**IGF - I : A LEGITIMETE SKELETAL MATURITY INDICATOR**

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**ABSTRACT :** Assessment of skeletal maturity is critical to the modality and timing of treatment of various skeletal abnormalities. Since lateral cephalometric radiographs are routinely taken for orthodontic patients, using the cervical vertebrae from these radiographs to assess skeletal maturity has been especially appealing to orthodontists. Apart from additional radiographic exposure and subjectivity of staging the x-rays, an inherent disadvantage of cervical vertebral stages and hand wrist radiographs is that the final stage of development does not necessarily indicate the completion of growth. In addition lateral tipping of a vertebrae by about 30° may lead to disappearance of curvature on an x-ray which accounts for the absence of curvature on the inferior borders of otherwise mature looking vertebrae. Keeping in view the radiographic artefacts associated with the lateral cephalograms which may mislead the practitioners, it was decided to conduct a study on 13 female and 10 male subjects to assess the skeletal maturity by testing serum insulin-like growth factor 1 (IGF-I) levels. Results from this study indicate that the IGF-I levels are low in the pre-pubertal cervical skeletal stages, rise sharply to their peak in puberty, and decline to approach pre-pubertal levels after puberty.

**KeyWords :** Skeletal maturity, IGF-I, residual growth

**INTRODUCTION**

In 1957, Salmon and Daughaday discovered IGF-I, or insulin - like growth factor I as a mediator of the growth hormone (GH) functions. IGF-I was first detected in serum and is a circulating growth hormone-dependent factor, the level of which correlates with sexual maturity. It is used to diagnose growth hormone deficiencies and excess. Precise assessment of IGF-I is useful diagnostic tool for determining GH status as its levels do not fluctuate throughout the day unlike the GH levels. IGF-I is measurable is serum, urine and saliva. The levels of IGF-I in saliva are considerably low, nearly less that 1% of serum levels. Additionally, measurements taken from Salivary IGF-I are likely to be inaccurate because of contamination with gingival
fluid or blood. Serum IGF-I measurement is a relatively new, minimally invasive technique and the samples are stable at room temperature for up to two weeks. Accurate determination of skeletal maturity is crucial to the timing of various orthodontic, orthognathic, and dental implant decisions. The current use of cervical vertebral stages and hand-wrist radiographs are subjective techniques that involve additional radiographic exposure and lack the ability to determine the intensity of the growth spurt. The use of the radiographs may bias the results as curvatures of about 300° disappear on an x-ray due to lateral tipping of visibly mature vertebrae. Moreover, studies have shown that chronologic age and dental age are both poor predictors of the pubertal growth spurt. Hence serum IGF-I levels could play a role in the determination of the pubertal status of the patient and as an indicator of residual growth.

AIM AND OBJECTIVES

1. To correlate IGF-I levels to the cervical vertebral stages for assessing skeletal maturity in males and females.
2. To compare the mean IGF-I levels with Cervical vertebrae maturation Index (CVMI)

MATERIAL AND METHODS

A. Sample :

The present study consisted of twenty three subjects – 13 females and 10 males - from the regular OPD of the Department of Orthodontics, D J College of Dental Sciences & Research, Modinagar. The inclusion criteria were patients between the ages of 9 and 23 years, who were either to begin orthodontic treatment, were in treatment, or were in post treatment follow-up. Exclusion criteria were systemic illness, growth abnormality, and bleeding disorders. The Study was cleared by the Institutional Ethical Committe.

B. Procedure :

Blood samples were collected by using kits supplied by Super Diagnostics. The samples were stored in an ice box (Fig I) and sent to the laboratory, where they were centrifuged (Fig II & III) to separate the serum (Fig IV). The samples were subsequently enzyme – immunoassayed for IGF - I levels at Super Religare Diagnostics, NewDelhi.

Lateral cephalograms were obtained as part of the standard treatment diagnostic protocol. The operators who staged the cephalograms were blinded about each patients age, pubertal status and IGF-I levels. The cervical staging technique as described by Baccetti was used to stage the vertebrae. Curvatures were defined when the depth of the curvature was 1 mm or greater, and a millimetric rules was used to measure the posterior and inferior borders to determine vertebral shape (Fig.V). IGF-I levels were then subsequently correlated to cervical vertebrae stages.

C. Statistical Analysis :

Analysis of variance (ANOVA) and Spearman’s RANK correlation coefficient were used to compare mean IGF - I levels corresponding to the cervical skeletal maturation stages. Correlations were performed to determine the IGF-I levels relating to the various cervical skeletal maturation stages. (Graph I).

Figure I : Blood samples stored in an ice box

Figure II : The Centrifuge

Figure III : Samples being centrifuged
RESULTS

The IGF - I levels in females were higher than in males at all ages. Table I & II Show the correlation of cervical staging with IGF-I levels in males and females respectively. The male subjects exhibited the highest (299.20 ng/ml) and the lowest values (135.36 ng/ml) of IGF-I with a mean of 212.31 ng/ml at the cervical vertebrae stages CS4 and CS6 respectively. Female subjects exhibited the highest (310.69 ng/ml) and the lowest (126.3 ng/ml) values at CS4 and CS6 with a mean value of 208.52 ng/ml. The mean value of IGF-I from the pooled data of the total sample was highest at CS4 with levels of 304.94 ng/ml and lowest at CS6 with 135.32 ng/ml (Table III). The results showed a positive correlation between IGF-I levels and cervical vertebral staging from CS1 to CS4 by showing a gradual increase from CS1 to CS2 (164.96 to 181.52 ng/ml) a sharp increase from CS2 to CS3 (295.12 ng/ml) a gradual increase in CS4 (304.94 ng/ml). A negative correlation was seen thereafter in CS5 222.20 and CS6 (and 135.32 ng/ml) to approach the pre-pubertal levels (Graph I). The Pearson linear correlation coefficient of +0.68(p>.01), whereas the correlation from CS1 to CS4 showed a correlation coefficient from CS4 to CS6 was -0.676 (p>.01). In CS6, IGF-I levels correlated negatively with chronologic age and the number of months reported to have passed since the onset of puberty with correlation coefficients of -0.531 and -0.522, respectively.

Table I : IGF - I levels correlated to the CVS in males

<table>
<thead>
<tr>
<th>C.S</th>
<th>n (%)</th>
<th>Mean IGF (ngm/mL)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>160.30</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>177.10</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>289.60</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>299.20</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>135.36</td>
</tr>
</tbody>
</table>

Table II : IGF - I levels correlated to the CVS in females

<table>
<thead>
<tr>
<th>C.S</th>
<th>n (%)</th>
<th>Mean IGF (ngm/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.38</td>
<td>169.62</td>
</tr>
<tr>
<td>2</td>
<td>15.38</td>
<td>185.94</td>
</tr>
<tr>
<td>3</td>
<td>15.38</td>
<td>300.64</td>
</tr>
<tr>
<td>4</td>
<td>15.38</td>
<td>310.69</td>
</tr>
<tr>
<td>5</td>
<td>15.38</td>
<td>222.20</td>
</tr>
<tr>
<td>6</td>
<td>15.38</td>
<td>144.3</td>
</tr>
</tbody>
</table>

Table III : Average pooled data to correlate cervical staging to mean IGF - I levels

<table>
<thead>
<tr>
<th>C.S</th>
<th>n (%)</th>
<th>Mean IGF (ngm/mL)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>16.66</td>
<td>164.96</td>
</tr>
<tr>
<td>2</td>
<td>16.66</td>
<td>181.52</td>
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<td>3</td>
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<td>304.94</td>
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<tr>
<td>5</td>
<td>8.33</td>
<td>222.20</td>
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<tr>
<td>6</td>
<td>25</td>
<td>135.32</td>
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DISCUSSION

Cervical vertebrae stages and hand-wrist radiographs currently used to identify peak mandibular bone growth lack the ability to determine the intensity of the growth spurt and its cessation. Additionally, the radiographic artefacts associated with lateral cephalograms justifies the need to look at serum IGF-I levels as a skeletal maturity indicator. Both GH and IGF-I are important factors for pubertal growth spurt as demonstrated by Mohan et al. IGF-I levels do not fluctuate and it has an added benefit of being directly stimulated by androgens in the pre-pubertal stages. It has also been found to play a principal role in local and systemic regulation of longitudinal bone growth. The results of the present study are similar to that of the study conducted by Juul A which reported mean serum IGF-I concentration increased slowly in pre-pubertal children from 80 to 200 g per litre with a further steep increase during puberty to approximately 500 g per litre. Post-pubertal circulating IGF-I levels continued to fall to approximately 250 g per litre at 25 years of age. The study conducted by Mohamed Masoud on Saudi Arabian population reported a sharp increase in IGF-I levels from CS3 to peak levels at CS5 (208.68 ug/L to 406.82 ug/L) whereas there was a decline between CS5 and CS6 (199.75 ug/L at CS6). In contrast the present study indicated maximum levels of IGF-I in CS4.

In the present study, two female subjects, both at CS6 stage of their skeletal maturity presented contrasting IGF-I levels of 126.3 and 143.3 ng/ml. This variance was essentially due to the differences in the number of years post-pubertal which was five and three years respectively. This indicated the negative correlation of IGF-I to cervical skeletal maturity with increasing chronologic age. One of the male subjects at CS6 stage exhibited high levels of IGF-I (222.2 ng/ml). This increased level of serum IGF-I is indicative of residual growth in this male subject.

CONCLUSION

1. IGF-I levels have a positive correlation with cervical skeletal maturity from the pre pubertal to the late pubertal stages and a negative correlation from the late pubertal to the post pubertal stages.
2. IGF-I may be used as a feasible skeletal maturity indicator and finds applicability as a virtual indicator of residual growth.

A multi-centered longitudinal study, with a larger sample size in the future could help to tabulate more authentic data.

BIBLIOGRAPHY