

The Ratio of the Second Finger to the Fourth Finger (2D:4D); Can it be a Marker for Dental Anxiety?

İkinci Parmağın Dördüncü Parmağa Oranı (2D:4D); Dental Anksiyete için Bir Belirteç Olabilir mi?

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ABSTRACT Objective: 2D:4D (the ratio of the second finger to the fourth finger) ratio has been used as a morphological marker in evaluating the relationship between androgen exposure in the prenatal period and developmental/neuropsychiatric disorders. **Material and Methods:** Ninety-one children between the ages of 5 and 10 years from whom teeth were to be extracted under local anesthesia were included in the study. Measurements were made of the second and fourth fingers of the children's right and left hands. At the end of the procedure, the physician was asked to evaluate the patient's dental anxiety levels using the Frankl Behavior Scale (FBS). **Results:** Based on the FBS, the right-hand 2D:4D ratio was 0.979 ± 0.074 in patients who refused treatment, 1.000 ± 0.044 in unwilling patients who could not cooperate, 1.017 ± 0.043 in cooperative patients, and 0.980 ± 0.020 in patients with interest ($p=0.092$). The left-hand 2D:4D ratio was 1.024 ± 0.045 in patients refusing treatment, 1.006 ± 0.046 in unwilling patients who could not cooperate, 1.018 ± 0.054 in cooperative patients, and 0.983 ± 0.025 in patients with interest ($p=0.526$). No relationship was found between successful extractions and 2D:4D ratios in children. **Conclusion:** As a result, no significant correlation was found between dental anxiety and 2D:4D of pediatric patients who are planned tooth extraction. It was determined that 2D:4D is not a morphological marker that we can use to predict dental anxiety in the preoperative period.

Keywords: Dental anxiety; 2D:4D; pediatric

ÖZET Amaç: Prenatal dönemde meydana gelen androjen maruziyeti ile gelişimsel/nöropsikiyatrik bozukluklar arasındaki ilişkinin değerlendirilmesinde, morfolojik bir belirteç olarak 2D:4D (2'nci parmağın 4'üncü parmağa oranı) oranı kullanılmıştır. **Gereç ve Yöntemler:** Çalışmaya, lokal anestezi altında diş çekimi planlanan 5-10 yaş arası 91 çocuk dâhil edildi. Ölçümler, çocukların sağ ve sol ellerinin 2'nci ve 4'üncü parmaklarından yapıldı. İşlem sonunda sorumlu doktordan, Frankl Davranış Ölçeği'ni [Frankl Behavior Scale (FBS)] kullanarak, hastaların dental anksiyete düzeylerini değerlendirmesi istendi. **Bulgular:** FBS'ye göre sağ el 2D:4D oranı, tedaviyi reddeden hastalarda $0,979 \pm 0,074$, iş birliği yapamayan isteksiz hastalarda $1,000 \pm 0,044$, koopere olan hastalarda $1,017 \pm 0,043$ ve ilgili olan hastalarda $0,980 \pm 0,020$ idi ($p=0,092$). Sol el 2D:4D oranı, tedaviyi reddeden hastalarda $1,024 \pm 0,045$, iş birliği yapamayan isteksiz hastalarda $1,006 \pm 0,046$, kooperatif hastalarda $1,018 \pm 0,054$ ve ilgili olan hastalarda $0,983 \pm 0,025$ idi ($p=0,526$). Başarılı diş çekimi uygulaması ile sağ ve sol el 2D:4D oranları arasında anlamlı ilişki bulunmamıştır ($p=0,691$, $p=0,086$, sırasıyla). **Sonuç:** Sonuç olarak, diş çekimi planlanan pediatrik hastalarda dental anksiyete ile 2D:4D arasında anlamlı bir ilişki bulunmamıştır. 2D:4D'nin preoperatif dönemde dental anksiyeteyi öngörmek için kullanabileceğimiz morfolojik bir belirteç olmadığı belirlenmiştir.

Anahtar Kelimeler: Dental anksiyete; 2D:4D; pediatrik

Rising androgens in the prenatal period are critical in fetal sexual dimorphism, and prenatal androgen activity affects and regulates neuropeptides, thus affecting structural and functional changes in the developing brain.^{1,2} Exposure of a fetus to high levels of androgens in the early intrauterine period may cause physical and mental adaptations that have lifelong ef-

fects. It is therefore thought that there may be a relationship between some neuropsychiatric conditions and a high androgen load.^{3,4} Measuring possible androgen exposure directly in the prenatal period may adversely affect the health of the fetus, so indirect methods and markers that do not affect the health of the fetus or the mother are needed to identify diseases

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that may be part of the etiology of intrauterine hyperandrogenism. In a review, Richards examined six studies and showed that there is a relationship between prenatal sex hormones and 2D:4D (the ratio of the second finger to the fourth finger) ratio in samples obtained from amniocentesis and cord blood, stating that a low 2D:4D ratio indicates a high intrauterine androgen level and vice versa.⁵

Many diseases and conditions are thought to be related to intrauterine androgen exposure and 2D:4D ratio have previously been investigated in some behavioral and psychiatric disorders, aggression, suicidal tendencies, sports success, and cerebrovascular diseases.⁶⁻⁹ Ribeiro et al. reported a negative correlation between 2D:4D ratio and physical aggression and, in another study conducted in men, stated that there is a significant relationship between suicidal tendencies and 2D:4D ratio and that the ratio may therefore be a sign that can be used to predict suicidality and to prevent suicide.^{7,8} Based on these studies, it was hypothesized that the 2D:4D ratio might be low in patients with high anxiety, which would mean that it could be used as a morphological marker for anxiety. In such patients, behavioral management techniques and evaluation for premedication and/or sedation could be recommended to avoid work and time loss.

In this study, the relationship between the hemodynamic parameters of patients and the 2D:4D ratio was also examined. Zhang et al. investigated whether there is a significant relationship between finger ratios and blood pressure in children and adolescents aged 8-15 years and reported a direct/indirect relationship.¹⁰ If the 2D:4D ratio is a hemodynamic morphological marker, physicians can take necessary precautions to keep hemodynamic parameters, such as blood pressure and pulse, under control.

This study investigated whether there is a significant relationship between the 2D:4D ratio and dental anxiety and hemodynamic parameters in pediatric patients from whom teeth were to be extracted under local anesthesia.

MATERIAL AND METHODS

This was a double-blind, prospective, randomized clinical study approved by the Ondokuz Mayıs University

Ethics Committee (date: 01.08.2019 / number: B.30.2.ODM.0.20.08/537). This study was carried out in accordance with the Helsinki Declaration Principles. Ninety-one children between the ages of 5 and 10 years from whom teeth were to be extracted under local anesthesia were included in the study. First, the study was explained to relatives and patients in the waiting room, and written informed consent was obtained. Measurements of the children's fingers were then made. Patients who did not allow measurement and those with musculoskeletal disease were excluded from the study.

Measurements were made of the second and fourth fingers of the children's right and left hands. The distance between the basal crease and the fingertip was measured with the help of a ruler (vernier caliper) and all measurements were recorded. The children taken into the treatment unit were monitored for blood pressure and pulse. Articain (40 mg/mL) was used as a local anesthetic in all patients; at the end of the procedure, the physician was asked to evaluate the patient's dental anxiety levels using the Frankl Behavior Scale. All tooth extractions were performed by the same dentist. Tooth extraction under sedation was planned for patients whose teeth could not be extracted under local anesthetic. And these patients were excluded from the study.

Perioperative heart rate (HR) and mean arterial pressure (MAP) were measured in the preoperative period, immediately after local anesthesia, and at 5-minute intervals during the procedure. Operation time, the number of teeth extracted, and any complications were recorded.

STATISTICAL METHOD

The data were analyzed using IBM SPSS v23. Comparisons between groups were conducted with independent samples t-tests and ANOVA. Categorical data were analyzed using chi-squared tests. The significance level was $p < 0.05$.

RESULTS

The right and left finger ratios of the patients were grouped as $2D:4D < 1$ and $2D:4D \geq 1$. Preoperative HR evaluated in the right and left hands was 97.4 ± 22 and

96.3±24.2 (p=0.126), respectively, in the 2D:4D<1 group and 103±14.8 and 103.6±13.9 (p=0.075) in the 2D:4D≥1 group. HR measured in the right and left hands after local anesthesia was 106.3±18.4 and 98.8±17 (p=0.483), respectively, in the 2D:4D <1 group and 109.5±18.2 and 112.4±17.3 (p=0.002) in the 2D:4D≥1 group. Fifth minute HR in the right and left hands was 104.1±17.1 and 98.6±15 (p=0.222), respectively, in the 2D:4D<1 group and 109.5±17.4 and 111.9±16.9 (p=0.002) in the 2D:4D≥1 group. Tenth minute HR in the right and left hands was 104.6±13.5 and 97.6±12.3 (p=0.283), respectively, in the 2D:4D<1 group and 110.8±17.4 and 114.5±13.4 (p=0.002) in the 2D:4D≥1 group.

Preoperative MAP measured in the right and left hands was 82.6±11.9 and 85.3±12 (p=0.255), respectively, in the 2D:4D<1 group and 85.8±11.9 and 84.6±11.9 (p=0.808) in the 2D:4D≥1 group. After local anesthesia, MAP in the right and left hands was 86.2±8.3 and 87.5±11.6 (p=0.440), respectively, in the 2D:4D<1 group and 88.4±16.5 and 87.8.4±15.7 (p=0.934) in the 2D:4D≥1 group. Fifth minute MAP in the right and left hands was 86.8±9.4 and 89.3±14.9 (p=0.564), respectively, in the 2D:4D<1 group and 88.9±13.8 and 88±12.1 (p=0.715) in the 2D:4D≥1 group. Tenth minute MAP in the right and left hands was 92±13.1 and 86.4±17.5 (p=0.706), respectively, in the 2D:4D<1 group and 88.7±17.4 and 90.7±16.1 (p=0.620) in the 2D:4D≥1 group.

Local anesthesia was successfully used in 23 of 27 patients with right-hand 2D:4D<1 and in 56 of 64 patients with right-hand 2D:4D≥1 (p=0.745). Local anesthesia was successfully used in 22 of 24 patients with left-hand 2D:4D <1 and in 57 of 67 patients with left-hand 2D:4D≥1 (p=0.506). The procedure was successfully completed in 22 of 27 patients with right-hand 2D:4D<1 and in 48 of 64 patients with right-hand 2D:4D≥1 (p=0.691). The procedure was successfully completed in 22 of 24 patients with left-hand 2D:4D<1 and in 48 of 67 patients with left-hand 2D:4D≥1 (p=0.086). The female to male ratio for the right hand measurements was 11:16 for 2D:4D<1 and 35:29 for 2D:4D≥1 (p=0.324). The female to male ratio for the left hand was 10:14 in 2D:4D<1 and 36:21 for 2D:4D≥1 (p=0.437) (Tables 1, 2).

The right-hand 2D:4D ratio was 1.002±0.047 in men and 1.015±0.047 in women (p=0.203). The left-hand 2D:4D ratio was found to be 1.008±0.049 in men and 1.021±0.052 in women (p=0.253) (Table 3).

Based on the Frankl Behavior Scale, the right-hand 2D:4D ratio was 0.979±0.074 in patients who refused treatment, 1.000±0.044 in unwilling patients who could not cooperate, 1.017±0.043 in cooperative patients, and 0.980±0.020 in patients with interest (p=0.092). The left-hand 2D:4D ratio was 1.024±0.045 in patients refusing treatment, 1.006±0.046 in unwilling patients who could not cooperate, 1.018±0.054 in cooperative patients, and 0.983±0.025 in patients with interest (p=0.526) (Table 4).

TABLE 1: Comparisons by right 2D:4D ratio.

	2D:4D<1	2D:4D≥1	p value
Preoperative HR	97.4±22	103.5±14.8	0.126
HR after local anesthesia	106.3±18.4	109.5±18.2	0.483
Minute 5 HR	104.1±17.1	109.5±17.4	0.222
Minute 10 HR	104.6±13.5	110.8±16.1	0.283
Preoperative MAP	82.6±11.9	85.8±11.9	0.255
MAP after local anesthesia	86.2±8.3	88.4±16.5	0.440
Minute 5 MAP	86.8±9.4	88.9±13.8	0.564
Minute 10 MAP	92±13.1	88.7±17.4	0.706
Number of patients allowing local anesthesia	23/27	56/64	0.745
Number of patients successfully completed	22/27	48/64	0.691
Gender (female/male)	11/16	35/29	0.324

Data presented as mean±standard deviation.

2D: 4D: Ratio of second finger to fourth finger; HR: Heart rate; MAP: Mean arterial pressure.

TABLE 2: Comparisons by left 2D:4D ratio.

	2D:4D<1	2D:4D≥1	p value
Preoperative HR	96.3±24.2	103.6±13.9	0.075
HR after local anesthesia	98.8±17	112.4±17.3	0.002
Minute 5 HR	98.6±15	111.9±16.9	0.002
Minute 10 HR	97.6±12.3	114.5±13.4	0.002
Preoperative MAP	85.3±12	84.6±11.9	0.808
MAP after local anesthesia	87.5±11.6	87.8±15.7	0.934
Minute 5 MAP	89.3±14.9	88±12.1	0.715
Minute 10 MAP	86.4±17.5	90.7±16.1	0.620
Number of patients allowing local anesthesia	22/24	57/67	0.506
Number of patients successfully completed	22/24	48/67	0.086
Gender (female/male)	10/14	36/31	0.437

Data presented as mean±standard deviation.

2D: 4D: Ratio of second finger to fourth finger; HR: Heart rate; MAP: Mean arterial pressure.

TABLE 3: Comparisons by gender.

	Female	Male	p value
Right 2D:4D	1.015±0.047	1.002±0.047	0.203
Left 2D:4D	1.021±0.052	1.008±0.049	0.253

Data presented as mean±standard deviation. 2D: 4D: Ratio of second finger to fourth finger.

TABLE 4: Comparisons according to Frankl Behavior Scale.

	Right 2D:4D	Left 2D:4D
Refusal/distress	0.979±0.074	1.024±0.045
Uncooperative/reluctant	1.000±0.044	1.006±0.046
Co-operative/reserved	1.017±0.043	1.018±0.054
Interested/enjoyed	0.980±0.020	0.983±0.025
p value	0.092	0.526

Data presented as mean±standard deviation. 2D: 4D: Ratio of second finger to fourth finger.

There was no significant difference in terms of operative time, number of extracted teeth and complications.

DISCUSSION

In this study, no relationship was found between either successful extractions or Frankl anxiety scores and 2D:4D ratios in children. However, the HRs immediately, 5 minutes, and 10 minutes after local anesthesia were higher in those with $2D:4D \geq 1$. No significant difference was found in terms of other hemodynamic parameters.

The effectiveness of 2D:4D ratio as a morphological marker has been tested in many different diseases.⁶⁻⁹ It has been reported that circulating androgens can cause hypertension in children and adolescents, which has been confirmed by animal experiments.^{10,11} It has also been reported that blood pressure may increase with increased androgen activity, especially during adolescence. Zhang et al. evaluated 2D:4D, blood pressure, and testosterone levels in children aged 8-15 years and reported that, although there was a positive correlation between circulating testosterone levels and systolic blood pressure, there was no significant relationship between the 2D:4D ratio and blood pressure. They suggested that this might be related to differences in ethnic ori-

gin.¹⁰ In the current study, no significant relationship was found between those with a 2D:4D ratio less than one and MAP, which may be related to the age range of the participants (prepubescent) and evaluation being limited to only mean arterial pressure.

2D:4D ratio has been used as a morphological marker in evaluating the relationship between androgen exposure in the prenatal period and developmental/neuropsychiatric disorders in children, adolescents, and adults.¹¹⁻¹⁴ Eichler et al. stated that 2D:4D ratio may be an early indicator of behavioral disorders based on their study in primary school boys.¹ Butovskaya et al. studied 1,296 children and adolescents using the aggression questionnaire by Buss and Perry and reported a negative relationship between right 2D:4D ratio and physical aggression in men.¹³ In a more recent study, they stated that 2D:4D ratio is an indicator of adult lung function, with low 2D:4D indicating low lung function.¹⁴

However, there are conflicting results; in a recent study, O'Brian et al. examined the relationship between 2D:4D ratio and aggression-related injuries in patients who attended a pediatric emergency department and stated that there was a significant relationship only in girls and that this rate was lower.¹⁵ In another study, no relationship was found between their aggression model and 2D:4D ratio in 275 undergraduate students.¹⁶

In the current study, no significant relationship was found between patients who either could not complete the procedure or had high dental anxiety scores and 2D:4D ratio. Although many researchers hypothesize that there is a negative relationship between 2D:4D ratio and many diseases and behavioral and psychiatric disorders, there are inconsistent results; significant differences in the conditions and diseases evaluated in the patient groups used in the various studies, whether those conditions are acute or chronic, and the sources of the diseases may all have affected the results.

The presence of a Y chromosome in the prenatal period and an increase in sex hormones prompt the development of male and female sexual characteristics. However, it has been reported that androgens increasing more than expected in the intrauterine period

may lead to male-type behaviors, such as physical strength, courage, independence, leadership, and assertiveness, when older.^{1,17} Studies have therefore focused on aggression and behavioral disorders.

In the literature review, studies on the effects of prenatal androgen on dental development and dimensions were found.^{18,19} Lakshmi et al. reported a positive relationship between caries risk and low 2D:4D ratio.²⁰ In the current study, dental anxiety levels and patient compliance were examined, but no significant relationship was found. Furthermore, no significant correlation was found between anxiety scores and 2D:4D ratios of pediatric patients whose teeth were planned to be extracted. It was therefore determined that 2D:4D ratio is not a morphological marker that can be used to predict dental anxiety in the preoperative period.

Prenatal androgens affect many organs and systems of the fetus with consequences that may only develop many years later. It has been reported that the second finger shows the effects of estrogen and the fourth finger shows the effects of testosterone. With the increase in testosterone, the length of the fourth finger increases and the 2D: 4D ratio decreases.^{21,22} Although there are many studies showing that low 2D:4D ratio can be a marker for aggression and behavioral disorders, there are many different results.^{14-16,23} Although many authors have been working on dealing with dental anxiety, more studies are needed on the predictors of dental anxiety.^{24,25}

CONCLUSION

As a result, no significant correlation was found between dental anxiety and 2D:4D of pediatric patients who are planned teeth extraction. It was determined that 2D:4D is not a morphological marker that we can use to predict dental anxiety in the preoperative period.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Aysun Çağlar Torun; **Design:** Aysun Çağlar Torun; **Control/Supervision:** Aysun Çağlar Torun; **Data Collection and/or Processing:** Aysun Çağlar Torun; **Analysis and/or Interpretation:** Aysun Çağlar Torun; **Literature Review:** Aysun Çağlar Torun; **Writing the Article:** Aysun Çağlar Torun; **Critical Review:** Aysun Çağlar Torun; **References and Fundings:** Aysun Çağlar Torun; **Materials:** Aysun Çağlar Torun.

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