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ORIGINAL RESEARCH

Growth and Development of Dentofacial Complex influenced by Genetic and Environmental Factors using Monozygotic Twins

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ABSTRACT

Aim: The purpose of this study was to determine the possible effects of genetic and environmental factors on dentofacial complex using monozygotic twins.

Materials and methods: The study sample was made of 21 pairs of monozygotic twins (14 female pairs and seven male pairs) between 10 and 25 years. Pretreatment lateral cephalograms were used which were traced and digitized, and various landmarks to determine the anteroposterior and vertical proportions were marked. Samples were divided into two groups. The correlation between groups was found by calculating Pearson's product moment correlation coefficients.

Results: The range of the correlation coefficient was from 0.705 to 0.952. Gonial angle showed the highest correlation coefficient (0.952), while saddle angle showed the lowest correlation coefficient (0.705).

Conclusion: The growth and development of craniofacial complex is under mutifactorial control. However, genetic influences do tend to play a dominant role.

Clinical significance: By studying identical twins, we can study about the interaction of the environment with the genes and how it affects the growth and development of the body in general and dentofacial complex in particular. By utilizing twin studies, we can identify whether a particular trait, disease, or disorder is influenced more strongly by genetics or by the environment. Success of orthodontic treatment depends on a proper diagnosis of the problem including its etiological factors. Genetic studies let the orthodontists to understand the effects of genetic and environmental factors in the growth and development of dentofacial complex better and allows to prevent or treat malocclusions and skeletal anomalies in better ways.

Keywords: Dentofacial complex, Genetic, Heredity, Monozygotic, Twin study, Twins.

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INTRODUCTION

The influence of genetic and environmental factors on the growth and development of dentofacial complex has been a matter for discussion for a long time. Various studies have shown a very significant genetic influence on dentofacial deformities and malocclusions. The genetic constitution of an individual is termed as genome, which is inherited from not one, but both of the parents. Conversion of the genetic information which is encoded in a person's genome into proteins or regulatory molecules, such as microribonucleic acid influences the growth and development of the person. How these factors affect growth has been discussed in length for years.[1-3] Family studies, as well as twin studies, have shown the role of heredity and the role of environmental factors in the growth and development of dentofacial complex. This may be better understood by utilizing twins as study subjects. Galton[4] was the first to suggest the merits of twin studies. Monozygotic twin

pairs are matched perfectly for age and sex, and also they occur from the early division of a single fertilized egg. Hence, each individual has the same chromosomal DNA, and they possess identical genetic constitutions. In case of dizygotic twins or trizygotic triplets, since each member of these originates from a separate zygote, they are similar or dissimilar as are siblings. The premise on which twin studies are based on is that any difference between monozygotic twins, phenotypically, must be the result of environmental influences only or of the interaction between different environmental factors acting on identical genes as they originate by the division of the same fertilized egg.[5]

Very few studies of the kind mentioned have been undertaken using the Indian control in general and the Kerala ethnic group in particular. For this reason, it was felt that valuable insight into the area would be provided by such a line of investigation.

Here, we aim to study the following:

- Heritability of anteroposterior and vertical facial proportions
- The heritability of mandibular growth patterns in monozygotic twins using lateral cephalograms.

MATERIALS AND METHODS

Materials

The study sample was made of 21 pairs of monozygotic twins, i.e., 14 pairs of female twins, and 7 pairs of male twins who have not undergone orthodontic treatment. The age range of the subjects was between 10 and 25 years. The details of the samples were collected in a pro forma sheet. The data for the study were obtained from the pretreatment lateral cephalograms of the samples. Different methods are available to identify monozygotic twins,[6-10] and in this study, monozygotic twins were selected based on their identical facial appearance, hair color and type, pupil color, blood grouping, and fingerprint records. Pretreatment lateral cephalograms obtained from the study subjects were used to obtain the required data for the study.

Methods

Each pretreatment lateral cephalogram was traced and the landmarks were digitized using a digitizer (RMO's Jiffy orthodontic evaluation). When shadows of both sides were seen on the radiograph, the midpoint of the margin of the two shadows was used. Each of the lateral cephalogram was digitized twice, and the average measurement was taken, so as to minimize intraobserver error. Definitions of the reference points and planes used in the study are given below.

Reference Points and Planes used

Tables 1 and 2 shows reference points and angular measurements.

Data files of the landmarks were used to compute the following cephalometric variables (Fig. 1).

Samples were divided into two groups. One twin was then assigned to group I while the other of the pair was assigned to group II.

Table 1: Reference Points

Definition	*Abbreviation*	*Landmarks*
The most anterior point of the frontonasal suture in the median plane	N	Nasion
The midpoint of the hypophyseal fossa. It is a constructed point in the median plane	S	Sella
The point of intersection of the posterior margin of the ascending ramus and the outer margin of the cranial base	Ar	Articulare
It is a constructed point at the intersection of the lines tangent to the posterior margin of the ascending ramus and the mandibular base	Go	Gonion
Most caudal point in the outline of the symphysis	Me	Menton
The tip of the anterior nasal spine in the median plane	ANS	Anterior nasal spine

Table 2: Angular Measurements

Formed by	*Abbreviation*	*Angle*
Formed by lines connecting Nasion-Sella-Articulare and provides means of measuring the shape of the cranial base	NSAr	Saddle angle
Formed by lines connecting Sella-Articulare-Gonion and shows the forward and rearward diversion of the mandible	SArGo	Articulare angle
Formed by a line from articulare and a tangent to the mandibular base	ArGoMe	Gonion angle
(NSAr + SArGo + ArGoMe)		Sum of the angles of the Bjork's craniofacial polygon
Measured from Nasion to Menton	AFH	Anterior facial height
Measured from Sella to Gonion	PFH	Posterior facial height
Measured in millimeters, horizontally between anterior nasal spine and posterior nasal spine		Maxillary length
Measured in millimeters horizontally between two points, Gonion and gnathion in the lower border of mandible		Mandibular length

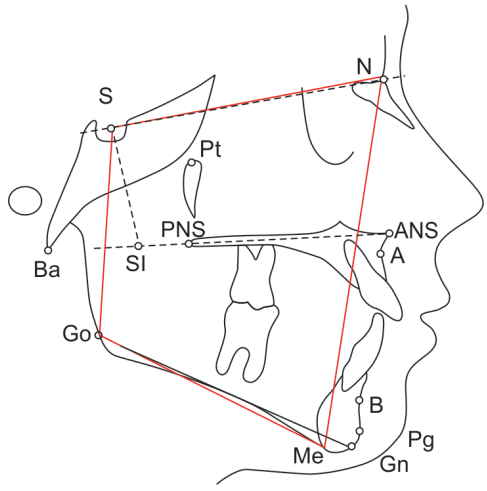

Fig. 1: Points and planes used in the study

RESULTS

Statistical Analysis

The data were collected and divided into two groups. Digitizing each lateral cephalogram twice followed by averaging out the value helped in minimizing chances of measurement error. Statistical analysis of the data was performed using the software Statistical Package for the Social Sciences version 7.5. Mean was used to measure the central tendency while standard deviation helped to map the spread of each parameter. These were calculated and are listed in Table 3. The correlation between groups was found by calculating the Pearson's product moment correlation coefficients for each of the aforementioned variables. The results obtained are given in Table 3.

The correlation coefficient for monozygotic twins ought to be 1 for all the variables as both the twins originate from a single ovum. However, in this study, it was observed that correlation coefficients for all the parameters studied were <1.0 and hence, different from the expected values. The range of the correlation coefficient was from 0.705 to 0.952. SArGo showed the highest correlation coefficient (0.952). NSAr showed the lowest correlation coefficient (0.705). The statistical analysis follows the mentioned values.

DISCUSSION

Each individualcell has 23 pairs of chromosomes, of which 22 pairs are autosomal, and 1 pair is sex chromosomes (XX or XY). One chromosome in the pair is inherited from the mother while the other is from the father. The genetic constitution of an individual is referred to as a person's genetic code or genotype. Surprisingly, studies have shown that in 99.9% of all humans the genetic sequences appear to be approximately identical,[11] and therefore, it is only a 0.1% of the genetic sequence information, i.e., responsible for the coding of differences between individuals. Variable expression of a single gene as well as interaction of proteins originated from another gene along with environmental factors on a single gene may cause a genetic expression of different characteristics/traits in an individual. Characteristics/traits known as complex or common diseases and traits do not stick to Mendelian inheritance patterns and show the interaction of environmental factors on multiple genes from multiple loci. Traits of polygenic nature reflect the effect of multiple genes on phenotypic expression and it may be multifactorial with the effect of environmental factors also.

The hypothesis that the etiology of malocclusion is multifactorial has been supported by various studies. Malocclusion can be defined as the final outcome of complex interactions of various genetic and environmental factors in the growth and development of the craniofacial region. Orthodontic interest in genetics to improve their knowledge regarding the reason for the occurrence of a particular occlusion or malocclusion in a patient, and to decide the apt mode of management for the malocclusion can be dated centuries back. As genetic mechanisms are seen to predominate during the embryonic stage of craniofacial morphogenesis and considered as the etiological factor in the development of many of the craniofacial abnormalities, genetic factors must definitely be considered as an etiological factor in the development of malocclusion also. However, postnatally, environmental factors are also believed to influence dentofacial morphology, especially during growth period, though in

Table 3: Means, SD, and correlation coefficients (n = 21)

	Mean		*SD*		
Variables	*Group I*	*Group II*	*Group I*	*Group II*	*Coefficient*
NSAr	127.45	126.1	5.99	6.12	0705 (+)
SarGo	139.93	138.8	7.27	6.58	0.952 (+++)
ArGoGn	127.71	128.4	6.86	6.3	0.744 (+)
Sum	395.18	394.28	6.41	8.31	0.753 (++)
AFH	116.93	118.21	8.27	6.34	0.791 (++)
PFH	76.89	77.66	5.36	4.84	0.830 (++)
Ratio	65.85	65.75	2.86	3.28	0.785 (++)
Max: Length	51.26	52.83	4.35	4.58	0.726 (+)
Mand: Length	75.22	75.05	4.23	4.98	0.826 (++)

+++degree of correlation >+0.9; ++degree of correlation +0.75 – +0.9; +degree of correlation 0.6–0.75; SD: Standard deviations

a smaller percentage. Since monozygotic twins are supposed to have identical genetic makeup, any difference in the developmental pattern of dentofacial complex of monozygotic twins residing in the same geographic location will be considered as due to environmental influence.

While considering genetic factors in the etiology of developmental variations and anomalies of dentofacial region in diagnosis, the significance of genetic influence on treatment outcome is not well appreciated often. Factors that influence the patient's response to the treatment of a particular malocclusion may not be the same ones as that causes development of that malocclusion. Malocclusion can be greatly affected by environmental factors also. Considering the effects of environmental factors in the development of malocclusion, it should be noted that the genetic constitution of individuals may modify his/her response to environmental factors. Similar malocclusions in siblings may often be the result of not just genetic or environmental factors common to them but also because of the similar response of their genetic factors to the shared environmental factors.

The role of genetics or heredity in forming the dentofacial complex of malocclusion was systematically assessed by making use of monozygotic twins as study subjects. The lateral cephalograms of 21 pairs of monozygotic twins were used to study nine predefined variables. Two study groups were formed from dividing the twins such that each twin in a pair was made part of any one group only. The data thus obtained were statistically compared.

In this study, all the parameters studied were having correlation coefficients between +0.7 and +1, which showed a very strong genetic influence on all nine studied variables. Environmental factors were also found to play a minor role in some of the variables. The three angles that make up Bjork's craniofacial polygon[12] have been investigated in this study. A Pearson's correlation value of 0.75 was obtained for the sum of the angles NSAr, SArGo, and ArGoGn. This strongly supports the influence of heredity in effecting clockwise or anticlockwise rotation of mandible with a role for environmental factors. Among the three angles, highest correlation value of 0.952 for the angle SArGo shows that orientation of mandible to cranial base during growth is linked much strongly to genetic control with a limited influence of environmental factors.

Correlation value 0.705 of the variable NSAr shows that shape of the cranial base is under the strong influence of heredity with a major component of environmental influences, which is in contrast to the findings of studies done by Manfredi et al[13] and also by Kosovcevic and Markovic[14] showing a very high degree of genetic influence. Correlation value 0.744 of the angle ArGoGn indicates a strong influence of heredity on shape of the mandible with predominant role for environmental influences, which is in agreement with the studies done by Lobb[15] and Watnick.[16]

Mandibular length was found to have greater genetic influence than maxillary length with a lesser component of environmental influence. High correlation coefficient of 0.830 showed a strong hereditary influence for posterior facial height (PFH). When correlation coefficient of PFH was compared with that of anterior facial height (AFH), it was found that hereditary influence was more for PFH than for AFH. This correlates with the findings of the study of Lundstorm and McWilliam[17] who found a strong genetic control for vertical parameters. Findings by Carels et al[18] also support this. When compared, mandibular dimension was found to be affected much more by genetic factors than craniofacial dimensions, which support the findings of Arya et al.[19] Posterior vertical dimensions showed more correlation to hereditary influences than anterior vertical dimensions. The heritability of vertical and horizontal dimensions was found to be very similar.

All the nine variables studied were under strong genetic influence. However, there was a minor component of environmental influence also. This suggests that etiology of most of the dentoalveolar as well as skeletal malocclusions is multifactorial, which means that interaction of various factors produces the observed outcome.

CONCLUSION

Based on the findings of this study, we have come to the conclusion that although growth and development of craniofacial complex is under multifactorial control, there is a predominant role for genetic influences. In the present scenario, to understand the genetic background of a patient in a better way with respect to the malocclusion as well as its response to treatment, further genetic studies are necessary. Developments in the field of genetics enabling identification of particular genes responsible for a malocclusion and a better understanding of the influence of genetic factors in response to environmental factors, which include orthodontic treatment also, can bring improvement in treatment outcome as well as its long-term stability.

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