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ORIGINAL RESEARCH

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Assessment of 2D:4D in Subjects with Anteroposterior Mandibular Dysplasia

Sridhar Premkumar, Bhuvaneswari Gurumurthy

ABSTRACT

Objectives: To compare 2D:4D ratio which is determined by testosterone levels with patients having orthognathic, retrognathic and prognathic mandibles.

Materials and methods: The study was performed at Chennai, on 320 subjects of which, 60 subjects (32 males and 28 females) had retrognathic mandible; 55 subjects (25 males and 30 females) had prognathic mandible and 205 subjects (98 males and 107 females) had normal mandible. All the subjects had a normal maxilla and were in the age group of 18 to 25 years. 2D:4D ratio was determined using the photocopies of the ventral surface of right hand made with vernier calipers of 0.01 mm accuracy. Statistical analysis was undertaken using Student's t- test, ANOVA test and TukeyHSD test.

Results: (i) Low 2D:4D is seen in subjects with mandibular prognathism, (ii) Among females, low 2D:4D is seen only in prognathic mandible.

Conclusion: These findings highlight the fact that testosterone plays an important role in mandibular growth. Thus 2D:4D, a least invasive and reproducible procedure can be used as an early marker for mandibular progathism, and as a diagnostic tool in correlating the mandibular growth with causal relations between hormones and craniofacial development.

Keywords: 2D:4D and mandible, 2D:4D and prognathic mandible.

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INTRODUCTION

Orthodontic diagnosis is an important factor in determining the success of any orthodontic treatment. Therefore, it is imperative for the orthodontist to have knowledge about the role of systemic factors, namely, the hormones in determining growth and development.

Sex steroids influence the growth of face and cranial base, and also, the eruption of teeth. The role of sex hormones on bone growth might be responsible, either by regulation of Homeobox genes, 'a' and 'd' in growth of digits, or independently of such genes. It has been established that 2D:4D is affected by exposure to sex hormones; most importantly the testosterone prenatally, and hence, it has been suggested as a tool to measure the levels of prenatal testosterone.[1]

2D:4D is the ratio of lengths between the second digit (index finger) and the fourth digit (ring finger) of the hand. It is measured from the bottom crease where the finger joins the palm to the tip of the finger. 2D:4D is determined as early as 2 years of age and does not change thereafter and remains constant.[2] The ratio on right hand is more responsive than that on the left and hence, is commonly used.[3]

The effect of hormones on bone growth can be substantiated by the fact that they serve as general epigenetic factors, contributing to craniofacial growth and development. Testosterone contributes to growth by acting as general epigenetic factor and also through the intrinsic genetic factor, Homeobox genes. The purpose of this work was to examine and compare the styles of 2D:4D in patients with discordant anteroposterior mandibular growth.

The decreased length of mandible is represented as retrognathic and increased as prognathic.

SUBJECTS

The subjects were 320 patients, who reported to the outpatient department for treatment, belonging to Dravidian population. Of this, 205 participants (98 males and 107 females) were with normal mandible. Sixty individuals (32 males and 28 females) had retrognathic mandible and 55 individuals (25 males and 30 females) prognathic mandible. The participants were aged between 18 and 25 years and had orthognathic or normal maxilla. None of the participants had (i) history of trauma to teeth, jaws, injury to fingers and orthodontic treatment, (ii) obesity, (iii) left handedness, (iv) medically compromised status (v) endomorphism and ectomorphism. The study was conducted after obtaining written and oral consent expressing their willingness to volunteer. The study was approved by the Institutional Ethical Committee, in January 2011.

MATERIALS AND METHODS

The sagittal relationships between the maxilla and the mandible of the participants were determined by cephalometric parameters using lateral cephalometric radiographs. The subjects were divided into three categories as normal, retrognathic and prognathic mandible based on the cephalometric findings. The cephalometric parameters used for normal maxilla were SNA = 82 ± 2°, SN-ANS = 87 ± 4° and FH-NA = 85 ± 4°. The cepahalometric criteria for considering mandible as orthognathic were SNB = 80 ± 2°, SN-Pog = 79 ± 2° and FH-NPog = 85 ± 5°. Increased and decreased values denoted prognathic or retrognathic mandible respectively.

We measured digit length from photocopies of the ventral surface of the right hand with vernier calipers measuring to 0.01 mm. The 2D:4D was calculated from digit length measured from the basal crease of digit proximal to palm, to the tip of the digit. It is known that this measurement can be made with high repeatability from photocopies of the hand and it correlates strongly with 2D:4D calculated from total digit length measured from X-rays of fingers.[4]

The data obtained were statistically analyzed using Student's t-test, ANOVA test and Tukey honestly significant difference test.

RESULTS

As found in previous studies (e.g. Manning et al 1998; Manning 2002), the males had a lower mean 2D:4D as females, using Students' t-test. The mean 2D:4D in normal mandible, retrognathic mandible and prognathic mandible were 0.983 ± 0.042, 0.982 ± 0.032 and 0.945 ± 0.031 (Table 1). Among the females, those with prognathic mandible had a lower ratio than the other two conditions of mandibular growth (Figs 1A and B). On comparing prognathic mandible with normal mandible, statistical significance was noted (p = 0.000) in the overall population (Table 2). The ratio was statistically significant when retrognathic mandible was compared with prognathic mandible, in males (p = 0.004). Among the females, statistical significance was noted when normal mandible was compared with prognathic mandible (p = 0.000) (Table 3).

DISCUSSION

Sex steroids stimulate growth centers of bones, either directly or indirectly through local production of insulin-like growth factor-1 (IGF-1) or other growth factors. They stimulate osteoclast differentiation indirectly[5] or directly[6] and endochondral ossification.[7] Male hormones have a powerful effect on bone extension by exhibiting a general stimulatory effect, resulting in coupling of the proliferation and differentiation processes essential for normal skeletal

Table 1: Mean 2D:4D ratio in normal mandible, retrognathic mandible and prognathic mandible

Class	*Sex*				*Overall*	
	Male		*Female*			
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*
I	0.963	0.037	0.996	0.041	0.983	0.042
II	0.982	0.035	0.981	0.029	0.982	0.032
III	0.944	0.033	0.947	0.029	0.945	0.031

Table 2: Comparison of 2D:4D ratio among normal mandible, retrognathic mandible and prognathic mandible

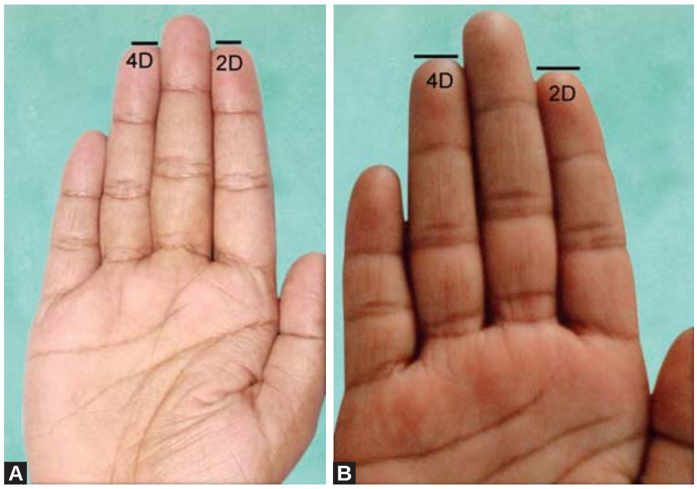
Dependent variable	*Class (I)*	*Class (J)*	*Mean difference (I-J)*	*Std. error*	*p*
2D:4D	I	II	0.0017	0.0081	0.974
		III	0.0382*	0.0081	0.000**
	II	I	– 0.0017	0.0081	0.974
		III	0.0364*	0.0092	0.000**
	III	I	– 0.0382*	0.0081	0.000**
		II	– 0.0364*	0.0092	0.000**

*The mean difference is significant at the 0.05 level, **p < 0.01

Table 3: Comparison of 2D:4D among normal mandible, retrognathic mandible and prognathic mandible between males and females

Dependent variable	*Male*					*Female*		
	Class (I)	*Class (J)*	*Mean difference (I-J)*	*Std error*	*p*	*Mean difference (I-J)*	*Std error*	*p*
2D:4D	I	II	– 0.0189	0.0109	0.200	0.0147	0.0122	0.458
		III	0.0187	0.0112	0.225	0.0493*	0.0116	0.000**
	II	I	0.0189	0.0109	0.200	– 0.0147	0.0122	0.458
		III	0.0377*	0.0113	0.004**	0.0346	0.0144	0.052
	III	I	– 0.0187	0.0112	0.225	– 0.0493*	0.0116	0.000**
		II	– 0.0377*	0.0113	0.004**	–0.0346	0.0144	0.052

* The mean difference is significant at the 0.05 level, ** p<0.01



Figs 1A and B: 2D:4D pattern seen in females (A) normal mandible, (B) prognathic mandible

growth. In an experiment with the animals, it was observed that the secretion levels of sex hormones changed the internal structure of mandibular condyle, which is a mandibular growth site and center.[8] One of the striking characteristics of mandibular growth disharmony is that it is strongly sex dependent,[9] which may be related to the differences in sex hormonal levels, notably, testosterone. This necessitates a noninvasive way of measuring the testosterone levels, preferably at a younger age itself.

Testosterone has a wide range of prenatal extragenital effects which include development of digits and CNS.[10] Prenatal testosterone can be held responsible for organization of certain features of the face, like bones (jaws and cheek bones) that will in turn be activated at puberty and remain relatively stable thereafter.[11] The combined effect of prenatal testosterone on postnatal growth has been proved.[12] A trait which is set *in utero* would provide an alternative way to investigate a testosterone linked etiology for altered anteroposterior growth of mandible.

The ratio between length of second and fourth digit (2D:4D) correlates with *in utero* testosterone. Physical features closely linked to fetal testosterone levels are more likely to be related to 2D:4D. The Homebox genes, 'Hoxa and d' control the differentiation of urogenital system and, indirectly influence the prenatal production of testosterone and the development of digits.[1] This ratio is sexually dimorphic[3] with women tending toward longer ratios than men. The relative digit length is established as early as 14th week of intrauterine life.[13]

2D:4D has been reported to be negatively correlated with testosterone and positively associated with estrogen in adults.[3] Testosterone stimulates prenatal growth of the fourth digit while estrogen promotes the growth of the second digit.[14] A low 2D:4D (4D longer than 2D) indicates a uterine environment high in testosterone and low in estrogen, and is most often seen in males. On the other hand, a high 2D:4D marks a uterine environment low in testosterone and high in estrogen, and is usually found in females. Jamison et al, in 1993 have hypothesized a positive correlation between prenatal and adult testosterone levels.[15]

The overall craniofacial growth presents large variations between individuals. In this population, difference in the 2D:4D among the three different patterns of mandible indirectly indicate the testosterone alterations.The variations in the ratio between the males and females in the overall population uphold the fact, that it is a dimorphic trait and matches with that of the ratios found in various other studies performed with 2D:4D. The variation found in the mean ratios has added to the differences that already exist between normal, retrognathic and prognathic mandible. Though there is not much difference in the ratios between normal and retrognathic mandible, the significant reduction in the ratio of prognathic mandible explains that the testosterone level in that condition is much higher than the other two. When the testosterone level increases above normal, there is increased growth as seen in mandibular prognathism. However, the ratio in retrognathic mandible is similar to that of the normal mandible. The restricted growth of mandible causing a retrognathic mandible may be because of the other factors influencing the mandibular growth and do not have a testosterone related etiology. Through this study, we have found that significantly low 2D:4D is associated with mandibular prognathism. This relationship is likely to reflect the fact that children with low 2D:4D have mandible that shows tendency for prognathism.

CONCLUSION

The present study has demonstrated that 2D:4D is decreased in subjects with prognathic mandible. Although numerous studies have assumed that the 2D:4D is linked with facial symmetry, no data is available on how this testosterone may contribute to facial asymmetry, leading to anteroposterior dysplasia of the mandible as one of its effects. The finding here, also puts in appearance that low 2D:4D may serve as one possible marker for mandibular prognathism. It can also contribute to the etiological relationships of the hormones in craniofacial syndromes and growth discrepancies. Thus, 2D:4D provides a window into the prenatal life of an infant which not only tells us about the behavior, probability of disease occurrence, intelligence, reproductive abilities, but also shows the possibilities and probabilities in the pattern of mandibular growth. Further research is needed in this context to understand the interactions between testosterone and 2D:4Ds that are involved in the bone growth and maturation, mostly the mandible leading to malocclusion.

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ABOUT THE AUTHORS

Sridhar Premkumar (Corresponding Author)

Professor, Department of Orthodontics, Tamil Nadu Government Dental College and Hospital, Chennai, Tamil Nadu, India e-mail: dr_premsridhar@yahoo.co.in

Bhuvaneswari Gurumurthy

Intern, Department of Orthodontics, Tamil Nadu Government Dental College and Hospital, Chennai, Tamil Nadu, India