negatively on oral health related quality of life.

STATEMENT CONTRIBUTION

ACC, FSR: design of the study, data collection and writing of the manuscript. MCAL, MACS, SSS: design of the study, training and supervision of fieldworkers and assisted in the writing of the manuscript. AR: design of study, analysis and interpretation of data and assisted in the writing of the manuscript. NPI and MVH: design of the study, analysis and interpretation of data, drafting the article and revising it critically. All the authors read and approved the final manuscript.

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