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Maxillary Tooth Sizes and Dental Anomalies in Schizophrenia Patients: A Case-Control Study

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ABSTRACT

Introduction: From the perspective of the developmental correlation between the face and brain, quantitative craniofacial findings such as tooth size may indicate important stages of neurodevelopment in the pathogenesis of schizophrenia. The aim of this study was to evaluate and compare maxillary tooth size and some dental anomalies in patients with schizophrenia in a blinded manner with non-psychiatric controls.

Methods: A total of 200 participants (100 patients with schizophrenia and 100 control subjects) aged 18–45 were included in the study. Plaster dental models were prepared from the measurements of the maxillary dental arch. The mesiodistal (MD) and buccolingual (BL) dimensions of the maxillary teeth were measured on dental casts by two observers using digital calipers. In addition to dimensional assessments, dental abnormalities such as tooth rotation, diastema, tooth crowding, and peg-shaped lateral incisors were also recorded.

Results: There was no statistically significant difference between the groups in terms of age and sex ($p > 0.05$). Statistical analyses showed that patients with schizophrenia exhibited significantly smaller measurements in both MD ($P < 0.001$) and BL ($p < 0.001$) dimensions across all teeth evaluated. Furthermore, multivariate binomial logistic regression revealed MD size ($B=-2.020$, $p < 0.001$) and the presence of diastema ($B=1.656$, $p < 0.001$) as significant independent predictors of schizophrenia.

Conclusion: Reduction in tooth size and increased presence of diastema in patients with schizophrenia may contribute to the hypothesis that there are possible variations that may represent specific markers of embryological dysmorphogenesis underlying schizophrenia.

Keywords: Diastema, maxilla, tooth abnormalities, tooth size, schizophrenia

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INTRODUCTION

The neurodevelopmental model of schizophrenia proposes that the origins of the disorder may be linked to prenatal events (1). Diverse evidence, such as epidemiological data (e.g., in-utero exposure to disease or stress), birth/pregnancy complications, developmental brain anomalies, pre-morbid behavioral and neuromotor deficits, and the presence of associated gross somatic abnormalities, supports this model (2,3). It is also noteworthy that there has been significant focus on the presence of minor physical anomalies (MPAs) in individuals diagnosed with schizophrenia (4). MPAs refer to minor structural differences that begin to develop in the early stages of pregnancy and remain present throughout a person's life. These physical anomalies originate from the same embryonic ectoderm layer as the brain and are thought to reflect abnormal development of the fetal central nervous system. Individuals with schizophrenia are known to consistently display a higher incidence of MPAs than those without the disorder. The origins of these anomalies, whether genetic or environmental, remain uncertain (5). This concept aligns with the neurodevelopmental theory of schizophrenia, which proposes that the disorder originates from disruptions in normal brain development. Moreover, MPAs have been proposed as endophenotypes and offer a promising approach for investigating schizophrenia. Gottesman and Gould defined endophenotypes as internal, intermediate

Highlights

- **All maxillary teeth showed reduced crown dimensions in patients with schizophrenia.**
- **Maxillary diastema was more prevalent and associated with schizophrenia.**
- **Reduced tooth size and dental anomalies support a neurodevelopmental basis.**
- **Dental morphology may serve as a potential biomarker for schizophrenia.**

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phenotypes that are not readily apparent and can bridge the gap between genes and diseases in complex disorders like schizophrenia (6).

Craniofacial anomalies, particularly dentofacial deformities, emerge as the foremost physical attributes that most accurately set apart patients with schizophrenia from other patient groups (7). Compton et al. (8) evaluated whether differences in facial measurements might offer potential clues to neurodevelopmental disorders associated with schizophrenia, as facial and brain development originate from the same ectodermal tissue. The researchers reported that some facial measurements differed in schizophrenia patients compared to controls, and that these differences were gender-related. They noted an increase in midface depth in females and a decrease in forehead and lower face height in males. They interpreted these differences as being related to neurodevelopmental abnormalities during the embryonic period of schizophrenia (weeks 8–16 of gestation) (8). Similarly, in a study by Kirkpatrick et al. (9) and a study by Delice et al. (10), the palatal morphology of patients with schizophrenia was compared with that of a control group. The researchers noted that the schizophrenia group had greater palate width and depth than the control group, suggesting that this may be related to the neurodevelopmental deformation observed during the early embryonic period in schizophrenia (9,10). Another study examined structural differences in the palatal rugae of schizophrenia patients to assess whether this anatomical feature serves as a biological indicator of the disease. The researchers noted significant differences in the palatal rugae patterns of schizophrenia patients, which may shed light on the neurodevelopmental basis of the disease (11). A retrospective study by Bahadir et al. reported statistically significant differences in linear measurements (e.g., ramus height, condylar height, and bigonial width) and angular measurements (e.g., antegonial and gonial angles) of mandibular morphology between patients with schizophrenia and controls. The researchers interpreted these results as suggesting that mandibular morphology varies in schizophrenia patients compared to controls and that these differences may indicate neurodevelopmental disorders (12).

In humans, odontogenesis begins early in prenatal development, characterized by the formation of primary teeth between the 6th and 8th weeks of gestation, and the first permanent tooth buds appear around week 20. The presence of dentofacial deformities may indicate defects in early brain development. Tooth size, like schizophrenia, is influenced by genetic and environmental factors, with genetic factors being predominant. A reduction in permanent tooth size has been documented in the literature in several genetic syndromes involving central nervous system abnormalities, such as Down, Turner, and Williams syndromes (13). The researchers emphasize that dental anomalies can be a valuable indicator for distinguishing children with developmental disabilities from their healthy equivalents and for supporting early diagnosis and screening (14). A study focusing on 13 genetic syndromes that affect craniofacial and dental structures showed that Kabuki, Treacher-Collins, Williams, and Coffin-Lowry syndromes, in particular, directly impact facial skeletal development and dental morphology (15). Notable differences were found in maxillomandibular proportions, arch form, tooth number anomalies, tooth size changes, and eruption patterns in these syndromes compared to controls (15). However, studies on tooth size and tooth abnormalities in patients with schizophrenia are limited in the existing literature (9,13,16). Kirkpatrick and colleagues reported that individuals with schizophrenia had a higher prevalence of a broad spectrum of tooth abnormalities (9). Elevated MPA scores in the mouth region, particularly those related to dental abnormalities, could potentially serve as markers of developmental defects contributing to the development of schizophrenia. Tooth size variation, influenced by genetic and environmental factors similar to those in schizophrenia, has been noted, with conflicting findings regarding size reduction in schizophrenia patients (13,16). Rajchgot et al. reported that patients with schizophrenia exhibited significantly reduced maxillary and mandibular tooth size in a small sample size (16), but reduced tooth size was not detected in a later study (13). Therefore, this study aimed to evaluate whether participants with and without schizophrenia differed in tooth size and dental abnormalities, including diastema, tooth crowding, rotated teeth, and peg-shaped lateral incisors.

METHODS

Participants and Eligibility Criteria

Ethical approval for this study was obtained from Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinical Research Ethics Committee (IRB: 05.09.2022—2022-17-06). Written informed consent was obtained from all individuals, confirming their understanding of the study's scope and their willingness to participate. The power analysis using the G*power software (version 3.1.9.7, University of Düsseldorf, Psychologia, HHU, Germany) was performed based on Bahadir et al's study (12) as a reference. Sample size calculations were conducted. Power analysis for the two groups showed that a total of 172 subjects (86 in each group) were required to demonstrate a clinically meaningful difference between the two groups, at a 2-sided significance level of 0.05 and 90% power; based on a moderate effect size (Cohen's d [d]=0.50). The schizophrenia group consisted of 100 patients who were admitted to Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatry, Neurology and Neurosurgery as outpatients between January 2023 and October 2023 and met the inclusion/exclusion criteria of the study. Participants' diagnoses were based solely on criteria defined by the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition). Each diagnosis was meticulously confirmed through independent evaluations by two experienced senior psychiatrists (HG and MN), ensuring the accuracy and reliability of the psychiatric assessments. Patients with schizophrenia who had any concurrent DSM-IV Axis I disorders were rigorously excluded from the study to ensure the homogeneity and validity of the patient group. The control group consisted of 100 subjects who were admitted with various dental complaints to the Bahçelievler Oral and Dental Health Center between January 2023 and October 2023. Personal history of these disorders was assessed with the Structured Clinical Interview for DSM-IV Axis I disorders (17). Family history was assessed by using an informal assessment technique of participants' verbal responses to several questions. The controls who had a confirmed personal or family history (in first- and second-degree relatives) of psychotic or mood disorders were excluded.

Participants in both groups were included in the study if they were between 18 and 45 years old and had permanent teeth from the second permanent molar on the left to the second permanent molar on the right. Participants with a history of neurological disorders, drug or alcohol dependence, any medical condition known to affect cognitive or cerebral function, indicators of potential intellectual disability, or somatic disorders, including neurological symptoms, craniofacial trauma, or orthodontic treatment, were excluded from both groups. Additionally, inclusion criteria for both groups included the absence of damage to the dental cast, a complete representation of the maxillary teeth, absence of trauma to the craniofacial region and to the teeth themselves, and absence of non-carious lesions (e.g., abrasion, abfraction) that could pathologically affect tooth dimensions. Teeth with interproximal caries, missing teeth, supernumerary teeth, and third molars were excluded from the measurements to prevent errors. An essential consideration for participant selection was ethnicity. This measure aimed to prevent potential ethnic or racial confounding in dental and craniofacial measurements by accounting for variability in tooth parameters. Both groups consisted exclusively of individuals of Turkish origin. Consequently, any potential participant whose parents or grandparents were not of Turkish ethnicity was excluded.

Comprehensive Assessment Protocol

Maxillary impressions of participants in both groups were taken using an irreversible hydrocolloid (Alginate, Zhermack, Italy) due to its favorable dimensional stability and ease of use, and standard clinical procedures. The impressions were poured within 10 minutes of taking, in line with the literature, which recommends prompt casting to minimise dimensional changes. All casts were stored in a controlled environment at 22–24°C and 45–55% relative humidity, protected from direct sunlight and vibration, to mitigate deformation. To further ensure dimensional stability, the stone models were allowed to set for at least 45 minutes before separation from the impression and were measured within 48 hours after pouring, consistent with standard protocols for Type III dental stone models. Two experienced examiners (ÖÖ and II), blinded to the subjects' group membership, carried out the measurements and recordings. The intraclass correlation coefficient (ICC) was used to assess intra- and inter-observer agreement for maxillary tooth size. Measurements were taken from dental casts of 200 participants (100 in the schizophrenia group and 100 in the control group). The dimensions of the teeth were carefully measured according to the methodology initially detailed by Moorrees and Reed (18,19). The maximum mesiodistal (MD) and buccolingual (BL) dimensions of each fully erupted permanent tooth were assessed. The MD dimension was defined as the largest distance measured between the tooth's most mesial (front) and distal (back) points, while the BL dimension was measured as the largest distance between the tooth's innermost lingual or palatal surface and the outermost buccal or labial surface. The method used to define mesiodistal (MD) and buccolingual (BL) dimensions is schematically represented in Figure 1. All these measurements were taken using a digital vernier (Mitutoyo Caliper, Japan), known for its precision, and recorded to the nearest tenth of a millimeter. The mesiodistal and buccolingual dimensions of maxillary permanent teeth in both groups were measured from dental casts.

The presence of four dental abnormalities, namely diastema/tooth rotation/tooth crowding/peg-shaped incisors, was evaluated on casts in both groups (19). All four qualitative parameters were assessed as present or absent by two experienced dentists (ÖO and II) using an observational, double-blind approach. The intraclass correlation coefficient (ICC) was used to measure the intra-observer and inter-observer agreement for dental abnormalities. A space greater than 0.5 mm between the proximal surfaces of the maxillary central incisors and other teeth was considered a maxillary diastema (20,21). Crowding tooth was defined as a discrepancy between tooth size and arch length. Tooth rotation was recorded as the angular deviation of the tooth from its standard position around its longitudinal axis, assessed biomechanically (22). The maxillary permanent lateral incisor was generally considered a peg-shaped tooth with a specific shape, defined as the mesiodistal width of the incisor crown being shorter than the cervical width (23).

Statistical Analysis

Statistical analysis for this study was performed using IBM Statistical Package for Social Sciences (SPSS) program software, version 25.0 for Mac OS (Armonk, NY: IBM Corp.). Initially, descriptive statistical methods were applied to systematically summarize and clearly present the data collected during the research. Before conducting comparative analyses, the distribution of the quantitative data was carefully evaluated to verify whether it conformed to a normal distribution. This evaluation was conducted using the Shapiro-Wilk test, complemented by visual graphical assessments such as histograms and Q-Q plots. To compare quantitative variables that demonstrated normal distributions between the schizophrenia patient group and the control group, an independent-samples t-test was employed. Additionally, the chi-square (χ^2) test was utilized to assess differences between groups for qualitative or categorical variables. Further statistical analysis involved multivariate binomial logistic regression to identify independent predictors of being categorized in the schizophrenia group. Logistic regression analysis was particularly appropriate, given its ability to handle binary outcomes and to clearly distinguish between individuals in the patient and control groups. A logistic regression model was constructed using variables identified as potentially significant in preliminary analyses, and the results were carefully interpreted to clarify the extent to which each predictor independently influenced the presence of schizophrenia. Throughout

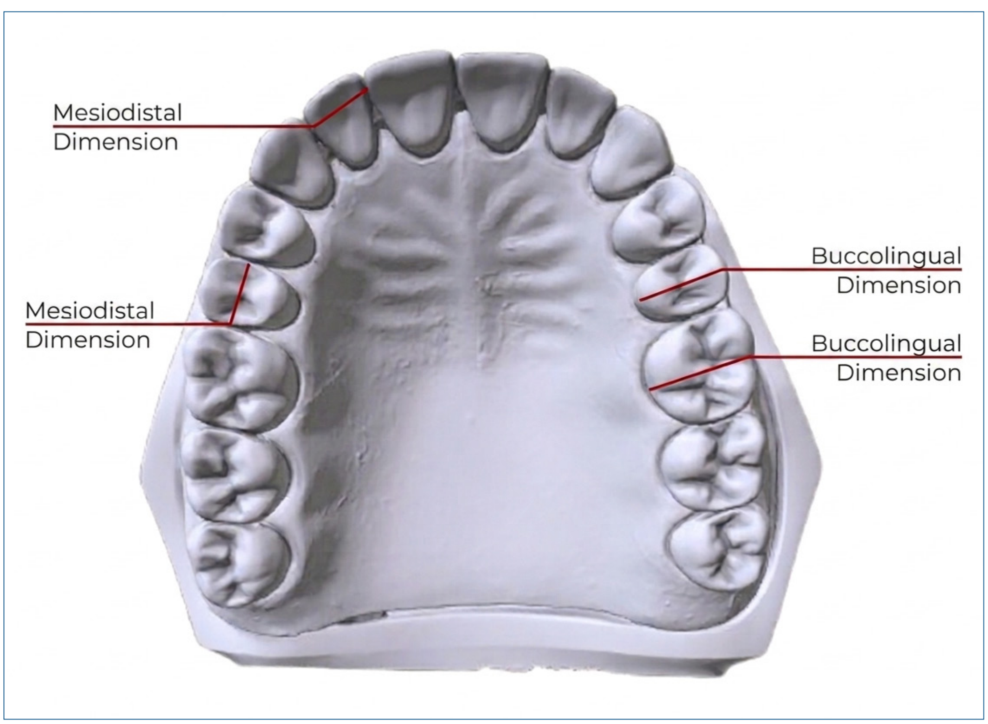

Figure 1. Representation of mesiodistal and buccolingual tooth dimensions in the maxillary model.

the analyses, the threshold for statistical significance was consistently set at p <0.05.

RESULTS

The mean ages of the two groups were very similar, and the male-to-female ratios were the same. The average age of schizophrenia subjects was 33.61±5.94 years, compared to 33.71±5.63 years in the control group (*p*=0.903). The ICCs for intra- and inter-observer assessments of tooth size and dental abnormalities were 0.70 or higher, indicating consistent measurements.

Table 1 and Table 2 present a comparative analysis of the mesiodistal and buccolingual dimensions of maxillary permanent teeth 11–17 and 21–27, respectively, in patients with schizophrenia and the control group. The results indicate that patients with schizophrenia exhibited significantly smaller measurements in both MD and BL dimensions across all assessed teeth (*p* <0.05). In addition to individual tooth measurements, the group-wise average values also revealed significant differences. The mean MD dimension across all evaluated teeth was 7.53±0.32 mm in the schizophrenia group, compared to 7.92±0.49 mm in the control group (*p* <0.001). Similarly, the average BL dimension was lower in patients (8.40±0.46 mm) than in controls (8.76±0.53 mm; *p* <0.001). Among all measured teeth, the highest percentage differences were observed in teeth 12 and 25. These findings underscore a consistent pattern of tooth size reduction in the schizophrenia group.

Patients with schizophrenia demonstrated significantly higher rates of certain dental abnormalities, specifically diastema (51% versus 15%, *p* <0.001), rotated teeth (24% versus 13%, *p*=0.045), and peg-shaped lateral incisors (13% versus 2%, *p*=0.003). However, no significant difference was found regarding the prevalence of tooth crowding between schizophrenia patients and the control group (25% versus 17%, *p*=0.165).

A multivariate binomial logistic regression analysis was performed using MD and BL dimensions together with the presence of diastema, rotated teeth, and peg-lateral incisors (Table 3). The overall model was statistically significant (χ^2=72.600, p <0.001) and accounted for 40.9% of the variance

Table 1. Mesiodistal dimensions of maxillary permanent teeth for schizophrenia and control groups

	Mesiodistal dimension (mean ± SD)			
No	**Schizophrenia**	**Control**	**Difference (%)**	**p**
11	8.21±0.6	8.52±0.72	0.30±0.89 (3.52)	0.001**
12	6.27±0.71	6.66±0.71	0.39±1.00 (5.85)	<0.001**
13	7.23±0.61	7.52±0.66	0.28±0.96 (3.72)	0.002**
14	6.43±0.6	6.83±0.7	0.40±0.90 (5.85)	<0.001**
15	6.33±0.65	6.75±0.81	0.42±1.05 (6.22)	<0.001**
16	9.50±0.56	10.03±0.69	0.52±0.88 (5.18)	<0.001**
17	9.20±0.77	9.54±0.7	0.33±0.99 (3.45)	0.002**
21	8.11±0.54	8.45±0.6	0.34±0.85 (4.02)	<0.001**
22	6.14±0.64	6.53±0.8	0.39±1.06 (5.97)	<0.001**
23	7.02±0.66	7.44±0.71	0.41±0.94 (5.51)	<0.001**
24	6.48±0.57	6.87±0.66	0.39±0.79 (5.67)	<0.001**
25	6.20±0.66	6.72±0.78	0.52±0.98 (7.73)	<0.001**
26	9.44±0.71	9.69±0.97	0.25±1.16 (2.57)	0.038*
27	9.01±0.76	9.43±0.79	0.42±1.01 (4.45)	<0.001**
Total	7.53±0.32	7.92±0.49	0.38±0.55 (4.79)	<0.001**

No: tooth number; Difference %: shows the % difference compared to the non-psychiatric controls; independent Samples T-test was used; *: p<0.05; **: p<0.01.

Table 2. Buccolingual dimensions of maxillary permanent teeth for schizophrenia and control groups

	Buccolingual dimension (mean ± sd)			
No	**Schizophrenia**	**Control**	**Difference (%)**	**p**
11	6.43±0.84	6.98±0.76	0.55±1.02 (7.87)	<0.001**
12	5.72±0.79	6.25±0.78	0.52±1.15 (8.32)	<0.001**
13	7.39±0.88	7.82±0.85	0.42±1.16 (5.37)	0.001**
14	8.66±0.83	8.9±0.85	0.24±1.08 (2.69)	0.040*
15	9.00±0.6	9.23±0.82	0.22±1.04 (2.38)	0.026*
16	10.91±0.75	11.3±0.83	0.39±1.01 (7.96)	0.001**
17	10.89±0.97	11.24±0.85	0.34±1.21 (3.02)	0.008**
21	6.36±0.88	6.85±0.82	0.48±1.22 (7.00)	<0.001**
22	5.72±0.91	6.04±0.82	0.32±1.23 (5.29)	0.009**
23	7.27±0.84	7.74±0.83	0.47±1.15 (6.07)	<0.001**
24	8.72±0.57	8.91±0.71	0.19±0.91 (2.13)	0.033*
25	8.99±0.54	9.21±0.84	0.22±0.95 (2.38)	0.028*
26	10.82±0.83	11.11±0.92	0.29±1.27 (2.61)	0.019*
27	10.8±0.84	11.13±0.86	0.33±1.09 (2.96)	0.006**
Total	8.40±0.46	8.76±0.053	0.36±0.66 (4.10)	<0.001**

No: tooth number; Difference %: shows the % difference compared to the non-psychiatric controls; independent Samples T-test was used; *: p<0.05; **: p<0.01.

Table 3. Evaluation of teeth dimensions with multivariate binomial logistic regression to predict inclusion in the schizophrenia patient group

Predictor	B	Sig.	OR (Exp (B))	95% CI for OR
Mesiodistal diameter (mm)	-2.020	<0.001	0.133	0.045 – 0.393
Buccolingual diameter (mm)	-0.422	0.352	0.656	0.270 – 1.595
Diastema (yes)	1.656	<0.001	5.241	2.443 – 11.242
Rotated teeth (yes)	0.877	0.054	2.405	0.984 – 5.877
Peg-shaped lateral (yes)	1.310	0.127	3.707	0.688 – 19.985
Constant	18.492	<0.001	–	–

$p<0.05$; statistically significant (bold values); logistic regression, model summary: $\chi^2=72.600$, $p<0.001$; Nagelkerke $R^2=0.409$; classification accuracy=71.7%.

in group classification (Nagelkerke $R^2=0.409$). Model fit was acceptable according to the Hosmer–Lemeshow test ($\chi^2=7.132$, p=0.523), and the model correctly classified 71.7% of participants. Among the predictors, MD dimension (B=−2.020, p <0.001, OR=0.133; 95% CI=0.045–0.393) and the presence of diastema (B=1.656, p <0.001, OR=5.241; 95% CI=2.443–11.242) were significant independent contributors to schizophrenia group membership. The presence of rotated teeth showed a trend toward significance (p=0.054), whereas BL dimension and peg-lateral teeth did not reach statistical significance (p>0.05).

DISCUSSION

The main finding of the current study is a significant reduction in both mesiodistal and buccolingual dimensions of the maxillary teeth in patients with schizophrenia compared to non-psychiatric controls. Based on the regression analysis used to identify independent factors that most accurately distinguished patients with schizophrenia from controls, patients with schizophrenia had significantly decreased mesiodistal dimension, and dental diastema was more common in patients with schizophrenia. The quantitative differences in tooth size and diastema presence between schizophrenia patients and controls are striking and consistent with the hypothesis of abnormal neurodevelopment in schizophrenia.

Tooth size is primarily regulated by genetic factors, with heritability rates similar to those observed in schizophrenia (59–91%) (24). Various syndromes and conditions, such as Down, Turner, and Williams syndromes, oligodontia, and cleft lip and palate, are also associated with decreased tooth size (25). Early environmental factors, such as childhood nutrition and lifestyle, may have a small effect on tooth size. For example, Chinese subjects raised in a more politically stable environment than their parents experienced slight increases in tooth size. Once dental crown development is complete in early childhood, tooth size remains relatively stable, except under extreme conditions, such as a prehistoric diet (26). Rajchgot et al. documented a statistically significant decrease in maxillary and mandibular tooth size in patients with schizophrenia compared to controls (16). The smaller maxillary tooth size in Turkish schizophrenia patients compared to controls in this study supports the data from a previous study (16) with a larger sample size.

Tooth development is a complex process influenced by both genetics and the environment. Genetic modifications can cause anomalies in tooth position, number, structure, and shape (25). These anomalies may include variations in number (hypodontia, anodontia, and hyperdontia), structure (dentinogenesis imperfecta, amelogenesis imperfecta, and dentin dysplasia), and shape (macrodontia, microdontia, and taurodontism) (21). They can occur either as part of a systemic disorder (syndromic) or independently (nonsyndromic) (23). Kirkpatrick et al. found that individuals with schizophrenia exhibited an increased frequency of various dental anomalies (9). Corroborating this, the study's observations further indicated that individuals with schizophrenia displayed a greater prevalence of numerous additional dental abnormalities. This included rotation and spacing of the teeth, along with the presence of small, cone-shaped lateral incisors (peg laterals). Notably, individuals with diastema were more than five times more likely to belong to the schizophrenia group, as detailed in Table 3. Maxillary midline diastema can result from developmental, functional, or dental anomalies. Hereditary variations in craniofacial structure and soft tissue characteristics are among the primary determinants of familial clustering of diastema. Therefore, diastema is considered a multifactorial and complex dental phenotype. Many of these skeletal and dental variations predispose to anterior space formation, and the risk of diastema development is significantly increased, particularly in syndromes associated with microdontia, lateral incisor agenesis, and arch narrowing (15).

To our knowledge, no studies have directly investigated the embryological basis of diastema. Studies have focused on the prenatal development of the premaxilla and the intermaxillary suture, and on the intrauterine formation of the upper labial frenulum. The distance between the central incisors is determined by the location of the central and lateral tooth buds and the direction of growth of the alveolar process (27,28). Also, studies report that papillary or papilla-penetrating, thick maxillary labial frenulum types that form in the fetal period and migrate apically in the postnatal period may cause a medial diastema (29,30). Studies show that developmental variations, tooth germ anomalies, or frenulum-related anomalies may disrupt this physiological process and cause permanent midline diastema (30,31). Diastema occurs in many genetic syndromes due to developmental anomalies in craniofacial growth patterns and dental morphogenesis (22,30). In Turner, Down, and Williams syndromes, reduced tooth size and decreased mesiodistal widths cause space in the anterior region, and the accompanying maxillary transverse narrowing, high palate, delayed eruption, and frenulum anomalies prevent the teeth from closing. Although midline diastema has been extensively evaluated in the literature in the context of many genetic syndromes, no studies have yet evaluated the potential relationship between diastema and schizophrenia. When examining syndromes associated with diastema, it was observed that diastema is frequently linked to dental morphological anomalies, such as microdontia and hypodontia, in various genetic and neurodevelopmental syndromes, particularly Down and Turner syndromes. In these studies, diastema has been identified as a component of the syndromic orofacial phenotype, but it has not been analyzed as an independent neurodevelopmental marker. For example, in a study by A. Szilágyi et al., which evaluated dental findings in individuals with Turner syndrome, midline diastema was reported as a characteristic oral phenotype of the syndrome, due to microdontia and increased spacing in the anterior region (22).

This study's findings about the presence of a higher prevalence of the diastema could be explained by developmental anomalies in craniofacial growth patterns and tooth morphogenesis in schizophrenia, as in the syndromes mentioned above. While data in this area require further support, this finding suggests that dental anomalies may be an important indicator in distinguishing schizophrenia and supporting early diagnosis and screening in the future.

This study has the following limitations: due to its uniqueness, there is a lack of comparative literature, leading to speculative interpretations. The sample consisted only of outpatients with schizophrenia who typically exhibit less severe psychopathology, limiting the generalizability of the findings to the broader schizophrenia population. Furthermore, the lack of information on the medications used by the schizophrenia patients included in the study for this diagnosis can be considered another limitation of this study in terms of analyzing the findings. Linear measurements and the identification of dental anomalies were performed on dental casts, but tooth development is three-dimensional, suggesting that three-dimensional imaging technology may provide more accurate assessments, particularly for determining tooth size and structure. Subjective assessment of dental anomalies may call the reliability of the qualitative method into question. The criteria we used for dental anomalies were intentionally kept simple because we were only interested in identifying key differences between subjects with and without schizophrenia. However, descriptive statistics and inter-rater reliability findings do not indicate significant outliers or excessive variation between the two measurements. Another limitation of the present study is the exclusion of mandibular teeth from the analysis, although significant associations between schizophrenia and mandibular morphology have been reported in the literature (12). The current study focused only on the maxillary dentition in accordance with the research design. Unlike the limited sample study by Rajchgot et al. (16) (n=16), the detailed evaluation of maxillary structures in a larger sample (n=200) provides valuable data for the literature. The oral region, particularly the palate, considered a typical site where MPAs associated with schizophrenia may occur, begins to develop between the 6th and 9th weeks of gestation and continues developing until approximately the 16th to 17th weeks. The focus on the maxilla was based on previous studies indicating a higher potential for MPAs in the oral region, particularly in the palate and related structures, among patients with schizophrenia. However, the omission of mandibular incisors and other tooth groups (canines, premolars, and molars) limits the interpretability of the findings. Future analyses, including mandibular morphology and dentition, could provide additional insights for the literature.

An another limitation is that only three dental anomalies (diastema, tooth rotation, and peg-shaped lateral incisors) were included in the analysis, whereas other anomalies (e.g., hypodontia, microdontia, macrodontia, and supernumerary teeth) were not evaluated. Several studies in the literature have examined the relationship between craniofacial morphology and schizophrenia. However, only one study (9), which performed a blind quantitative assessment of the palate, reported that patients with schizophrenia had significantly wider palates and a higher incidence of dental developmental abnormalities such as diastema, tooth rotation, crowding, peg-shaped lateral incisors, and interarch tooth size discrepancies compared with controls. However, that study had a relatively small sample size and consisted predominantly of male patients with schizophrenia. In the present study, we focused only on maxillary tooth dimensions, and only the dental anomalies examined in the previous study (9) were referenced. In addition, individuals with missing teeth, a history of trauma, interproximal caries, and dental wear were excluded from the study to ensure standardized measurements and minimize the margin of error in mesiodistal dimensions. In accordance with these criteria, developmental anomalies that can directly affect tooth size and alignment, especially the presence of diastema, such as hypodontia, microdontia, and macrodontia, were also excluded from the assessment. While these criteria increase measurement accuracy, they limit the ability to reflect the full prevalence of dental anomalies in patients with schizophrenia. Expanding the scope of the analysis could provide additional meaningful insights

In conclusion, the present study demonstrated significant reductions in maxillary tooth size among individuals with schizophrenia, particularly reduced mesiodistal tooth dimensions and a higher prevalence of diastema. Although these findings do not indicate a specific abnormality in dental development, they support the possibility of altered neurodevelopmental processes in schizophrenia. Further research integrating genetic, histological, and embryological approaches, supported by modern methodological designs, is needed better to understand the relationship between tooth morphology and schizophrenia. Confirming quantitative differences in tooth size and morphology between schizophrenia patients and controls may provide valuable insights into the neurodevelopmental mechanisms underlying the disorder.

Ethics Committee Approval: Ethical approval for this study was obtained from Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinical Research Ethics Committee (IRB: 05.09.2022—2022-17-06).

Informed Consent: Written informed consent was obtained from all individuals, confirming their understanding of the study's scope and their willingness to participate.

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