Original Article

Mandibular Prognathism and Genetic Transmission in Turkish Families

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ABSTRACT

Objective: Mandibular prognathism (MP), defined as the difference in the size and relationship of maxilla and mandible, is the most serious anomaly in the practice of orthodontics. Incidence of MP varies among different populations; it is highest in Asian populations (15–23%) and lowest in Caucasian populations (0.48–4%). Genetic and environmental factors are suggested in the etiology of MP, but the contribution of these factors is not known. This study was designed to determine patients with MP in 3 generations of the families and to evaluate familial transmission of MP in Turkish families.

Materials and Method: To reveal the effect of genetic factors on MP, we created pedigree charts for 99 subjects with severe skeletal Class III MP who planned to undergo or had undergone orthognathic surgery. Three generations of each patient's family was assessed on pedigree charts. The relatives of the probands were evaluated with photos and a detailed interview to confirm the prognathic phenotype.

Results: The average ANB, SNA, and SNB angles in the probands were −2.65°, 79.92°, and 82.57°, respectively. A total of 1847 family members were examined, and 12.7% had MP. Men were slightly more affected than women. Most families (89%) had at least 1 member with MP other than the proband. The affected ratios of the first- and second-degree relatives were 20% and 7.3%, respectively. The affected ratio of fathers of probands (25.7%) was more than twice that of mothers of pronbands (9.9%), and siblings showed a 17.8% affected ratio.

Conclusion: A high frequency of MP was seen in families of patients with skeletal Class III, suggesting a genetic transmission. (*Turkish J Orthod* 2013;26:114–118)

KEY WORDS: Affected ratio, Heredity pattern, Mandibular prognathism

INTRODUCTION

Skeletal Class III malocclusion with a prognathic mandible is one of the most severe maxillofacial skeletal deformities in the practice of orthodontics.[1] The prevalence of mandibular prognathism (MP) varies among different populations. Prevalence of MP is highest in East Asian populations (approximately 15–23%), moderate in sub-Saharan Africans (3–8%), and lowest in Caucasian populations (0.48–4%).[2,3] Sarı and colleagues[4] and Sayin and Turkkahraman[5] reported the incidence of Class III malocclusion in Turkish population at 10.2% and 12%, respectively.

Environmental and genetic components have both contributed to the development of MP.[6] Various environmental factors, such as enlarged tonsils;[7] endocrine imbalances;[8] posture, trauma, and disease;[9] hormonal disturbance;[10] congenital anatomic defects;[11] and instrument deliveries[12] have been associated with MP. It has been known for many years that heredity plays a substantial role in the etiology of MP. When the Habsburgs, one of Europe's foremost royal families, were examined, autosomal dominant hereditary pattern was observed in 23 generations.[13] However, the inheritance pattern of MP is heterogeneous; findings have suggested autosomal-recessive inheritance,[8,14] autosomal-dominant inheritance,[15,16] dominant inheritance with incomplete penetrance,[2,13] or a polygenic threshold model.[17] Overall, polygenic or multifactorial factors are thought to be responsible for the phenotype in a vast majority of families with MP.

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Various authors have researched MP in family studies and determined the affected ratio of this phenotype in their populations. These studies were usually carried out in Asian populations because of the high incidence of the condition.[18–22]

Orthodontic treatment with maxillofacial surgery is necessary to treat patients with MP, but this treatment approach is quite difficult for patients. Understanding the specific genetic variables contributing to MP could allow clinicians to advance new preventive strategies for this condition.

The aim of this study was to determine patients with MP in 3 generations of families and to evaluate familial transmission of MP in Turkish families.

MATERIALS AND METHODS

Participants in this study were101 Turkish patients with MP and severe skeletal Class III malocclusion who planned to undergo or had undergone orthognathic surgery at the Orthodontics Department of Selçuk University Faculty of Dentistry. Patients were chosen according to the following inclusion criteria:

1. Patients were older than 16 years and had completed their growth and development
2. Patients had severe Class III malocclusion with MP
3. Patients had no congenital anomalies (eg, cleft lip and palate), hereditary diseases, or endocrinologic problems
4. The ANB angle was $<0°$ and the Wits value was <0.

Two subjects were excluded from study because of family members were not available to examine for MP. Pedigree charts were created in 3 generations of the families of 99 patients with MP to determine how genetic factors affect MP. The relatives of the probands were evaluated with a detailed interview and photos to confirm the prognathic phenotype by one of the authors (S.B.). Demographic characteristics of the probands are shown in Table I.

In this study, family members defined as having "prominence of the lower jaw" were assumed to have MP. Each pedigree chart was carefully created to differentiate between maxillary retrusion and MP.

Table 1. Demographic characteristics of probands

	Females	Males
No.	46	55
Mean age	17.2	17.1

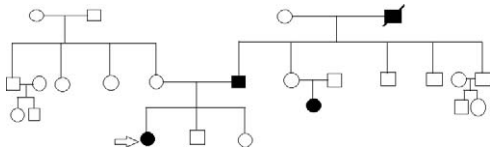

Figure 1. Pedigree chart of a proband.

A sample pedigree chart of a proband is shown in Figure 1. Pedigree charts allowed us to predict heredity patterns of MP in the study subjects. Autosomal dominant or recessive inheritance patterns were determined from these charts.

RESULTS

A total of 99 probands (52 male, 47 female) were identified, and pedigree charts were created by the same author (S.B.). The average ANB angle was $-2.65° \pm 1.63°$ (males$=-2.87° \pm 1.63°$; females$=-2.43° \pm 1.67°$) and the average Wits value was -7.43 ± 2.55 (males$=-7.15 \pm 2.25$; females$=-7.55 \pm 2.75$). The average SNA and Sn-GoGn angles were within a standard deviation of the Turkish norm. The average SNB angle was much higher than the norm (Table 2).[23]

A total of 1847 first-, second-, and third-degree relatives were identified from the 99 probands (Table 3); of these, 217 relatives (93 females, 124 males) had MP, and 1488 (776 females, 712 males) did not (Table 3). The affected ratio was 12.7% in all defined (affected and unaffected) relatives (1705 people); 7.6% of the 1847 relatives could not be defined from the examination whether they had MP. Of these undefined relatives, 66.2%, 21.1%, and 12.7% were grandparents, cousins, and uncles or aunts, respectively. In total, 89% of families had at least 1 member with MP other than the proband. (Table 4).

The affected ratio of first-degree relatives (20%) was about 3 times higher than that of second-degree relatives (7.3%). The ratio of third-degree relatives (cousins) was 19.7%. In 36% of the pedigrees, one of the parents of the proband was also affected (10 mothers and 26 fathers); however, in no families were both parents affected. In first-degree relatives, the affected ratio of father of probands (25.7%) was more than twice that of mother of probands (9.9%), and siblings showed an affected ratio of 17.8% (Table 5). In second-degree relatives, the affected ratios of grandparents and uncles/aunts were 17.8% and 5.2%. respectively (Table 5).

The affected ratio of total relatives was slightly higher in men (Table 3), and this was more than

Table 2. Cephalometric values of the probands and Turkish norms

Probands	SNA Angle	SNB Angle	ANB Angle	Wits	SN-GoGn	U1-SN	IMPA
Males	79.82 ± 3.83	83.25 ± 4.31	–3.45 ± 2.87	–7.15 ± 2.25	32.13 ± 4.17	107.07 ± 6.81	80.06 ± 8.33
	83.27 ± 3.60[a]	80.40 ± 3.59[a]	–2.87 ± 1.63[a]		31.40 ± 6.01[a]	102.90 ± 9.87[a]	96.83 ± 8.43[a]
Females	79.47 ± 3.34	82.48 ± 3.72	–3.05 ± 2.41	–7.55 ± 2.75	32.22 ± 3.64	107.35 ± 7.16	82.27 ± 8.75
	81.81 ± 3.41[a]	79.43 ± 3.27[a]	–2.43 ± 1.67[a]		31.93 ± 4.43[a]	101.23 ± 9.68[a]	96.16 ± 6.56[a]
Total	79.63 ± 3.68	82.82 ± 4.03	–3.27 ± 2.63	–7.43 ± 2.55	32.17 ± 4.39	107.12 ± 6.94	81.52 ± 8.54
	82.57 ± 3.55[a]	79.92 ± 3.44[a]	–2.65 ± 1.63[a]		31.66 ± 5.25[a]	102.07 ± 9.73[a]	96.50 ± 7.50[a]

[a] Turkish norm according to Basciftci and colleagues.[23]

twice that of first-degree relatives (Table 5). The affected ratio of total relatives determined from the female probands (12.7%) was higher than that for the male probands (10%) For first-degree relatives, the ratio of the women was almost 1.5 times higher than that of the men (Table 6).

When pedigree charts of 99 probands were evaluated, autosomal dominant and autosomal recessive heredity patterns were observed in 83.8% and 16.2% of families, respectively. In 37 pedigree charts, autosomal dominant with incomplete penetrance was noticed.

DISCUSSION

This is the first report that examined the mandibular prognathic phenotype in detail in Turkish families. The subjects who planned to undergo or had undergone orthognathic surgery had prognathic mandible with negative ANB angle and Wits appraisal. As distinct from previous studies,[2,20,24] we used ANB angle with Wits similarly to the way it was used by Li and colleagues[25] in order to complete the missing aspects of each measurement.

One of the authors (S.B.) interviewed patients about their family history and created their pedigree charts. Each family member was carefully examined and photographs were reviewed in case of doubt. In particular, prognathic mandible was assessed rather than retrusive maxilla in relatives. All probands identified MP from the facial profile of their relatives, so the accuracy of this study will differ from that of others.

According to the study by Sarı and colleagues,[4] which had a sample size of 1602 patients, the incidence of Class III malocclusion in Turkish population was found to be 12%. Although the incidence was reported as 10.2% in a similar study,[5] the subjects examined in these studies include not only patients with MP but also patients with maxillary retrusion. Compared with these data, the incidence of MP (12.7%) is higher than expected in this study. This may be related to the fact that skeletal Class III malocclusion is most often mentioned as an inherited trait in previous studies.[2,8,13–17]

The affected ratio of male probands (47 female, 52 male) and male relatives (93 female, 124 male) is higher than female probands and relatives in this study. Many diseases present differences in incidence rates between females and males. In a Japanese study,[20] for example men were slightly more affected with MP than women; this is in contrast to the findings of Cruz and colleagues,[22] who examined 2562 Brazilian family members.

The affected ratio was much higher in first-degree relatives than in second- and third-degree relatives (Table 5), but it was also higher in third-degree relatives than in second-degree relatives in this study. The reason for this is unclear, but the percentage of undefined relatives was highest in second-degree relatives (66.2%). Some grandpar-

Table 3. Ratio of affected relatives

Phenotype	Relatives with Mandibular Prognathism (No.)	Ratio of Affected Relatives (%)
Affected	217	12.7
Males	124	14.8
Females	93	10.7
Unaffected	1488	
Males	712	
Females	776	
Total	1705	

Table 4. Distribution of families with at least one affected person other than the proband

Probands	Affected	Unaffected	Total
Male	45	7	52
Female	43	4	47
Total (%)	88 (89)	11 (11)	99 (100)

Table 5. Mandibular prognathism in first-, second-, and third-degree relatives

Relatives	Ratio of Those Affected (%)
First-degree relative	20
Father	25.7
Mother	9.9
Sibling	17.8
Male	26.1
Female	10.3
Second-degree relative	7.3
Grandparents	17.8
Uncle or aunt	5.2
Male	8.4
Female	6.3
Third-degree relative	19.7
Male	17.5
Female	21.9

ents were no longer living, and the probands could not ascertain their prognathic profile. Also third-degree relatives and the probands are of similar ages, and it is easier for the probands to recognize facial profiles and determine MP.

The affected ratio of male relatives was higher than that of female relatives (Tables 3 and 5). Moreover, the affected ratios of total and first-degree relatives ascertained from the female probands were higher than those from the male probands (Table 6). This is known as the Carter effect, which involves a multifactorial threshold model with sex dimorphism of inheritance.[26] According to this theory, females, who are less commonly diagnosed with MP, appeared to require a greater genetic load to become affected and were therefore more likely to transmit this phenotype to their offspring.

Watanabe and colleagues[20] examined 105 subjects with severe skeletal Class III MP via a questionnaire and determined MP in 3 generations of each subject's family. According to this study, 1480 family members were examined and 11.2% had MP. In addition, 68.6% of families had at least 1 member with MP other than the proband. In a similar study conducted in Korea with 103 patients, 58.3% had at least 1 member with MP other than the proband.[21] The affected ratio of 12.7% in this study is similar, but the percentage of at least 1 member other than the proband is higher than in those studies. Because MP was seen more frequently in Asian populations, we were expecting lower ratios from these studies. Recently, Cruz and colleagues[22] found a 14.4% incidence of MP in members of

Table 6. Ratio of affected relatives ascertained from the probands

Probands	Ratio of Affected Relatives			
	First Degree	Second Degree	Third Degree	Total
Male	13.7	8.4	20	10
Female	18.2	5.1	18.1	12.7

affected families, which is higher than our results. In Brazil, Cruz and colleagues[22] studied 55 MP pedigrees that comprised 2562 members and identified 158 males and 214 females affected with MP.

Different heredity patterns for MP were observed in different studies in different ethnic populations. In the United States, 57 Hispanic subjects in 4 families were evaluated, and the heredity pattern was reported as autosomal dominant with incomplete penetrance.[27] In a Chinese population, 2 families consisting of 42 subjects were evaluated and autosomal dominant with 0.95 incomplete penetrance was reported.[28] In another study, the heredity pattern was found to be autosomal dominant with 0.70 incomplete penetrance.[25] Ko and colleagues[29] examined 100 Korean subjects with MP and concluded that both genetic and environmental factors are responsible for susceptibility to MP in Korean patients with Class III rather than Mendelian inheritance.

In this study, an autosomal dominant heredity pattern was seen in 83.8% of families; furthermore, in 37 pedigree charts, autosomal dominant with incomplete penetrance was observed. These results are consistent with the results of Cruz and colleagues,[22] who evaluated 2562 subjects in 55 families. Similarly, El-Gheriani and colleagues[2] reported the heredity pattern of MP in Libya as autosomal dominant.

CONCLUSIONS

The affected ratio of total relatives was 12.7%, and in 99 examined families, 89% had at least 1 member other than the proband with MP. The affected ratio in first-degree relatives was higher than that for second-degree relatives. It can be concluded that the heredity pattern of MP in the Turkish population is close to autosomal dominant. These results indicate the presence of genetic transmission in the etiology of surgically treated

patients with MP. For a better understanding of the genetic factors that contribute to the mandibular prognathic phenotype, there is need for molecular-level genetic studies to understand factors causing prognathic mandible.

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