Correlation of dental anxiety with oral health status and treatment needs among 12-year old indian school going children

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Summary. *Background and aim:* Dental anxiety is primarily associated with learning negative behaviour which may be attributed to the aggressive condition process during childhood and adolescence and is considered to be the main reason for avoiding dental care. Hence the present study aimed to assess the correlation of Dental Anxiety with Oral Health Status and Treatment Needs. *Methods:* Cross sectional study was carried out among 12-year old school going children of Hyderabad City, India. Dental anxiety was assessed using the Modified Child Dental Anxiety Scale (MCDAS). Oral Health Status and Treatment Needs were assessed using Gingival Index and Dentition status and treatment needs based on Basic Oral Health Survey. Multigroup analysis was done using Analysis of Variance. p<0.05 was considered statistically significant. *Results:* In the present study, females had higher significant total mean MCDAS score as compared to males (22.8±5.4 vs.19.66±6.0) (p=0.00001*). Study participants with no history of previous dental visits (21.55±5.6) showed a statistically higher significant total MCDAS score compared to their counterpart (p=0.006*). On the other hand, Decayed component (r=0.1335*) and overall DMFT (r=0.1384*) had a significant positive correlation with MCDAS score. *Conclusion:* The study concluded that there is a correlation between dental anxiety and dentition status and treatment needs among 12 year old children. (www.actabiomedica.it)

Key words: dental anxiety, fear, dentition status; dental caries

Introduction

Fear and anxiety are two protective conditions induced by threats that serve to detect and avoid danger. In other words, fear is an emotional response to internal or an external realistic threat, whereas, anxiety is a response to a situation in which the source of the threat is not well defined, is ambiguous or not immediately present and is also known as "anticipatory anxiety" (1).

It has been proposed that people have innate tendencies to be fearful and anxious, where few have speculated that both fear and anxiety are byproducts of learning through one's interaction with the surrounding environment (2). The most appropriate reaction to nearby threat seems to be escaping, whereas if the threat is far away, avoidance can be a better option. Likewise, fear and anxiety also play a vital role in determining their compliance to dental care treatment.

The general term 'Dental Anxiety' might have diverse meanings in the dental literature, covering a rather wide range of emotions, from a relatively mild feeling of apprehension of extreme anxiety and dental phobia. Literature reviews have revealed no difference between dental fear, dental anxiety and thus have been used interchangeably. Dental anxiety has been defined "as a situation-specific trait anxiety and as disposition to experience anxiety in dental situations" (3). 2

The onset of dental anxiety is thought to originate in childhood, peak in early adulthood, and decline with age (4). Several factors, especially direct and indirectly conditioning experiences have been reported to contribute to dental fear and anxiety in children. The first community based survey of dental fear was conducted by Agras et al (5) who reported that fear of dentist ranked fourth among common fear and seventh among intense fear in the United States. Thomson et al (6) has argued that dental fear may be a component in a cycle of dental disadvantage, with dentally anxious individuals avoiding dental care and thereby worsening their problems and increasing the likelihood that subsequent dental visits will be for only emergency reasons.

A study among Finnish children reported that 15% of children don't seek care because of fear of dental treatment (7). Thus, children with dental anxiety may change their dental visit behavior and as reported by some parents their children's fear may act as a barrier to taking their children to visit a dentist. Further, Lahti et al (8) reported that children with active caries were more fearful than other children. Therefore, dental anxiety is considered to be the main reason for behavior management problems and avoiding dental care resulting in lack of regular dental care and delay in necessary treatments (9).

Despite the recent interest in the psychological impact of dental anxiety on daily living, there is limited information about its impact on oral health and a little is known about such a relationship among children. Since altering health behavior's after adolescence is difficult, the preventive measures are crucial during childhood. Recognizing this importance, the present study aims to correlate Dental Anxiety using Modified Child Dental Anxiety Scale with Oral Health Status and Treatment Needs among 12-year old school going children in Hyderabad city, India.

Materials and method

Ethical clearance was obtained from the Institutional Review Board. The study have compiled with the World Medical Association Declaration of Helsinki.

A pilot study was conducted to assess the feasibility, to estimate the sample size and to finalize the survey proforma among one of the schools among 12year old children. The minimum number of Sample required (n) was 663 Children. The list of 5 zones in Hyderabad city was obtained by Greater Hyderabad Municipal Corporation (GHMC) (10). However, a final sample of 1000 was considered. In order to get an equal number of samples in each zone, the final sample was divided by five zones. (1000/5=200); i.e approx 200 students. Assuming that a sample of 50 to 60 children could be obtained from each school, around four schools per zone was considered (200/50=4). Since, there are 5 zones; it implied that, on the whole 20 schools (4 schools X 5 zones) have to be included in the study.

Students of age 12- year present in the school on the day of survey and willing for the oral examination were included in the study. Children with systemic disorders (eg. Down's syndrome, Autism etc) or with any medical condition (eg. Children on antibiotic therapy etc) were excluded.

The survey tool included: Demographic detailsage, gender, previous dental visits and brushing frequency. A questionnaire measuring the Dental anxiety: Modified Child Dental Anxiety Scale. Wong et al (1998) (11). Gingival health status was assessed using Gingival Index by Loe and Silness (1963) (12). DMFT was derived from Dentition status and treatment needs according to the Basic Oral Health Survey method by World Health Organization 1997 (13).

The data was analyzed using Statistical Package for Social Sciences (SPSS) package version 20.0. Comparison of mean MCDAS score and Gingival Index score according to variables was done using Student t-test and Mann- Whitney U test. Decayed, Missing and Filled teeth (DMFT) and its individual components were compared with variables using Student t- test. Correlation of MCDAS scores with Gingival Index and DMFT score was done using Karl Pearson's and Spearman's correlation method respectively. Multiple linear regression was used to analyze regression equation for MCDAS with Gingival Index score, DMFT score and other variables. p< 0.05 was considered statistically significant.

Results

A sample of 1026 school children comprising of 525 (51.2%) males and 501 (48.8%) females participated in the study. Zone-wise distribution of study population showed 206 (20.1%) belonged to North zone, 205 (20.0%) to the East, 208 (20.2%) to the West and 203 (19.8%), 204 (19.9%) to the South and Central zones, respectively. The majority of the study population had no history of previous dental visits (682; 66.5%) and had the habit of brushing once daily (760; 74.1%).

Based on the responses to questions of Modified Child Dental Anxiety Scale (MCDAS), a significant difference based on gender was observed for all questions apart from Questions Q1 (p=0.17), Q2 (p=0.06) and Q7 (p=0.21). Most of the males felt relaxed/not worried for Modified Child Dental Anxiety Scale as compared to females. Based on previous dental visits, a statistical significant difference was observed for questions like Q4 ($p=0.004^*$), Q6 ($p=0.001^*$) and Q8 ($p=0.001^*$), wherein participants with past dental history were more worried compared to those with no history of dental visits. However, comparison based on brushing frequency showed significant difference merely for Q4 ($p=0.05^*$). Majority of participants with habit of brushing twice daily were more relaxed/not worried compared to participants with habit of brushing once daily (Table 1).

Based on gender, females (22.8±5.4) had higher significant total mean MCDAS score as compared to males (19.66±6.0) (p=0.00001*). Likewise, when question-wise mean MCDAS was taken into account, females showed higher significant mean scores for all the questions except for question like Q_2 (p=0.34) (Table 2).

| Table 1. (| Comparison | of responses t | o modified | child denta | l anxiety sca | ale based | on variables |
|------------|------------|----------------|------------|-------------|---------------|-----------|--------------|
| | | | | | | | |

| | | p-Value | | | | |
|----|--|---------|---------------------------|-----------------------|--|--|
| | Questions | Gender | Previous dental visits | Brushing frequency | | |
| Q1 | How do you feel about going to the dentist generally | 0.17 | 0.12 | 0.15 | | |
| Q2 | How do you feel about having your teeth looked at | 0.06 | 0.34 | 0.59 | | |
| Q3 | How do you feel about scraped and polished | 0.001* | 0.12 | 0.08 | | |
| Q4 | How do you feel about having an injection in the gum | 0.001* | 0.004* | 0.05* | | |
| Q5 | How do you feel about having a filling | 0.001* | 0.60 | 0.56 | | |
| Q6 | How do you feel about having a tooth taken out | 0.001* | 0.001* | 0.82 | | |
| Q7 | How do you feel about being put to sleep to have treatment | 0.21 | 0.72 | 0.07 | | |
| Q8 | How do you feel about having a mixture of "gas and air " which will help you feel comfortable for treatment but cannot put you to sleep | 0.001* | 0.001* | 0.09 | | |

*p≤0.05 statistically significant

| | Mean ±SD | | | | | | | | | |
|-------|----------|----------|----------|------------------------|-----------|----------|--------------------|-----------|---------|-----------|
| | Gender | | | Previous dental visits | | | Brushing frequency | | | |
| | Males | Females | p-Value | Yes | No | p-Value | Once | Twice | p-Value | Total |
| Q1 | 2.17±1.2 | 2.39±1.2 | 0.0007* | 2.29±1.3 | 2.27±1.2 | 0.49 | 2.30±1.2 | 2.21± 1.2 | 0.40 | 2.27±1.2 |
| Q2 | 1.83±1.2 | 1.93±1.2 | 0.34 | 1.80±1.2 | 1.92±1.2 | 0.09 | 1.88± 1.2 | 1.88± 1.2 | 0.65 | 1.88±1.2 |
| Q3 | 2.00±1.3 | 2.46±1.4 | 0.00001* | 2.33±1.4 | 2.17±1.3 | 0.15 | 2.27±1.4 | 2.14± 1.3 | 0.38 | 2.22±1.4 |
| Q4 | 3.48±1.5 | 4.04±1.2 | 0.00001* | 3.56±1.5 | 3.85±1.4 | 0.005* | 3.82±1.4 | 3.60± 1.4 | 0.01* | 3.76±1.4 |
| Q5 | 2.58±1.4 | 3.07±1.4 | 0.00001* | 2.85±1.5 | 2.80±1.4 | 0.74 | 2.87±1.4 | 2.83± 1.4 | 0.75 | 2.82±1.4 |
| Q6 | 3.31±1.5 | 3.96±1.3 | 0.00001* | 3.33±1.5 | 3.78±1.4 | 0.00001* | 3.66±1.4 | 3.67± 1.4 | 0.93 | 3.63±1.5 |
| Q7 | 1.96±1.3 | 2.16±1.3 | 0.02* | 2.08±1.2 | 2.04±1.3 | 0.17 | 2.13±1.4 | 2.00± 1.2 | 0.59 | 2.06±1.3 |
| Q8 | 2.43±1.4 | 2.89±1.5 | 0.00001* | 2.37±1.5 | 2.80±1.5 | 0.00001* | 2.73±1.5 | 2.59± 1.4 | 0.28 | 2.66±1.5 |
| Total | 19.66±6 | 22.8±5.4 | 0.0000 | 20.48±6.4 | 21.55±5.6 | 0.006* | 21.4±5.9 | 20.6±5.9 | 0.001* | 21.19±5.9 |

Table 2. Question wise mean score comparison of MCDAS score based on variables

*p≤0.05 statistically significant

Comparison based on previous dental visits revealed that, study participants with no history of previous dental visits (21.55 \pm 5.6) showed a statistically higher significant total MCDAS score (p=0.006*). Furthermore, study population with no past dental history were more worried about having their tooth looked at Q2 (p=0.09), having an injection in gums Q4 (p=0.005*), having tooth taken out Q6 (p=0.00001*) and having a relative analgesia (RA), Q8 (p=0.00001*) compared to participants with previous dental visits (Table 2).

Based on brushing frequency, participants with habit of brushing once daily (21.4 ± 5.9) had higher significant total mean MCDAS score as compared to participants with habit of brushing twice daily (20.6 ± 5.9) (p=0.001*). However, question wise comparison revealed, though participants who brush once daily were more anxious for most of the treatment options, it was statistically significant only for question Q4 (p=0.01*) (Table 2).

Out of 1026 study population, 717(72.7%) had no gingivitis, very few presented with mild form of gingivitis 269 (27.3%) and none of them had moderate or severe forms of gingivitis. In addition, a higher percentage of males (50.5%), participants who never visited a dentist (66.3)% and with habit of brushing once daily (71.4%) had no gingivitis However, this difference didn't show statistical significance based on gender, previous dental visit and brushing frequency.

The majority of the study population was caries free 542 (52.8%). In addition, the prevalence of dental caries (Decayed Component) for males was 50.5% which was comparable to that of females (49.5%) (p=0.67). Likewise, although study participants with no past dental visit 352(65%) had higher prevalence of dental caries, it was not statistical significant (p=0.27)). On the contrary, participants with brushing frequency of once daily 404(74.5%) showed a significantly higher prevalence of dental caries as compared to their respective counterparts (p=0.05).

The overall mean gingival index score for the study population was 0.04 ± 0.09 which revealed mild gingivitis (0.1-1.0). Mean gingival index scores based on gender, previous dental visits (p=0.97) and brushing frequency (p=0.42) were comparable with no statistical significance (Table 3).

The total mean DMFT recorded for the study population was 1.08 ± 1.3 . When total mean DMFT scores was compared based on variables, a comparable mean score was observed for gender (p=0.82) and previous dental visits (p=0.08). Whereas, study subjects with habit of brushing once daily (1.12±1.3) had higher significant mean DMFT score compared to those brushing twice daily (0.93± 1.2) (p= 0.04*). When individual components of DMFT were considered, the mean scores for males (DT-1.04±1.3; MT- 0.01±0.13 and FT- 0.03±0.2) were comparable to females (DT-1.04±1.2; MT- 0.01±0.1 and FT- 0.02±0.1) (Table 3).

Comparison of individual component of DMFT mean scores based on previous dental visits, study population with past dental history had a comparable mean scores for individual component of DMFT except for missing component score, wherein higher mean score was recorded among participants who had visited the dental office (0.03 ± 0.2) as compared to participants who had never visited a dentist (0.01 ± 0.1) (p= 0.007*). The mean score of individual component of DMFT were comparable based on brushing frequency except for decayed teeth component wherein a higher significance was noted among participants with habit of brushing once daily (1.09 ± 1.3) compared to

When MCDAS score was correlated to gingival index score based on gender, only females showed a significant positive correlation (r=0.1015). On the other hand, MCDAS score had significant positively correlated with D component of DMFT based on all variables. Nevertheless, overall DMFT revealed a significant positive correlation with MCDAS score for all the variables apart from for those brushing twice daily (Table 4).

The results of multiple regression showed that MCDAS score was significantly associated with higher scores of gingival index (p=0.00001), overall DMFT (p=0.01), gender (p=0.00001), previous dental visits (p=0.03), whereas brushing frequency (p=0.19) was not significantly associated with MCDAS (Table 5).

| Variables | | Mean±SD | | | | | | | |
|---------------------------|---------|-------------------------|---------------|---------------|--------------|---------------|--|--|--|
| | | | | | | | | | |
| | | Gingival Index Score | Decayed Teeth | Missing Teeth | Filled Teeth | Total DMFT | | | |
| | Males | 0.05±0.1 | 1.04±1.3 | 0.01±0.13 | 0.03±0.2 | 1.08±1.3 | | | |
| Gender | Females | 0.04±0.1 | 1.04±1.2 | 0.01±0.1 | 0.02±0.1 | 1.07±1.2 | | | |
| | p-Value | 0.55 | 0.94 | 0.93 | 0.24 | 0.82 | | | |
| | Yes | 0.04±0.1 | 1.11±1.3 | 0.03±0.2 | 0.03±0.2 | 1.2±1.3 | | | |
| Previous dental visits | No | 0.04±0.1 | 1.0±1.2 | 0.01±0.1 | 0.02±0.1 | 1.03±1.3 | | | |
| | p-Value | 0.97 | 0.22 | 0.007* | 0.10 | 0.08 | | | |
| | Once | 0.07±0.4 | 1.09±1.3 | 0.01±0.1 | 0.01±0.1 | 1.12±1.3 | | | |
| Brushing frequency | Twice | 0.05± 0.1 | 0.89± 1.2 | 0.01± 0.1 | 0.02± 0.1 | 0.93± 1.2 | | | |
| | p-Value | 0.42 | 0.03* | 0.94 | 0.29 | 0.04* | | | |
| Total | | 0.04±0.09 | 1.04±1.3 | 0.01±0.1 | 0.02±0.2 | 1.08±1.3 | | | |

Table 3. Comparison of total mean of Gingival Index score and individual components of DMFT scores based on variables

*p≤0.05 statistically significant

| | MCDAS | | | | | | | | |
|-------------------------|---------|---------|---------|------------------------|---------|--------------------|---------|--|--|
| Variables | | Gender | | Previous Dental Visits | | Brushing frequency | | | |
| | Total | Males | Females | Yes | No | Once | Twice | | |
| Gingival Index Score | 0.0357 | -0.0071 | 0.1015* | 0.0601 | 0.0177 | 0.0384 | 0.0344 | | |
| Decayed Teeth | 0.1335* | 0.1467* | 0.1299* | 0.2260* | 0.0834* | 0.1670* | 0.0286 | | |
| Missing Teeth | 0.0280 | 0.0278 | 0.0291 | 0.0365 | 0.0406 | 0.0392 | -0.0310 | | |
| Filled Teeth | 0.0226 | 0.0784 | -0.0515 | 0.0802 | -0.0229 | 0.0409 | 0.0022 | | |
| DMFT | 0.1384* | 0.1598* | 0.1279* | 0.2428* | 0.0830* | 0.1751* | 0.0248 | | |

Table 4. Correlation of MCDAS with overall Gingival Index and DMFT score based on variables

*p≤0.05 statistically significant

Table 5. Multiple linear regression analysis of Modified Child Dental Anxiety Scale (MCDAS) by variables

| Independent variables | Regression coefficient | SE of Regression coefficient | t-value | p-value | | | |
|--|------------------------|---------------------------------|---------|----------|--|--|--|
| Intercept | 14.6222 | 0.9555 | 15.3034 | 0.00001* | | | |
| Gingival Index | 4.9035 | 1.9414 | 2.5257 | 0.01* | | | |
| DMFT | 0.6821 | 0.1368 | 4.9854 | 0.00001* | | | |
| Gender | 3.1550 | 0.3533 | 8.9290 | 0.00001* | | | |
| Previous dental visit | 0.8292 | 0.3821 | 2.1703 | 0.03* | | | |
| Brush frequency | -0.4126 | 0.3212 | -1.2844 | 0.19 | | | |
| R=0.3202, R ² =0.1025, F(5,1020)=23.305 p<0.01, Std.Error of estimate: 5.6111 | | | | | | | |

*p≤0.05 statistically significant

Discussion

According to Hmud and Walsh (14), several factors have been related to dental anxiety including fear of pain, personal traits, traumatic dental experience during childhood and having family members or friends who are dentally anxious. Other studies (15,16) have reported that dental anxiety is primarily associated with learning negative behavior which may be attributed to the aggressive condition process during childhood and adolescence. Hence, identifying this impact of dental anxiety on compliance to dental care, an attempt was made in the present study to correlate Dental Anxiety using Modified Child Dental Anxiety

Scale (MCDAS) with Oral Health Status and Treatment Needs among 12-year old school going children In Hyderabad City, India.

Modified child dental anxiety scale (MCDAS) by Wong et al (1998) was used in the present study as it has high internal reliability (17) and this measure can discriminate between children with and without dental anxiety. In addition, anxiety-provoking dental situations like dental injections, general anaesthesia, extraction and sedation were included. In this study, oral health status was quantified using the Gingival Index (GI) by Loe and Silness (1963) (12) and DMFT derived from Dentition status and treatment needs (13). These indices reflect reversible oral condition like gingival inflammation (gingivitis) and irreversible conditions like filling, extraction, can be measured with Dentition status and treatment need based on Basic Oral Health Survey (1997). The World Health Organization has regarded 12 years as the global monitoring age for caries for international comparisons and monitoring of disease trends. Hence, 12-year old school children were included in the current study (13).

In the present study, out of 1026 school children, 525 (51.2%) were males and females constituted in 501 (48.8%), this was in accordance with the 2011 census where the gender ratio for 5-14 years old in Hyderabad, was 51.8% for males and 48.2% for females (18). In this study, 66.5% of the study participants had never visited the dentist which was in contrary to the findings of the study by Amin et al (19) on African school children where 52% of them had never been to the dentist. When brushing frequency was considered most of them brushed once daily 74.1% which was higher than that reported among Chennai school children by Ahad and Gheena (20) (46%) and Priya et al (21) (36.1%).

In this study, more than 60% of study population were "very worried" for treatment options like having an injection in the gums Q4 (65.1%) and tooth being taken out Q6 (60.5%). Similar findings were reported by Wong et al (11) among children aged 8-15 years old at Liverpool, United Kingdom. The authors reported majority were "very worried" about Injection (34.6%) and tooth taken out (19.0%).

When overall mean and question-wise MCDAS scores were considered, females (22.8 ± 5.4) had higher significant total mean MCDAS score for most of the questions (p=0.00001*). This was in agreement with the study done by Rantavuori et al (22), that 12 year old Finish girls (34%) were more likely to be afraid of drilling than boys (23%) (p=0.039).

In this study, participants with no history of previous dental visits (21.55 \pm 5.6) showed a significant higher total MCDAS score (p=0.006*) and for Q2 (p=0.09), Q4 (p=0.005*), Q6 (p=0.00001*) and Q8 (p=0.00001*) compared to participants with history of previous dental visits. This was in contrast with the findings of the study by AlSarheeda (23) among children of Riyadh aged 9-12 years old. They established that children with a past dental history were more anxious to injection (74%), tooth extraction (31%), teeth drilled (27%), restorations (14%), and set of dental instruments (12%).

In the present study, 72.7% of study participants had healthy gums. However, Sharva et al (24) reported slightly higher values of gingival inflammation among 12 and 15 years old school going children in Bhopal district (53.09%-mild gingivitis, 5.5%- moderate to severe gingivitis). In addition, a greater number of males had absence of gingival inflammation (50.5%) and mild inflammation (52.1%) than females ((absence of inflammation; 49.5%) and (mild gingivitis; 47.9%)) no statistical significance (p=0.66). This could be attributed to improper oral hygiene practices among boys. Similar findings were reported in a study conducted by Das et al (25) among 6 and 12 years old children in Bangalore.

In this study, though higher number of study participants with a habit of brushing once daily had no gingivitis (536; 74.7%) compared to the participants with a habit of brushing twice daily (181; 25.3%); no statistical significant difference (p=0. 29) was observed. This could be because as the frequency of brushing increased, prevalence of gingivitis decreased; significant correlation between plaque retention and gingival inflammation as reported by Kurt et al (26).

In the present study, most of the study populations were caries free (52.8%). This findings were comparably lower on comparison to the study by Sukhabogi et al (27) where around 70% of Hyderabad private school children were caries free (p<0.01).When total mean DMFT score was compared based on variables, a comparable mean score was observed for gender (p=0.82). This was in accordance, with the results of a study by Sukhabogi et al (27) where mean scores were comparable among males (0.3±0.7) and females (0.3±0.5) (p<0.01).

In the current study, participants with a brushing frequency of once daily 74.5% showed a higher significant prevalence of dental caries as compared to those brushing twice 25.5% (p=0.05). This supports the fact that the prevalence of dental caries is depended on the oral hygiene status of an individual.

Even though in females, teeth erupt earlier and are exposed for longer time to the oral environment in the present study no significant difference was seen in the decayed and missing teeth among males and females (28). On the other hand, greater number of males 52 (64.1%) were having trauma or fractured teeth compared to females 29 (35.9%) (p=0.01). Similar finding was noted among Brazilian school children where males had more tooth fractures than females; which could be attributed to their aggressive and energetic nature (29).

In the current study, participants who never visited a dentist showed a greater prevalence for decayed teeth (65.6%), Missing as a result of caries (66.6%) and trauma (fracture) (70.4%). Also, positive correlation was observed between MCDAS score and overall DMFT based on previous dental visit. This might be the impact of dental anxiety leading to avoidance of dental visits contributing to poor oral and dental health status.

In the present study subjects, participants who brushed once daily had poorer oral health with higher values of all variables of dentition status. This result corresponded with the findings of Taani et al (30) among Jordanian school children, where they concluded that those who didn't brush regularly or brushed on irregular basis had poor and slightly varied oral health status. In the present study population, MCDAS score was significantly and positively associated with D component and Overall DMFT scores based on the study variables.

However, this study acknowledges certain limitations such as cross-sectional study design and the self-reporting nature of the questionnaire. Using a validated questionnaire and representative sample may diminish the outcomes of these limitations. Also, a sample larger than the estimated sample size, can also add to the merit of the study.

Conclusion

In this study, females were more dentally anxious compared to males. Likewise, participants with no history of previous dental visits were more anxious than their respective counterparts and there was a correlation between dental anxiety and dentition status and treatment needs among 12 year old school children. **Conflict of interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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