SKELETAL MATURITY ASSESSMENT BY CORRELATING SALIVARY INSULIN LIKE GROWTH FACTOR-1 WITH MIDDLE PHALANX OF THIRD FINGER STAGING

DISSERTATION

Submitted to The Tamil Nadu Dr. M.G.R Medical University
in partial fulfillment of the requirement for the degree of

MASTER OF DENTAL SURGERY

BRANCH V

ORTHODONTICS AND DENTOFACIAL ORTHOPEDICS

2016 - 2019

CERTIFICATE

This is to certify that the dissertation entitled **"Skeletal Maturity Assessment by Correlating Salivary Insulin like Growth Factor-1 with Middle Phalanx of Third Finger Staging"** is a bonafide record of the work done by **Dr. Shreevidhya Vijayan,** a Post graduate student during the period 2015-2018 under my guidance and supervision. This dissertation is submitted in partial fulfilment of the requirements for the award of **Master of Dental Surgery** on Branch V (Orthodontics and Dentofacial Orthopedics) under **The Tamil Nadu Dr. M.G.R Medical University, Guindy, Chennai.** It has not been submitted (partial or full) for the award of any other degree or diploma.

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I hereby declare that this dissertation **"Skeletal Maturity Assessment by Correlating Salivary Insulin like Growth Factor-1 with Middle Phalanx of Third Finger Staging"** is a bonafide record of work undertaken by me during the period 2015-2018 as a part of post graduate study. This dissertation, either in partial or in full, has not been submitted earlier for the award of any degree, diploma, fellowship or similar title of recognition.

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LIST OF ABBREVIATIONS

MP3	:	Middle phalanx of third finger
IGF-1	:	Insulin - Like Growth Factor 1
PHV	:	Peak height velocity
IOPA	:	Intraoral periapical radiograph
SMI	:	Skeletal maturation index
ELISA	:	Enzyme-linked immunosorbent assay
ANOVA	:	Analysis of variance
CVM	:	Cervical vertebrae maturation
CVMI	:	Cervical Vertebrae Maturity Index
RIA	:	Radio Immuno assay
pM	:	picometer
mm	:	millimeter
ml	:	milliliter
C	:	Celsius
Pg	:	picogram
CS	:	Cervical stage
IGFBP	:	Insulin like growth factor binding protein
SPSS	:	Statistical Package for Social Sciences
Yrs	:	Years
GH	:	Growth hormone
HIV	:	Human Immunodeficiency Virus
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ABSTRACT

ABSTRACT

Aims and objectives:

This invivo study aims to assess skeletal maturity by measuring salivary IGF-1 levels. The objectives were i) to assess whether salivary IGF-1 levels can be used as a skeletal maturity indicator; ii) to compare the mean IGF -1 levels at different stages of skeletal maturity using MP3 staging.

Materials and method:

MP3 radiographs and saliva samples of 30 patients divided into 3 Groups (10 in each group) between the age range 7-18 yrs were collected. Saliva would be aspirated from the floor of mouth using a 3ml micropipette by use of gentle suction and then it would be transferred to individual centrifugable collector. Saliva samples from each patient would be collected and transferred in a standard thermal box with icepacks maintained at temperatures between 2˚-8˚ C to the Biogenix Research centre, Trivandrum on the collection day itself. Before the assay, thawed saliva would be centrifuged for 10minutes at 3000rpm at 4˚ C and a clear, non-viscous sample would be analyzed. The samples would then be analyzed by human IGF-1 Enzyme-Linked Immunosorbent Assay kits (ELISA) specific for salivary IGF-1 protein structure. The absolute concentration of IGF-1 in unit sample (pg/ml) would be found out and recorded.

For capturing the digital radiographic image, the subjects would be instructed to place his/her left hand with palm downward on a flat table, marked for placing the middle finger. The middle finger was centered on a 31 x 41 mm periapical dental x-ray film parallel with the long axis of film. The cone of the dental

radiograph machine was positioned in slight contact with the middle phalanx of the third finger, perpendicular to the IOPA film. All MP3 radiographs would be classified according to Modified MP3 staging criteria by R. Rajagopal, Sudhanshu Kansal by two independent blindfolded examiners.

Result

The study showed that the mean of IGF-1 values of pubertal group was significantly higher than that of post pubertal and prepubertal group. Also Post HOC test values showed that the comparison between prepubertal and pubertal group showed statistically significant higher mean of pubertal group as compared to prepubertal group. Comparison between prepubertal and post pubertal group showed statistically significant higher mean of postpubertal group as compared to pre pubertal group. But when comparing pubertal and postpubertal group no statistically significant difference between the two groups was found.

Conclusion

In the present study the salivary IGF-1 levels follow the same pattern of a sharp acceleration to a peak in puberty and a more gradual fall thereafter. The levels obtained in prepubertal stage was lowest, and in pubertal group was highest. Whereas the levels at post pubertal stages showed almost same value as pubertal. Longitudinal data are necessary to confirm the usefulness of this technique in predicting the timing, intensity, and the end of growth spurt.

Keywords:

Insulin- like growth factor 1, Saliva, MP3 radiographs.

INTRODUCTION

INTRODUCTION

One of the most important factor in orthopaedic and myofunctional treatment planning is the growth potential of the patient.[1] In devising a treatment plan, an orthodontist considers not only dental and facial relationships but also the amount of jaw growth anticipated and whether this would aid in correcting any sagittal discrepancies. Hence the timing of the commencement of treatment is of paramount importance. Growth modification is advocated as an early intervention in treatment of growing patients. It would appear that functional appliance will be more successful during a period of rapid growth. Peak Height Velocity is the period where maximum rate of growth occurs. To identify stages of skeletal growth certain parameters in the form of chronologic age, dental assessment, sexual maturation, voice changes and increase in body height has been suggested in the past.[2] However, studies have shown poor correlation between pubertal growth spurt and chronologic and dental age. Other classic methods include use of hand-wrist radiographs and cervical vertebra maturational stages[2]. Newer possibilities are provided with biochemical markers representing agents that are directly involved in bone growth and remodeling. They could be measured from various biologic fluids such as blood, saliva, and urine, there by overcoming the subjectivity associated with radiographs.[3]

In 1957, IGF-1 (Insulin-like growth factor-1) was discovered by Salmon and Daughaday as a mediator of growth hormone function. Since then, IGF-1 has been extensively studied and shown to play a principal role in systemic and local regulation of prenatal and postnatal longitudinal bone growth[4]. Insulin-like growth factors (IGFs), originally isolated from plasma, are GH-dependent factors that

stimulate growth in cartilage and many other tissues. IGF-1 is measurable in serum(in which it was first detected) as well as in urine and saliva.[1,3]

Saliva can be collected noninvasively, which eliminates the risk of infection for the healthcare worker, avoidance of needle stick injuries, acceptable to those with needle phobias and furthermore transmission of HIV via saliva is unlikely. Complexity in identification of landmarks and subjectivity of staging the x-rays are an inherent disadvantage of cervical vertebrae maturation (CVM) and hand wrist radiographs. Also, because of the radiation exposure involved with these two methods, x-rays cannot be performed if needed for reevaluation. IGF-1 (Insulin like growth factor-1), a polypeptide hormone, is considered to be a mediator of growth hormone function. IGF-1 stimulates growth locally as well as systemically. An increase in level of IGF-1 has been correlated with pubertal growth spurt. IGF-1 levels have been proposed as an alternative method to detect pubertal growth spurt timing in comparison to Cervical Vertebrae Maturity Index (CVMI) staging in different populations.[5] Also, IGF-1 levels have been correlated with hand wrist skeletal maturation pattern by Masoud et al.[6] A marked positive correlation was observed between IGF-1 levels and hand-wrist stages from prepubertal stages to the stages of highest velocity of mandibular growth, whereas there was a moderate negative correlation between IGF-1 levels and hand-wrist radiograph stages from the levels associated with peak mandibular growth to the final hand-wrist stages.[5]

Skeletal growth has been shown to be closely related to GH status. IGF-I is a useful diagnostic tool for determining GH status as its levels do not fluctuate throughout the day unlike the GH levels.[2] IGF- 1 has been reported to play an important role in growth of long bone as well as in growth of mandibular condyle.[7]

These hormonal markers are a better alternative to radiological skeletal maturity indicators in certain conditions such as in residual mandibular growth which is accelerated growth seen in some individuals who had attained radiographic skeletal maturity and also in some individuals who before attaining pubertal growth stage shows accelerated growth which is termed as juvenile acceleration.

In this study we are measuring salivary IGF – 1 levels and the mean IGF-1 levels at various stages of skeletal maturity. The values are then compared with skeletal maturity stages identified with MP3 staging. In this way trying to achieve a correlation of IGF-1 levels in saliva and the stages of growth including growth spurt.

AIMS & OBJECTIVES

AIMS AND OBJECTIVES

Aim:

To assess skeletal maturity by measuring salivary IGF-1 levels.

Objectives:

- To assess whether salivary IGF-1 levels can be used as a skeletal maturity indicator.
- To compare the mean IGF-1 levels at different stages of skeletal maturity using MP3 staging.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Marshall WA et al (1969) [55] Variations in pattern of pubertal changes in girls. The girl's curve begins to rise more steeply at about the age of 10.5 and the boy's at about 12.5. This inflection represents the adolescent spurt in stature which occurs, on average, about 2 years earlier in girls than in boys. The spurt occurs at different ages among children in any population, whereas the mean age may vary considerably from one population to another.

Chapman SM (1972)[56] Ossification of the adductor sesamoid and the adolescent growth spurt. In his study it was concluded that the adductor sesamoid bone is found to occur regularly in accordance with the development of the first metacarpophalangeal joint. Onset of ossification of the sesamoid takes place at the time the adolescent spurt in statural height begins. The duration of the latter is observed to coincide with the duration of the sesamoid development. Commencing epiphyseal- diaphyseal fusion of the proximal phalanx at the thumb joint is found to mark the completion of the two maturational events which have been related.

Bowden BD (1976) [45] Much of the treatment for growth anomalies, including the orthodontic correction of malocclusions, is dependent upon the intensity of skeletal growth and therefore, indirectly upon the prediction of the precise stages of skeletal growth. Because the postnatal skeletal growth rate in primates is dominated by the adolescent phase, so its prediction has assumed increasing importance in clinical orthodontics.

Grave KC et al (1976) [40] Fourteen ossification events in the hand and wrist were studied in relation to the age of peak growth velocity in body height in fifty-

two boys and thirty-six girls. The subjects were aborigines enrolled in a longitudinal growth study. The results indicate that the ossification events can be used by the orthodontist to assess a child's growth activity. The accelerative phase of the adolescent growth spurt is accompanied by epiphyseal widths reaching diaphyseal widths in the fingers and radius and by ossification of the pisiform and hamate Stage 1. Peak growth velocity occurs at about the time of epiphyseal capping in the fingers and radius and ossification of the sesamoid and hamate Stage 2. The decelerative phase of growth is indicated by epiphyseal union in the third finger, progressively from distal to proximal phalanges, and in the radius.

Roche AF et al (1976) [50] The reliability of skeletal maturity assessments of the hand-wrist (Greulich-Pyle) was determined using 60 roentgenograms that were assessed twice by each of two observers. There was a reduction in both the comparability and replicability of bone specific ages; these were particularly unreliable for the carpals, especially the hamate and triquetral. The ranges of bone-specific ages within groups of bones were increased markedly.

Houston WJB et al (1979) [49] The prediction of the timing of the pubertal growth spurt could be helpful in planning some types of orthodontic treatment. It has been suggested that information from hand-wrist radiographs could be used for this purpose. Insufficient attention has been paid to the distinction between ossification events and bone stages. In the present paper it is shown that the uncertainty of prediction of the timing of the peak height Velocity from ossification events in the hand and wrist, is generally large and so they are of limited value for this purpose.

Hägg U & Taranger J (1980) [38] Longitudinal data on adolescent growth in height and skeletal development of the hand and wrist were collected as part of a

prospective study of the growth and development of 212 randomly selected Swedish urban children. The onset , highest value and attaining completion of the pubertal growth spurt were defined on the unsmoothed incremental curve of height. The analysis of the relationship in lime between the growth events and the skeletal stages showed that these stages can be used to indicate which period of adolescent growth an individual has reached

Houston WJB (1980) [44] The roles of ossification events, bone stages and bone ages in the prediction of the timing of the pubertal growth spurt are examined using data from the Harpenden growth study . Radius ulna and short bone score (RUS) bone age is more closely related to the timing of peak height velocity than is carpal age, and it is the most convenient and reliable way of estimating the age at peak height velocity, although the confidence limits of such a prediction are appreciable. It may be very misleading to assume that the growth spurt will be advanced or delayed to the same extent as ossification events or bone age and the appropriate regression equations must be used.

Riad-Fahmy D et al (1982) [12] in their study to evaluate Steroids in Saliva For Assessing Endocrine Function shows storage of saliva samples before assay poses no problems since steroid concentrations in saliva show no significant differences on storage at - 20° C for periods ranging from 6-9 months or at 4° C for about 7 days. Problems of viscosity, which restrict processing of freshly collected saliva, maybe resolved by deep-freezing the samples in a freezing mixture, and storage of samples at -20 C for prolonged periods is acceptable. Patients find little difficulty in salivating directly into disposable tubes, providing adequate volumes for determining a steroid hormone profile in approximately 10 minutes. Assay of

samples collected 1 to 2 hour intervals during waking hours provides an accurate assessment of baseline endocrine activity. Since smaller aliquots can be collected at 15 or at 10 minute interval, salivary sampling could well be more useful than that of either plasma or urine in short term dynamic tests.

Wikland KA (1986) [33] A study of 31 children with short stature was initiated in 1982. They received subcutaneous injections of pituitary hGH, 0.1 IU/kg/day; no adverse effects were seen and none of the patients acquired antibodies. Only the results of the first year are presented, as final height has not yet been attained. A high growth response was seen in 29 of the 31 children; they experienced an initial rise of IGF-1, IGF-2, alkaline phosphatase and procollagen III. The best response was obtained in the child with the lowest levels of endogenous pulsatile hGH secretion.

Sierra AM (1987)[37] A comparison of radiographic methods of assessing skeletal and dental maturation, and an evaluation of the correlations among the various maturity indicators in the 8–12 year age range.

Costigan DC et al (1988)[3], performed a study in human saliva to detect free IGF I and II , which showed that mixed saliva could be stored at room temperature for up to 24 hours without altering its IGF concentration and without any damage or loss of structural stability. Normal and stimulated mixed saliva had no significant difference in IGF -1 concentration. Salivary IGF concentration was not influenced by flow rate. It was neither affected by time of day nor proximity to food intake as opposed to diurnal variation in serum growth hormone concentration. It was found that human saliva contains both insulin like growth factor-1 and insulin like growth

factor-2 but no significant binding proteins, and that salivary IGF-1 levels correlated with the plasma growth hormone levels. Mixed saliva had globular proteins precipitated by freezing / thawing. The lower limits of detection of IGF-1 and 2 were 0.7ng/ml and 1.2 ng/ml respectively. Iodinated IGF added to saliva was not degraded. IGF-1 level was measurable from all the saliva samples of the subjects, while IGF-2 was not detected in few saliva samples. Human saliva contained no significant insulin like growth factor binding protein. Salivary IGF-1 concentrations did not change with increasing salivary flow rates above normal, with time of day, or with storage at room temperature for upto 24 hours before freezing. Salivary IGF-1 levels reflect the growth hormone status of the donor.

Guler HP et al (1989)[16] insulin like growth factor I and II in humans. Using the half-lives of the tracer studies and the levels of the different molecular weight forms of IGF in serum, the production rates for IGF-I and -II were calculated to be 10 mg and 13 mg per day.

Darendeliler F, et al (1990)[28] they had performed a retrospective analysis of pubertal parameters of 134 children with isolated growth hormone insufficiency on growth hormone treatment and compared them to the standards of tanner and a recent longitudinal study done in United Kingdom. The results suggest that growth hormone accelerates the pubertal spurt.

Moore RN et al (1990)[48] The purpose of this study was to assess the relevance of hand-wrist radiographs to craniofacial growth and clinical orthodontics. Serial annual cephalometric and hand-wrist radiographs and standing height measurements were obtained from a sample of 47 girls (ages 10 through 15 years)

and 39 boys (ages 11 through 16 years) from the Bolton-Brush data base. The results of the study indicated that statural height and hand-wrist skeletal maturation in both sexes are significantly related.

Hauspie R et al (1991) [27] The following interpretation of skeletal maturity is proposed. The onset of the spurt depends, ultimately, upon some maturational processes going on in the hypothalamus and shows little relationship with the advancement of the long bones at that time. Therefore, the spurt can begin at any level of skeletal maturity within the range normally observed at the chronological age at which it happens to begin in the individual. Peak height velocity, on the other hand, is reached when skeletal maturity is sufficiently advanced for testosterone to change its influence upon the bones from one which consists in stimulating cartilage growth to one which consists in stimulating epiphyseal fusion. Therefore, peak height velocity is bound to occur within a range of skeletal maturity much more restricted than that within which take-off can occur.

Ryan J et al (1992) [34] Insulin-like growth factor 1 (IGF 1) concentrations in mixed saliva samples, collected from a normal population (n = 327, ranging in age from birth to adolescence), were determined by radioimmuno assay. Salivary IGF 1 concentrations remained steady over a 24 hour period when collected at basal rates, but were diminished in saliva samples collected at a maximally stimulated flow rate. A similar pattern was observed for males and females, when IGF 1 levels in saliva were plotted as a function of age. The pattern was that of low levels seen in childhood, the values increased with age, maximum possible values during puberty and going back to near adult levels in adolescence. The IGF-1 in saliva level differed from plasma measurement in three ways: 1) salivary IGF 1 concentrations

(70 +/- 50 pM) were 100- to 200-fold less than plasma IGF 1 levels; 2) salivary IGF 1 levels in age-matched male and female samples were not different outside of pubertal influences; 3) salivary IGF 1 levels in neonates were highly variable with concentrations ranging up to pubertal concentrations. The study provides salivary IGF 1 reference data for a pediatric population.

Clemmons DR (1992) [24] in their studies showed the adherence to cell surfaces appears to be one important property of the IGF proteins that results in their ability to potentiate or inhibit growth. Likewise, phosphorylation of Insulin like growth factor binding protein-1 on serine residues appears to be a structurally modifying change which results in altered growth regulation.

Ryan J et al (1992) [61] Salivary insulin-like growth factor-I originates from local synthesis. Insulin-like growth factor-I (IGF-I) is a growth hormone-dependent growth factor found in its highest concentrations in plasma. It is also measurable in saliva. The origins of salivary IGF-I concentrations were studied. Intracardial administration of Sprague-Dawley rats with 125I-labelled IGF-I and subsequent analysis of plasma and saliva samples by exclusion gel chromatography and SDS-PAGE, followed by autoradiography, demonstrated the apparent inability of IGF-I to cross from the plasma pool through to saliva. 125I-Labelled IGF-I was not chromatographed immediately before injection, resulting in administration of free iodide along with the iodinated peptide. This free iodide was demonstrable in saliva, indicating that movement of substances from plasma to saliva was measurable using the levels of 125I activity administered. Free iodide in saliva was not contributed to by 125I-labelled IGF-I degradation since 125I-labelled IGF-I was shown to be stable in saliva over 24 h. These data indicated that IGF-I in saliva is produced locally.

Identification of a 4.7 kb IGF-I mRNA transcript in rat parotid salivary gland was consistent with IGF-I synthesis within that tissue.

Argente J et al (1993)[15] The normal levels of IGF following extraction, IGF binding proteins and high infinity GH binding proteins couldn't be established in infancy or childhood. This study tried to find correlation with serum IGF-I, IGF-II, IGF-binding proteins and GH binding protein in 600 normal Spanish children. Insulin like growth factor-I levels in serum increases gradually during childhood in both males and females, with a peak increase in puberty and significant decline during adulthood. The pubertal peak occurs approximately 2 years earlier in girls than in boys. In contrast, serum IGF-II levels remain stable throughout childhood, showing no pubertal peak. In boys, there is a significant decline in IGF-II levels during adulthood. Serum IGFBP- 3 levels show a pattern similar to that of IGF-I, with a significant increase during childhood and a significant decline during adulthood in both males and females. In contrast, serum IGFBP-1 levels decrease dramaticallv during childhood in both boys and girls. A significant decline in serum GH-binding protein levels is observed between prepubertal and pubertal children of both sexes. There is a close linear correlation between the sum of serum IGF-I plus IGF-II levels versus serum IGFBP-3. In contrast, there is a nonlinear correlation between serum IGF-I versus serum IGFBP- 3 (concave curve) as well as between serum IGF-II and serum IGFBP- 3 (convex curve). A negative correlation was found between serum IGFI versus IGFBP-1 as well as between the sum of serum IGF-I plus IGF-II versus IGFBP-1, but not between serum IGF-II and IGFBP-1. These data emphasize that when these tests are performed in the clinic, their interpretation should be based upon age- and sex-specific criteria.

Fielder PJ et al (1996) [25] All treatments increased serum IGF. The molecular size distribution of IGFBP-3 in recombinant human GH-treated rats was similar to that of normal rats (IGFBP-3 in the 150K mol wt range), due to rhGH increasing serum acid-labile subunit (ALS), but was altered by rhIGF-I (IGFBP-3 in the 200-300K and 44K mol wt range). In a Growth hormone-deficient animal, restoring the IGF/IGFBP-3/Acid labile subunit axis towards normal is associated with greater growth promotion.

Bonjour JP (1997) [32] During growth, protein undernutrition results in reduced bone mass and strength. Genetic defect impairing the production of IGF-I markedly reduces bone development in both length and width. The serum level of IGF-I markedly increases and then decreases during pubertal maturation in parallel with the change in bone growth and standing height velocity. The impact of physical activity on bone structure and strength is enhanced by increased dietary protein consumption. This synergism between these two important environmental factors can be observed in prepubertal boys, thus modifying the genetically determined bone growth trajectory.

So LLY (1997) [43] The maturation status of each hand and wrist bone age of 117 12-year-old Southern Chinese girls was studied using the Greulich and Pyle Atlas (1959) Method. The bone ages were found to range from 12.14 years (scaphoid) to 12.80 years (middle phalanx). , Skeletal maturation of 102 of these Southern Chinese girls was correlated to the developmental status of their permanent dentition. The skeletally below average group had on average 1.1 more erupted permanent teeth than the skeletally advanced group.

Abdel- Kader HM et al (1998)[17] illustrated a clinical study to provide a simple and practical method to assess the pubertal growth spurt stages of a subject by recording MP3 stages with the dental periapical radiograph and the standard dental x-ray machine. The high degree of clarity of the radiographs, the ease with which the MP3 stages can be interpreted, the simplicity of the method, and the significantly low patient radiation exposure highly recommends it as a practical and sensitive technique that meets the requirements of the clinicians.

Vogelsang F et al (2000)[41] Derived from a model based segmentation algorithm for hand radiographs proposed in their former work, here they present a method to determine skeletal maturity by an automated analysis of regions of interest (ROI). These Regions of interests including the epiphyseal and carpal bones, which are most important for skeletal maturity determination.

Floyd B. (2000)[63] This study uses longitudinal height records of girls in two urban and one rural area in Taiwan. Results support the view that rapid socioeconomic change in Taiwan influenced the relationship between the timing and intensity of adolescent growth in stature. Children in the more stable environments in both urban areas had patterns of correlations typical of population samples from developed countries. The most atypical correlations in both areas were found among those who likely experienced the greatest improvement in socioeconomic status during primary school.

Sato K et al (2001)[42] Mandibular growth prediction provides important information for planning treatment and for evaluating occlusal stability after treatment. This study compared the predictive error of several methods by using skeletal maturity indicators. Twenty-two longitudinal cephalograms and hand-wrist

radiographs of female subjects (average initial age, 8.3 years; final age, 18.4 years) were collected to construct the prediction formula. Another 22 female subjects (initial age, 10.8 years; final age, 18.6 years) were examined to compare differences between the predicted values and the actual values. Mandibular total length (condylion-gnathion) at the final stage can be accurately predicted by (1) the ossification events of the third middle phalanx and the radius, (2) the growth potential method, (3) the growth percentage method, (4) the multiple regression method, and (5) the growth chart method.

Rogol AD et al (2002) [30] in their review demonstrated the hormonal regulation of the growth spurt and the alterations in body composition depend on the release of the gonadotropins, leptin, the sex-steroids, and growth hormone. It is very likely that interactions among these hormonal axes are more important than their main effects, and that alterations in body composition and the regional distribution of body fat actually are signals to alter the neuroendocrine and peripheral hormone axes. These processes are merely magnified during pubertal development but likely are pivotal all along the way from fetal growth to the aging process.

Krailassiri S et al (2002) [36] The purpose of this study was to investigate the relationship between the stages of calcification of various teeth and skeletal maturity stages among Thai individuals. The study subjects consisted 139 male subjects and 222 female subjects ranging in age from 7 years to 19 years. A total of 361 hand-wrist and panoramic radiographs were obtained and analyzed. The tooth development of the mandibular canines, first and second premolars, and second and third molars were assessed according to the Demirjian's system. Skeletal age and skeletal maturity stages were determined from hand-wrist radiographs by using the method outlined in the atlas

of Greulich and Pyle and the Fishman's system, respectively. The Spearman rank order correlation coefficient revealed significant relationships ($r = 0.31–0.69$, $P < .01$) between dental calcification stages and skeletal maturity stages.

Baccetti T et al (2002)[53] elaborated a different method or version of cervical vertebral maturation method that was used for assessing mandibular growth. The study aimed to provide a version of the Cervical Vertebral Maturation (CVM) method for the detection of the peak in mandibular growth based on the analysis of the second through fourth cervical vertebrae in a single cephalogram. The new CVM method presents with five maturational stages (Cervical Vertebral Maturation Stage [CVMS] I through CVMS V, instead of Cvs 1 through Cvs 6 in the former CVM method). The peak in mandibular growth occurs between CVMS II and CVMS III, and it has not been reached without the attainment of both CVMS I and CVMS II. CVMS V is recorded at least two years after the peak. The advantages of the new version of the CVM method are that mandibular skeletal maturity can be appraised on a single cephalogram and through the analysis of only the second, third, and fourth cervical vertebrae, which usually are visible even when a protective radiation collar is worn.

Madhu S et al (2003) [10] Assessment of skeletal maturity is an integral part of interceptive diagnosis and treatment planning. The present day methods of skeletal maturity assessment like the hand-wrist radiographs or cervical vertebrae radiographs are expensive, require elaborate equipment and accounts for high radiation exposure, especially for growing children. The present study was thus undertaken to provide a simple and practical method of skeletal maturity assessment using the developmental stages of the middle phalanx of the third finger (MP3) as

seen on an IOPA film taken using a standard dental x-ray machine. The results of the study showed that this simple method was highly reliable and could be used as an alternative method to assess the skeletal maturity of growing children.

Floyd B (2003) [64] Patrilineal family values, family planning and variation in stature among taiwanese six-year-olds**.** This study first addresses the extent of son preference as inferred from family composition data for 772 Taiwanese first-graders born in the mid-1970s in two socioeconomically distinct communities in Taipei, Taiwan. It then uses linear regression to consider whether the model criteria help account for statural variation among children in each study area when controlling for differences in measurement age, parental education and housing. With respect to family composition and gender preference, available evidence was consistent with previous surveys. This study shows that the environmental and socioeconomic factors can greatly influence timing and pattern of growth in a particular ethnic group.

Flores-Mir C et al (2004) [9] a study evaluating use of skeletal maturation based on hand-wrist radiographic analysis as a predictor of facial growth concluded that the total vertical and horizontal facial growth velocity is related to skeletal maturity index determined by analysis of hand-wrist radiographs. Maxillary and mandibular growth velocities are related to skeletal maturity, but the correlations are less robust than those for overall facial growth velocity.

Suzuki S et al (2004) [7] a study to assess administration of insulin like growth factor-1 locally and showed accelerated growth of mandibular condyle in mature rats concluded that the local injection of IGF-I into mature condyle

seemed to reactivate the process of endochondral bone formation and induced actual bone growth in mature condyle. The effects of local administration of IGF-I on the condyle were analyzed in the 15 week-old mature rats using a vital staining technique. Histological changes, such as an increase in the thickness of the cartilaginous layer and a decrease in bone area in the subchondral cancellous bone layer, were observed in the IGF-I-treated group. In addition, the measurement of labeling lines produced by vital staining revealed that the amount of endochondral bone growth in the experimental group was greater than that in the control group. These results indicate that the local injection of IGF-I induced not only temporary histological changes, but also actual skeletal growth of the condyle.

Juul A et al (2004) [35] they in their study concluded that easily dissociable and ultrafiltrated free IGF-I serum levels are increased in boys with normal and precocious puberty and suggest that the increased free IGF-I serum concentration in puberty primarily reflects changes in total concentrations of IGF-I and IGFBPs secondary to increased growth hormone secretion, but that it is not influenced by changes in Insulin like growth factor binding protein-3 proteolysis.

Delatte M et al (2004) [62] Growth stimulation of mandibular condyles and femoral heads of newborn rats by IGF-I. Primary and secondary cartilage differ in embryonic origin and are generally considered to have a different mode of growth. However, few experimental studies exist that directly compare the two types of cartilage and their growth regulation. The regulation of cartilage growth is a complex mechanism involving growth factors like insulin-like growth factor-I (IGF-I). The purpose of this study was to compare the growth of mandibular condyles of 4-day-old rats with that of femoral heads in vitro and to analyze the

effects of IGF-I. IGF-I increased glycosaminoglycan synthesis of both condylar and femoral cartilage. However, only the DNA synthesis of the mandibular condyles was significantly increased by IGF-I while that of the femoral heads was not affected. It is concluded that IGF-I stimulates growth of both secondary condylar cartilage and primary femoral cartilage. The mandibular condyle appears to be more sensitive to IGF-I than the femoral head, which may partly be due to the different developmental stage.

Flores-Mir C et al (2004)[9] elaborated use of Skeletal Maturation Based on Hand-Wrist Radiographic Analysis as a Predictor of Facial Growth. It was concluded that (i) the overall horizontal and vertical facial growth velocity is related to skeletal maturity index determined by analysis of hand-wrist radiographs. (ii) Maxillary and mandibular growth velocities are related to skeletal maturity, but the correlations are less robust than those for overall facial growth velocity. (iii) Skeletal maturity analysis of hand-wrist radiographs for use in predicting facial growth velocity should include bone staging as well as ossification events.

Baccetti T et al (2005) [54] outlined the cervical vertebral maturation method for assessing optimal treatment timing in Dentofacial Orthopedics. The study introduces a further modified version of the Cervical Vertebral Maturation (CVM) method for the detection of the peak in mandibular growth, based on the analysis of the second through fourth cervical vertebrae in a single cephalogram. The new clinically improved CVM method is comprised of six maturational stages (cervical stage 1 through cervical stage 6, ie, CS1 through CS6). CS1 and CS2 are prepeak stages; the peak in mandibular growth occurs between CS3 and CS4. CS6 is recorded at least 2 years after the peak. The use of the CVM technique would enable

to identify the optimal treatment time for a series of dentoskeletal disharmonies in all three planes of space.

Yeung HY et al (2006) [26] Interestingly, IGF-I polymorphism affects the curve severity of adolescent idiopathic scoliosis (AIS) though it was not associated with onset of adolescent idiopathic scoliosis per se. It specifies that IGF-I may be a disease modifying gene. The significance of insulin-like growth factor-1 in skeletal growth makes it a good candidate gene which would play a role in the documented association of rapid growth with curve progression in adolescent idiopathic scoliosis.

Uysal T et al (2006) [39] The aims of this study were (1) to investigate the relationship between chronologic age and maturation of cervical vertebrae, (2) to identify the relationship between chronologic age and maturation stage evaluated by hand-wrist radiographs, and (3) to determine whether the maturation of cervical vertebrae correlates with maturation indicated by hand-wrist radiographs in a Turkish population. The cervical-vertebrae maturation stages are clinically useful maturity indicators of the pubertal growth period Turkish subjects.

Masoud M et al (2008) [4], a study to assess skeletal maturity by using insulin like growth factor-1 in serum shows blood spot IGF-1 could be used as a skeletal maturity indicator and might be useful in detecting residual mandibular growth in young adults. Blood spot IGF-1 levels are low in prepubertal cervical skeletal stages, rise sharply to their peak in late puberty, and decline to approach prepubertal levels after puberty. Our results showed that IGF-I levels were still relatively high in many subjects who were at cervical stage-6 and had supposedly

completed their growth. In that stage, we found that IGF-I levels were negatively correlated with time since the onset of puberty. Thus, IGF-I might be a good indicator of residual mandibular growth.

Chen LL et al (2008)[52] performed a study to establish a quantitative cervical vertebral maturation (CVM) system for adolescents with normal occlusion. An equation that can accurately estimate the maturation of the cervical vertebrae was established: CVM stage = –4.13 + 3.57 x H4/W4 +4.07 x AH3 / PH3+0.03 x @2. It was concluded that the quantitative CVM method is an efficient, objective, and relatively simple approach to assess the level of skeletal maturation during adolescence.

Gabriel DB et al (2009)[11] a study to evaluate cervical vertebrae maturation method documented that CVM staging involved subjective errors and has a decreased reproducibility. Furthermore, subtle changes in the vertebra are difficult to assess when the radiographs are taken in incorrect posture and posturing correctly is cumbersome for patients as well as radiographers. Based on these results, the CVM method cannot be recommended as a strict clinical guideline for the timing of orthodontic treatment

Masoud M et al (2009) [6], a study to find any correlation between that of hand –wrist skeletal maturity assessment and insulin like growth factor1 in serum showed The pattern that mean IGF-1 levels followed at various skeletal stages mirrored the mandibular growth velocity pattern that Fishman observed, with a sharp acceleration to the peak late in puberty and a more gradual decline thereafter. In the postpubertal stage, IGF-1 levels were higher in the younger subjects and decreased as they aged. The findings demonstrate that IGF-1 levels start below 200 mg/L at the prepubertal

stage. The acceleration stage had IGF-1 levels that varied tremendously, with a mean of 235 mg/L. IGF-1 levels rose sharply between the acceleration stage and the high growth velocity stage to a mean of 359 mg/L. There was a mild decline in IGF-1 levels from the high growth velocity stage to the deceleration stage to a mean of 329 mg/L. The difference in IGF-1 levels between these two stages was not statistically significant, indicating that IGF-1 levels probably stay high for some time after the peak levels are reached. However, both stages were significantly higher than the postpubertal stage, with a mean IGF-1 level of 234 mg/L.

Kaur N et al (2010) [29] 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.

Bala M et al (2010) [47] The purpose of the study was to assess skeletal age using MP3 and hand-wrist radiographs and to find the correlation amongst the skeletal, dental and chronological ages. Skeletal age from MP3 and hand-wrist radiographs shows high correlation in all the age groups for both sexes. Females were advanced in skeletal maturation than males. Skeletal age showed high correlation with dental age in 12-14 years age group. Chronological age showed inconsistent correlation with dental and skeletal ages.

Singh S et al (2010)[22] highlighted timing of Myofunctional Appliance Therapy. It was concluded that the maximum response to myofunctional therapy can

be expected in patients during the stages 3 to 4 of cervical vertebrae maturation index, i.e., during or slightly after the pubertal peak.

Morris JM et al (2012) [31] There have been many attempts to correlate dental development with skeletal growth. The relationship is generally considered to be moderate at best. However, there is evidence that hand-wrist radiographic interpretation of remaining growth can be augmented by taking into account the developing dentition. In addition, the practicality of evaluating routine dental radiographs and avoiding additional radiation is advantageous. To this point, no system has been described to match apical development by Demirjian's stages and compare it to skeletal development and remaining growth. This study reviewed articles pertinent to the relationship between developing teeth and skeletal maturity and remaining growth, and a system is proposed to give practitioners an additional assessment for growth and development.

Hegde DY et al (2012) [46] To evaluate the reliability of the digital radiograph of the middle phalanx of the third finger (MP3) in skeletal maturity assessment, The correlation determined between the MP3 stages and cervical vertebrae maturity index (CVMI) stages, the peak-wise distribution of the MP3 stages, and the correlation between the MP3 stages and the chronological age were found to be highly significant.

Ishaq RAR et al (2012)[19] elaborated Insulin-like growth factor I as a biologic maturation indicator. The mean value of IGF-1 got at each cervical maturation stage was different statistically from the mean values at the other stages. The highest mean values were observed in stage 4, followed by stage 5 in males and

stage 3 in females. The study stated that IGF-I serum level is a reliable maturation indicator that could be applied in orthodontic diagnosis.

Gupta S et al (2012) [21] To investigate the validity of Insulin like Growth Factor -1(IGF-1) as a skeletal maturity indicator by comparing serum IGF-1 levels with the stages in cervical vertebral maturation (CVM) and in the middle phalanx of the third finger (MP3). Serum IGF-1 levels in females correlated well with skeletal maturity determined by CVM and MP3 stages and increased sharply during early pubertal stages followed by a decrease in late puberty. In addition it was hypothesised that serum IGF-1 testing can be undertaken as a preliminary screening test in patients in whom the orthodontist predicts the possibility of using myofunctional appliance but in whom the chronologic age is not suggestive for a growth modification therapy. The study highlights the fact that the serum IGF-1 estimation can be a valuable tool in assessing skeletal maturation.

Jain S et al (2013)[18] outlined insulin – like growth factor-1 levels in serum as a clinical tool for optimal orthodontic treatment timing. Serum IGF-1 levels showed good association with skeletal age in male subjects.

Sinha P et al (2014)[1] , did a study about assessment of skeletal maturity by correlating Insulin like growth factor-1 with hand-wrist radiographs, showed that IGF-1 levels were significantly higher in pubertal stage as compared to prepubertal and postpubertal stages. The levels of postpubertal stage declined to almost the same level as prepubertal stage. Concluding that IGF-1 levels might prove to be a valuable skeletal maturity indicator.

Nayak S et al (2014) [2] in their study observed the correlation between insulin-like growth factor-1 in saliva and quantitative cervical maturational stages of skeletal maturity was assessed and concluded that salivary IGF- I levels or its secretion rate can be used as an indicator of skeletal growth. Salivary IGF-I levels and its secretion rate follow the same pattern of a sharp acceleration to a peak late in puberty and a more gradual fall thereafter. Levels of salivary IGF-I and its secretion rate are lowest at the accelerated velocity stage and gradually increase to a peak level in the high velocity stage. There is gradual decrease in salivary IGF-I and its secretion rate levels in the deceleration velocity and completing velocity stages. Salivary IGF-I can be used as a marker of residual mandibular growth.

Masoud MI et al (2015) [20] Predicted annual growth rate changes in mandibular length and total anterior facial height using IGF-1 together with cervical stage, skeletal classification, and gender . This method which combines IGF-1 levels with information that is readily available to clinicians could be used to predict the timing and intensity of the growth spurt.

Tripathi T et al (2017) [51] studied biochemical markers as skeletal maturity indicators. Precise estimation of the stage of skeletal growth is essential for the formulation of accurate treatment planning and employing orthodontic intervention through functional orthopedic appliances for the shortest time possible yielding stable results. Along with clinical and radiological techniques, biochemical markers play an important role in the growth assessment for differential treatment application. Isolation and characterization of various systemic and local factors having a significant role in the growth process provided the sight to tap their potential to be used as skeletal maturity indicators. Different methods for the

assessment of biomarkers in use are enzyme‑linked immunosorbent assay, radioimmunoassays, and immunoradiometric assays. These methods of assessment of biochemical markers are noninvasive and when interpreted correctly give useful information.

Jain N et al (2017)[5] made a study to evaluate Serum IGF-1, IGFBP-3 and their ratio concluded that IGF-1 and IGFBP-3 can serve as a potential biochemical indicator for assessment of skeletal maturity. Mean serum IGF-1 levels were found to be highest (403.3 ± 12.3 ng/ml) at CVMI3 stage of CVMI. The posthoc test revealed a significant difference in IGF-1 levels between all stages of CVMI, thereby indicating a specific range of IGF-1 levels for a specific skeletal stage. Mean serum IGFBP-3 levels were found to be highest (5186.8 ± 1384.2 ng/ml) at CVMI4 stage of CVMI. The mean serum IGFBP-3 levels at CVMI4 were found to be significantly higher than the levels at all other CVMI stages except CVMI3 stage.

MATERIALS & METHODS

MATERIALS AND METHODS

Study Setting:

The present study was carried out in the Department of Orthodontics and Dentofacial Orthopedics, Sree Mookambika Institute of Dental Sciences, Kulasekharam after obtaining clearance from the Institutional Ethical Committee Board.

Study period:

Study period is 12 months.

Study design:

This is a Cross sectional comparative study.

Study subjects:

Patients attending Sree Mookambika Institute of dental science for orthodontic treatment who fulfilled the inclusion criteria were randomly selected and explained about the procedure and study was conducted in Department of orthodontics and dentofacial orthopaedics.

Total 30 individuals who fulfilled the inclusion criteria formed the study group.

Number of groups to be studied: Three

Detailed description of the groups:

Group I : which included subjects in MP3F through MP3FG stage, was considered Prepubertal

Group II : which included subjects in MP3G stage, was considered Pubertal

Group III : included subjects MP3H through MP3I stage, was considered Postpubertal

Sample size of each group: 10 each for all Groups

Total sample size of the study: Total Sample -30

SAMPLING:

Sample Size[13] , n = $\frac{2Z^2S^2}{d^2}$

Z =Z value associated with alpha=1.644

S = $\frac{S_1+S_2}{2}$

S_1 = Standard deviation of I group = 0.3

S_2 = Standard deviation of II group = 0.9

d= absolute precision = 0.5

N=9.7 (sample size taken 30).

EXCLUSION CRITERIA:

- Subjects suffering from any serious illness like growth abnormality, systemic diseases and disorders like liver disorders.
- Bleeding disorders.
- History of any accident or injury to the face, hand and wrist region.

INCLUSION CRITERIA:

- Age: 7 to 18 years (both females and males).
- Healthy subjects with information about birth date, whom were classified using Modified MP3 staging by R. Rajagopal, Sudhanshu Kansal criteria[14] and assigned to each group.

MATERIALS:

1. Micropipette (3ml transfer graduated pipettes graduated 0.5ml)
2. Eppendorf tubes. (3ml)
3. Human IGF-1 Enzyme-Linked Immunosorbent Assay kits (ELISA) specific for salivary IGF-1 (Immuno Tag- GB Bioscience, USA)
4. No 2 size IOPA film (31x41 millimeter, Kodak E-speed).
5. Standard thermal box
6. Tracing sheet (Garware Economy)
7. 0.7 mm lead pencil.
8. X-ray viewer.
9. Lead Aprons with Thyroid shield

EQUIPMENTS

1. Standard dental radiographic machine (Villa – Sistemi Medicali, Explor-X 70, Italy)
2. Centrifuger – Remi R12 refrigerated centrifuge
3. Incubator – Remi C12

PROCEDURE IN DETAIL:

The parents and subjects undergoing study was explained about the research and their informed consents was obtained for using their saliva samples and MP3 radiographs for the study. Ethical approval was obtained from the research ethical committee of the institute.

Patients were asked to rinse mouth with 300ml of plain water, and saliva was aspirated from the floor of mouth using a 3ml micropipette by use of gentle suction

and then it was transferred to individual centrifugable collector (provided by the centre). Saliva samples from each patient were collected and transferred in a standard thermal box with icepacks maintained at temperatures between 2˚-8˚ C to the Biogenix Research centre, Trivandrum on the collection day itself. Before the assay, thawed saliva was centrifuged for 10minutes at 3000rpm at 4˚ C and a clear, non-viscous sample was analyzed. The samples were then analyzed by human IGF-1 Enzyme-Linked Immunosorbent Assay kits (ELISA) specific for salivary IGF-1 protein structure. The absolute concentration of IGF-1 in unit sample(pg/ml) was found out and recorded.

For capturing the digital radiographic image, the subjects were instructed to place his/her left hand with palm downward on a flat table, marked for placing the middle finger. The middle finger was centered on a 31 x 41 mm periapical dental x-ray film parallel with the long axis of film. The cone of the dental radiograph machine was positioned in slight contact with the middle phalanx of the third finger, perpendicular to the IOPA film. All MP3 radiographs were classified according to Modified MP3 staging criteria by R. Rajagopal, Sudhanshu Kansal by two authors. Two independent examiner (senior lecturer from department of oral medicine and orthodontics) were blinded about the patient's age, pubertal status and IGF-1 levels during the staging of MP3 radiograph.

Modified MP3 staging by R. Rajagopal & Sudhanshu Kansal

MP3-F stage: Start of the curve of pubertal growth spurt

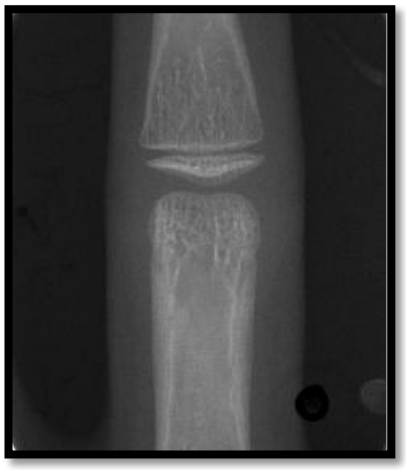


Fig.1 MP3-F stage

Features observed:

i) Epiphysis is as wide as metaphysis.

ii) Ends of epiphysis are tapered and rounded.

iii) Metaphysis shows no undulation.

iv) Radiolucent gap (representing cartilaginous epiphyseal growth plate) between epiphysis and metaphysis is wide.

MP3-FG stage: Acceleration of the curve of pubertal growth spurt

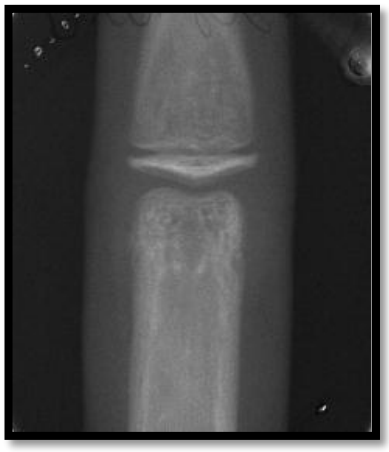


Fig 2. MP3-FG stage

Features observed:

i) Epiphysis is as wide as metaphysis.

ii) Distinct medial and/or lateral border of epiphysis forms line of demarcation at right angle to distal border.

iii) Metaphysis begins to show slight undulation.

iv) Radiolucent gap between metaphysis and epiphysis is wide.

MP3-G stage: Maximum point of pubertal growth spurt

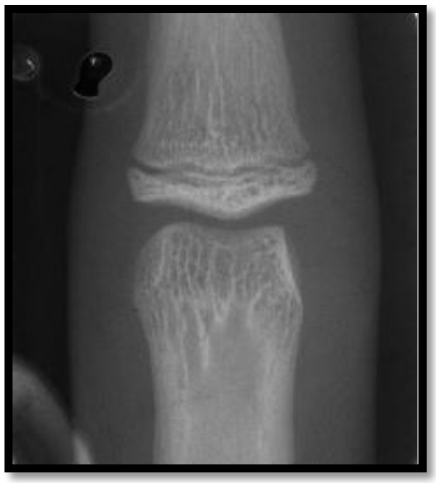


Fig 3. MP3-G stage

Features observed:

i) Sides of epiphysis have thickened and cap its metaphysis, forming sharp distal edge on one or both sides.

ii) Marked undulations in metaphysis give it "Cupid's bow" appearance.

iii) Radiolucent gap between epiphysis and metaphysis is moderate.

MP3-H stage: Deceleration of the curve of pubertal growth spurt

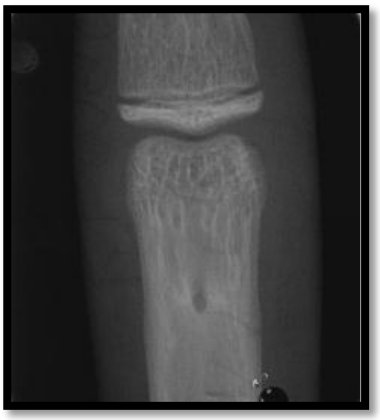


Fig. 4: MP3-H stage

Features observed:

i) Fusion of epiphysis and metaphysis begins.

ii) One or both sides of epiphysis form obtuse angle to distal border.

iii) Epiphysis is beginning to narrow.

iv) Slight convexity is seen under central part of metaphysis.

v) Typical "Cupid's bow" appearance of metaphysis is absent, but slight undulation is distinctly present.

vi) Radiolucent gap between epiphysis and metaphysis is narrower.

MP3-HI stage: Maturation of the curve of pubertal growth spurt

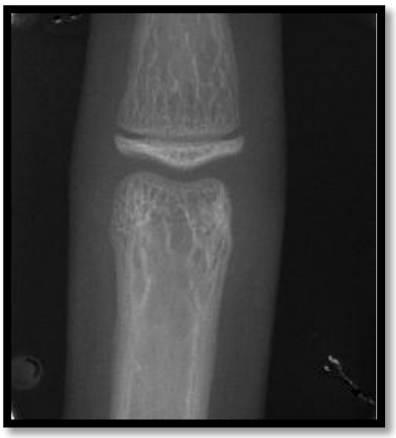


Fig. 5: MP3-HI stage

Features observed:

i) Superior surface of epiphysis shows smooth concavity.

ii) Metaphysis shows smooth, convex surface, almost fitting into reciprocal concavity of epiphysis.

iii) No undulation is present in metaphysis.

iv) Radiolucent gap between epiphysis and metaphysis is insignificant.

MP3-I stage: End of pubertal growth spurt

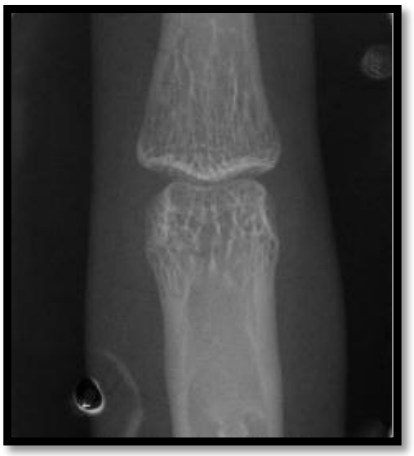


Fig. 6: MP3-I stage

Features observed:

i) Fusion of epiphysis and metaphysis complete.

ii) No radiolucent gap exists between metaphysis and epiphysis.

iii) Dense, radiopaque epiphyseal line forms integral part of proximal portion of middle phalanx.

Based on Modified MP3 staging[14], the 6 stages are regrouped into 3 phases. The first phase, including MP3F through MP3FG stage, was considered Prepubertal. The second phase, which included MP3G stage, was considered Pubertal. The third phase, including MP3H through MP3I stage, was considered Postpubertal.

The mean IGF-I concentration in mixed saliva was 2.3 ± 0.3 (±SE) ng/mL (/xg/L), and their mean plasma IGF-I level was 315 ± 27 ng/mL (/xg/L).[3]

The pattern of salivary IGF 1 concentrations, like the concentrations in plasma, are age and sex dependent, peaking during puberty, before declining in adolescence. However, unlike plasma IGF 1, where female values are higher than male; salivary IGF 1 concentrations are similar in both sexes.

The IGF-1 levels at the pubertal stage were significantly higher than the prepubertal and post pubertal stages.[1]

Salivary IGF-1 levels and its secretion rate follow the same pattern of a sharp acceleration to a peak late in puberty and a more gradual fall thereafter.[2]

COLOR PLATES

Fig 7: No 2 size IOPA film

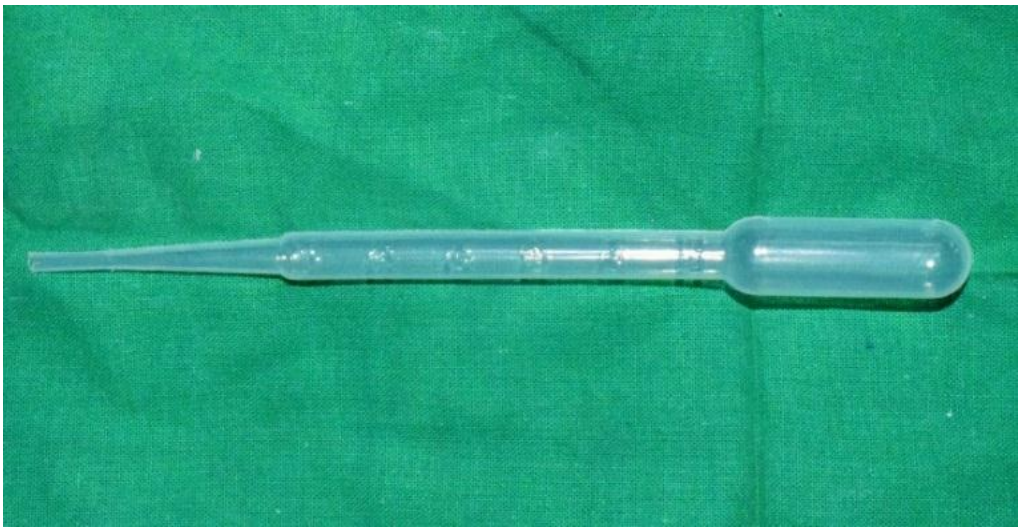


Fig 8: Micropipette (3ml)

Fig 9: Eppendorf tubes (3ml)

Fig 10: Standard Thermal box

Fig 11: Gel Frost packs

Fig 12: Lead Aprons with Thyroid shield

Fig 13: 0.7 mm lead pencil

Fig 14: 0.003-inch matte acetate tracing sheet

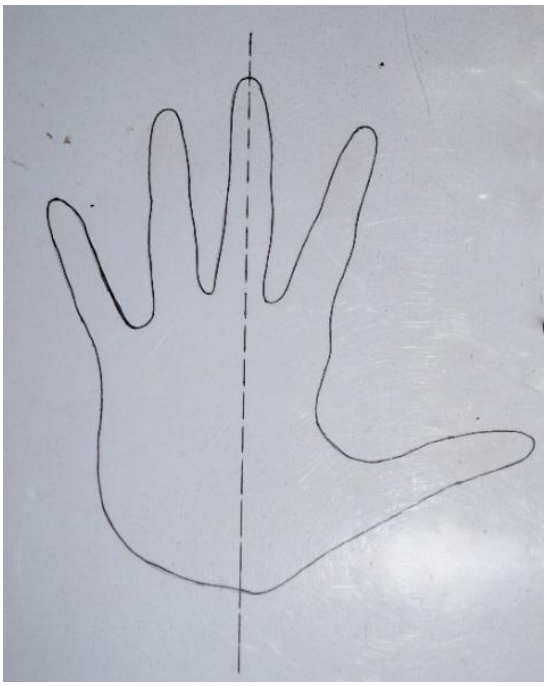


Fig 15 : Marking to place hand

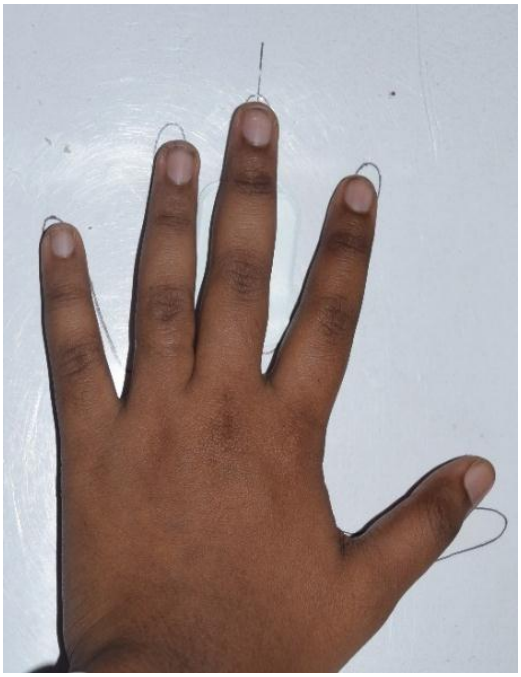


Fig 16: Left hand kept on the marked surface

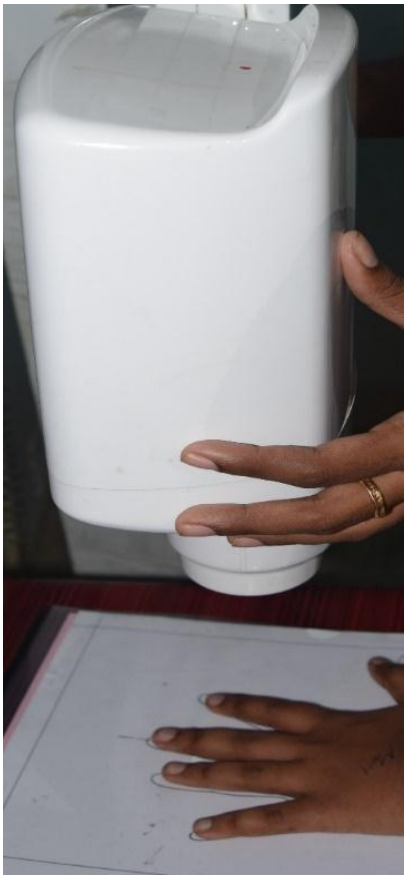


Fig 17: Standard dental radiographic machine (Villa – Sistemi Medicali Explor-X70, Italy)

Fig 18: X-ray Viewer

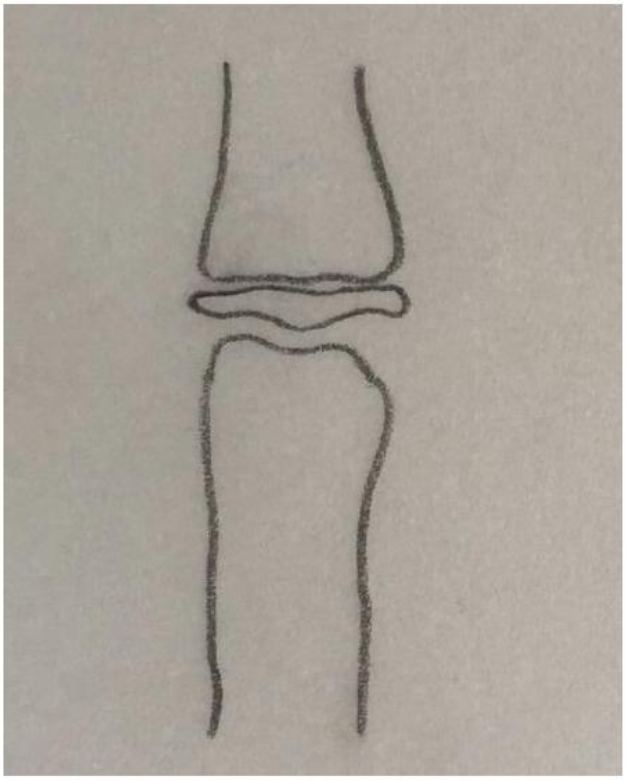


Fig 19: MP3 tracing

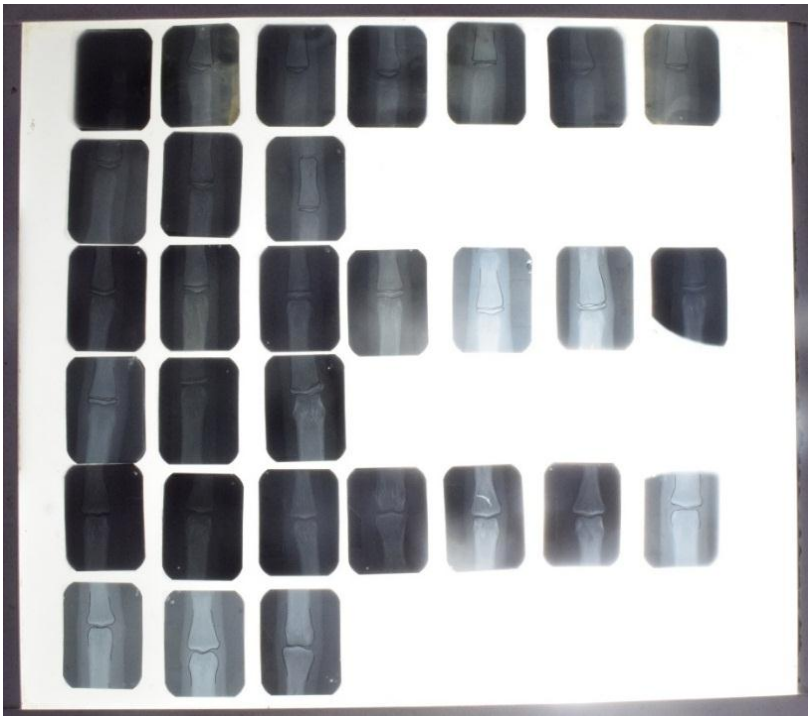
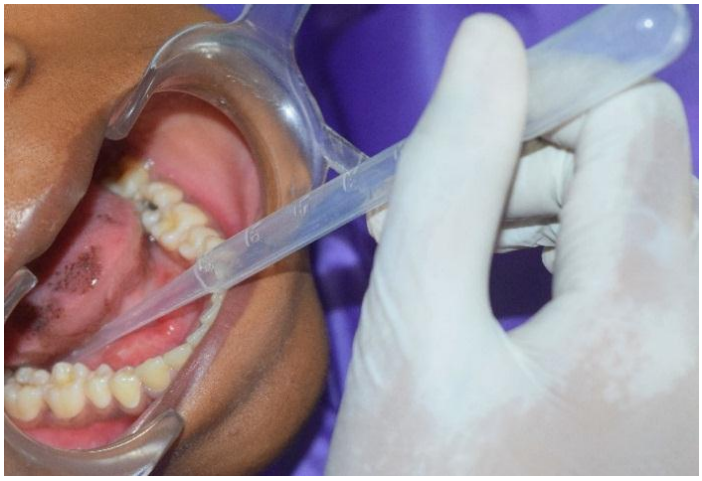


Fig 20: Collected MP3 radiographs



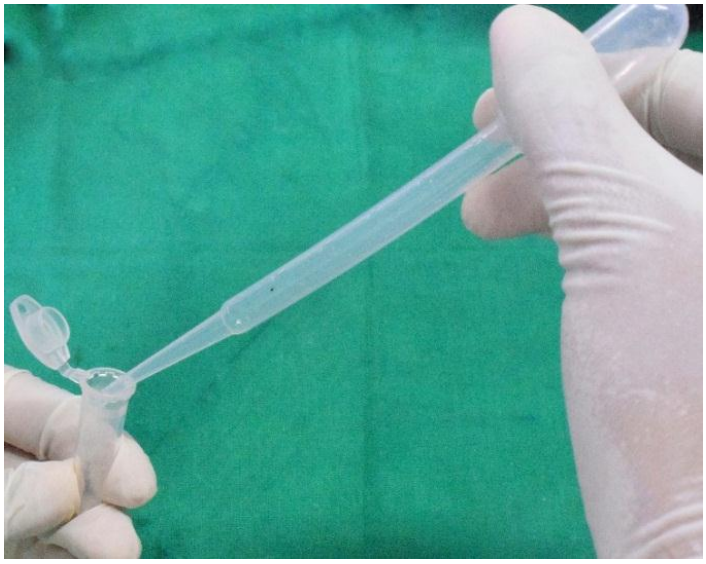


Fig 21: Collection of Saliva

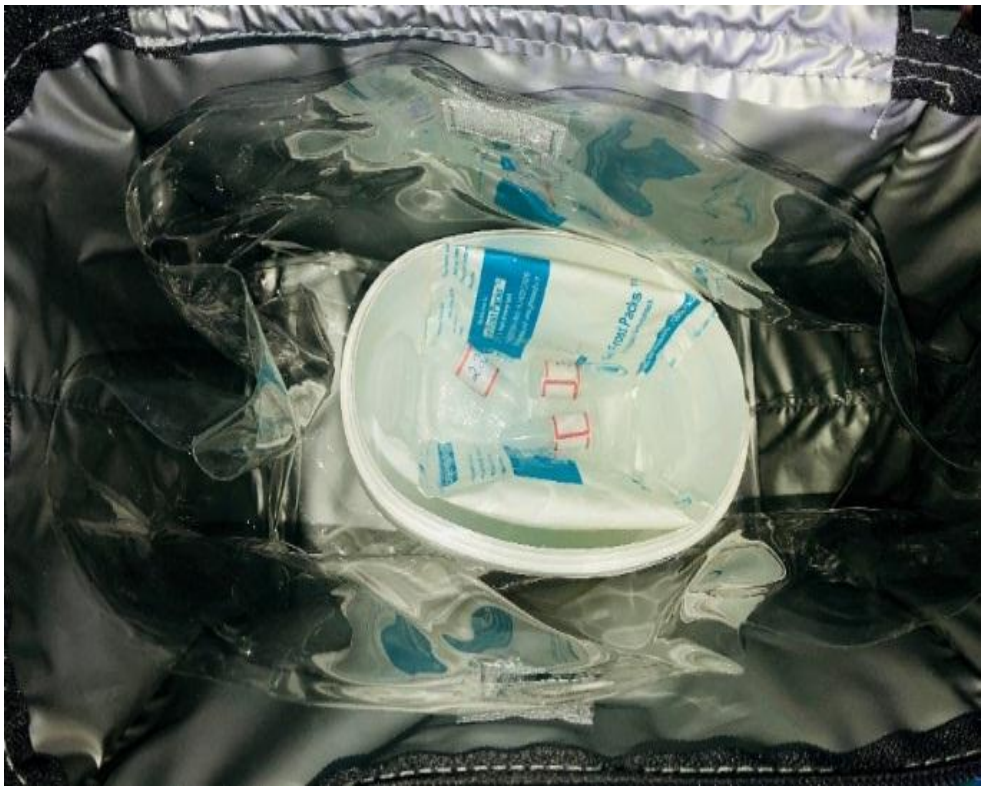


Fig 22 : Transportation of samples in thermal bag with gel frost packs and ice

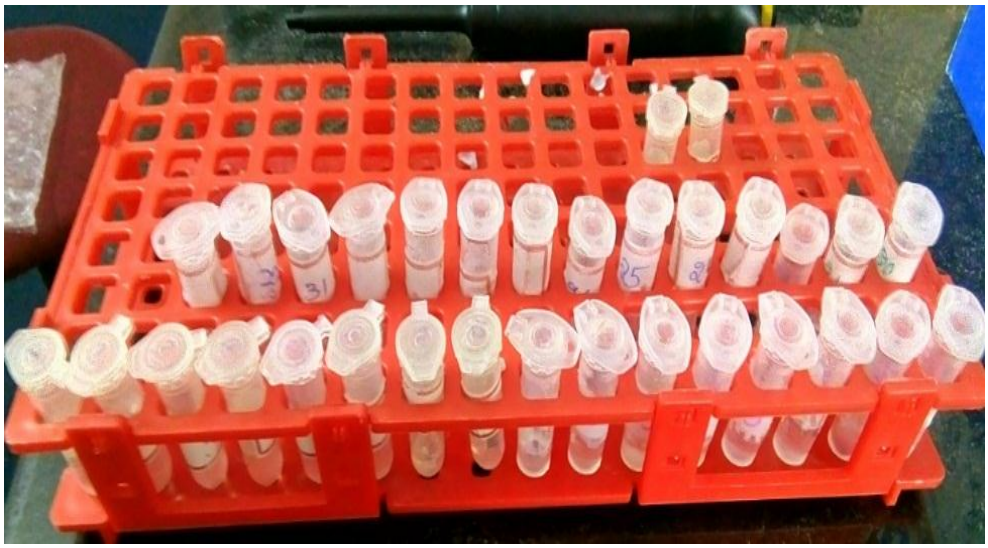


Fig 23 : Collected Saliva samples

Fig 24: Subzero -8^0 C cooler

Fig 25: Centrifuge- Remi R12 refrigerated centrifuge

Fig 26 : Microbiological incubator

Fig 27: Human IGF-1 ELISA kit

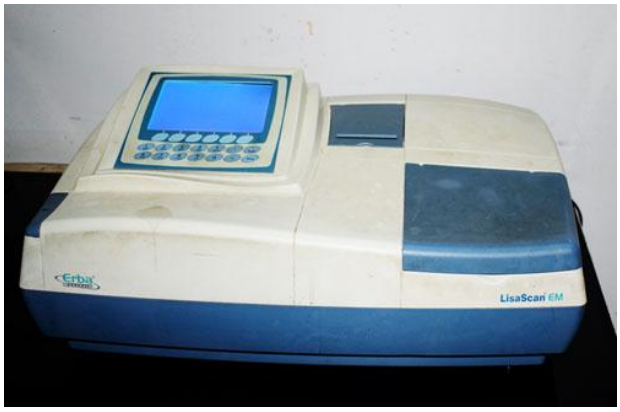


Fig 28 : Elisa Reader

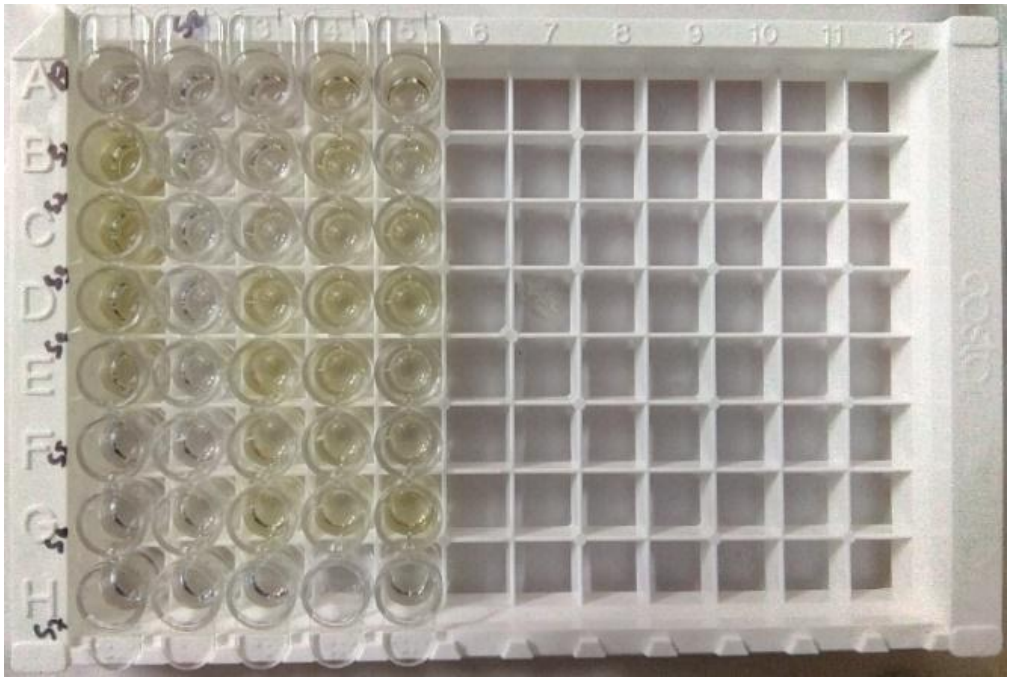


Fig 29: Saliva samples kept in the wells before ELISA test

Fig 30: Reagents

RESULTS & OBSERVATIONS

RESULTS AND OBSERVATION

The study was done to compare salivary IGF-1 values and modified MP3 stages using periapical radiograph for assessment of skeletal maturity and also to determine whether the six modified MP3 stages described by Rajagopal and Kansal could be correlated with the six stages of cervical vertebrae maturation indices (CVMI), as described by Hassel and Farman.

A total of 30 patients were divided into 3 groups, based on the MP3 staging.

Group 1: MP3F-MP3FG.

Group 2: MP3G.

Group 3: MP3H- MP3I.

All the patients were subjected to dental periapical radiographs to determine the six modified MP3 stages and were traced. The data so obtained was subjected to statistical analysis for obtaining mean and standard deviation for the respective variables.

The results were tabulated for each variable in different tables.

The following results were obtained while comparing the MP3 and Salivary IGF-1:

Statistical Package for the Social Sciences (SPSS) 22.0, IBM Analytics, New York, U.S.A was used to carry out the statistical analysis.

Table 01: Mean IGF values in the 3 groups

	Group I (MP3F-MP3FG)	**Group II (MP3G)**	**Group III (MP3H- MP3I)**	**Total**
Total number of samples in each group	10	10	10	30
Mean	130.787	673.5856	620.1736	
Standard deviation	95.9416	406.1727	100.8365	

The above table (table 01) shows the correlation between IGF-1 levels to that of MP3 stages in their respective groups showing IGF-1 levels increasing in growth phase. The study shows that the mean of the IGF values in Group 1 was 130.787 (±95.9416), group 2 was 673. 5856 (±406.1727) and group 3 was 620 (±100.8365). The mean value was highest for Group 2 followed by group 3 and it was least in group 1.

ANOVA was carried out to compare the difference in the mean values in between the 3 groups.

Table 02: ANOVA for comparison of the mean

	Sum of squares (SS)	**Degree of Freedom (df)**	**Mean Squares (MS)**	**F ratio**	**P value**	**Interpretation**
Between-treatments	1789941.3539	2	894970.6769	14.564283	0.000051	The result is significant at $p < .05$.
Within-treatments	1659141.6016	27	61449.6889			
Standard Error	1165613.6083	18	64756.3116			

Table 02 shows that the mean of IGF values of group 2 was significantly higher than that of group 3 and group 1. The result is significant at $p<.05$. Therefore showing that there is correlation between mean IGF levels to that of skeletal maturity assessment using MP3.

Tukey HSD Post-hoc Test

Table 03: Post HOC test values for comparison between the 3 groups at Confidence Interval (CI) 95%.

Group	Difference	Lower limit	Upper limit	P value	Explanation
Group 1 vs Group 2	542.8000	267.9265	817.6735	0.0001	Statistically significant higher mean of group 2 as compared to group 1
Group 1 vs Group 3	489.4000	214.5265	764.2735	0.0004	Statistically significant higher mean of group 3 as compared to group 1
Group 2 vs Group 3	53.4000	328.2735	221.4735	0.8805	No Statistically significant difference between group 2 and group 3

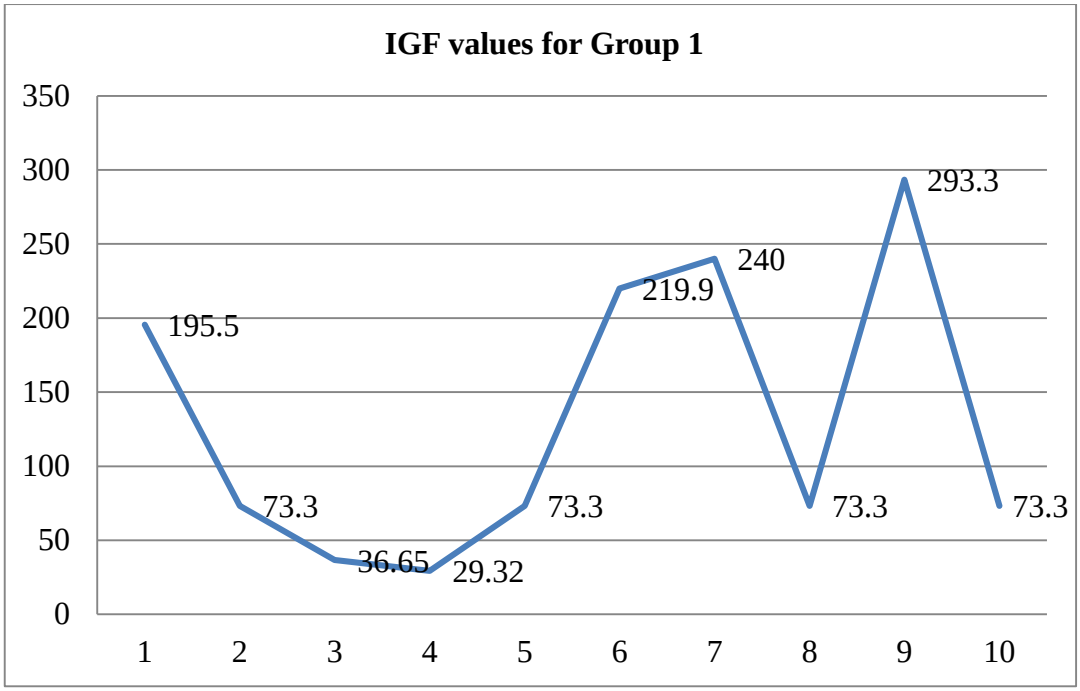
Post hoc test (table 03) was done to determine if there was statistically significance in higher values of mean in between groups. Which showed that comparison between prepubertal and pubertal group showed statistically significant higher mean of pubertal group as compared to prepubertal group. P value: 0.0001

Comparison between prepubertal and post pubertal group showed statistically significant higher mean of postpubertal group as compared to pre pubertal group. P value: 0.0004.

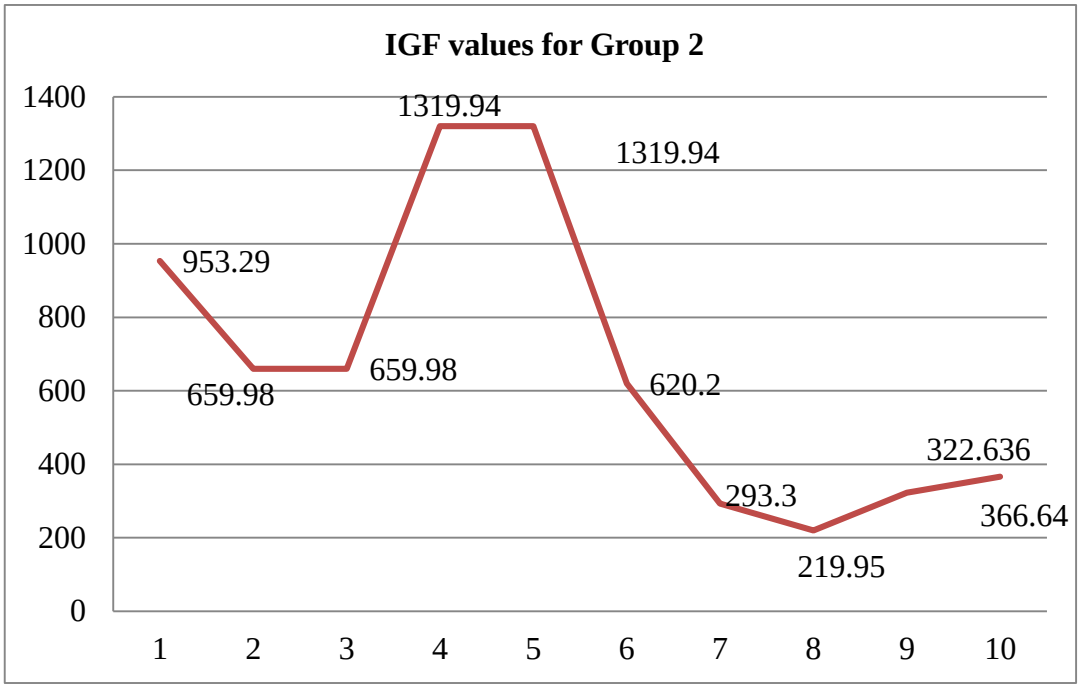
But in this study when comparing pubertal and postpubertal group no statistically significant difference between the two groups was found. P value: 0.8805

Therefore the second objective cannot be proved. The possible reasons maybe due to low number of samples included in the study. Also random cluster of females in postpubertal group. Further longitudinal studies are necessary to prove whether salivary IGF-1 could be used as a skeletal maturity indicator.

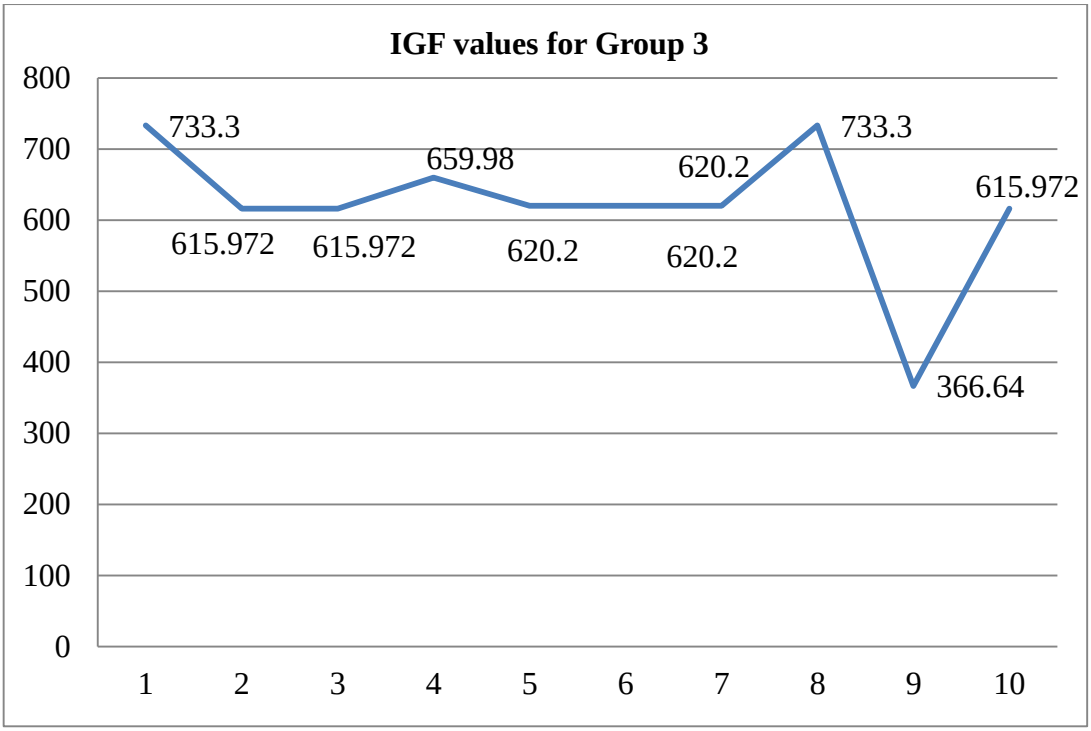
GRAPHS



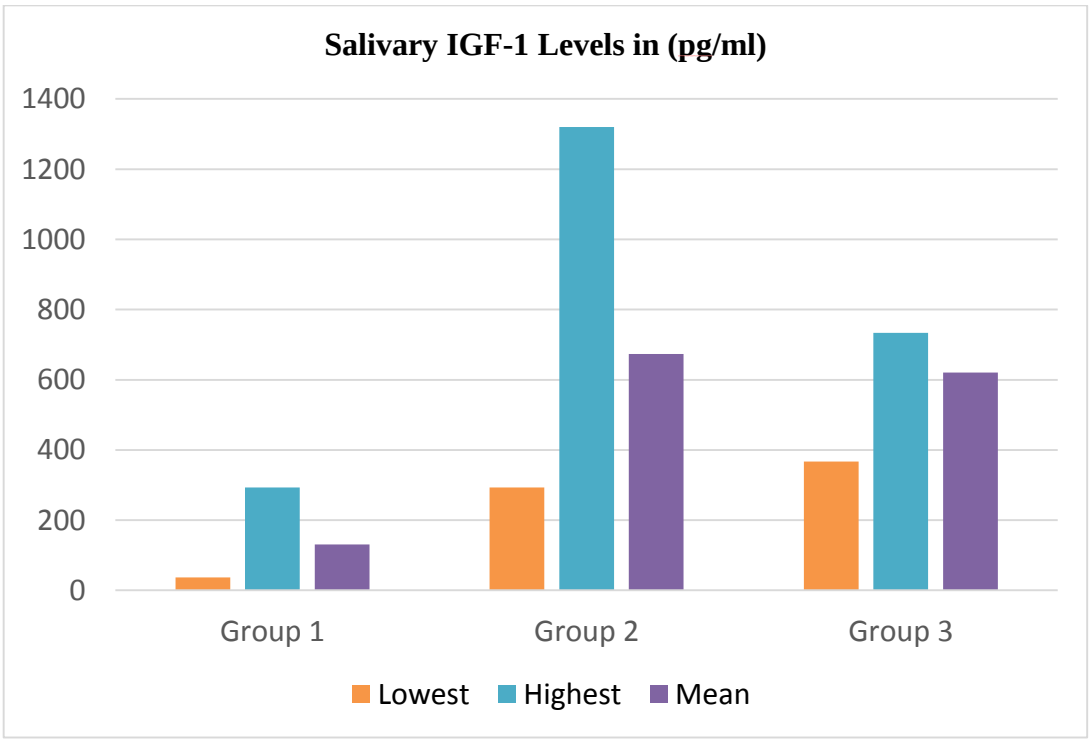
Graph 01: Distribution of Group 1 samples based upon the IGF values



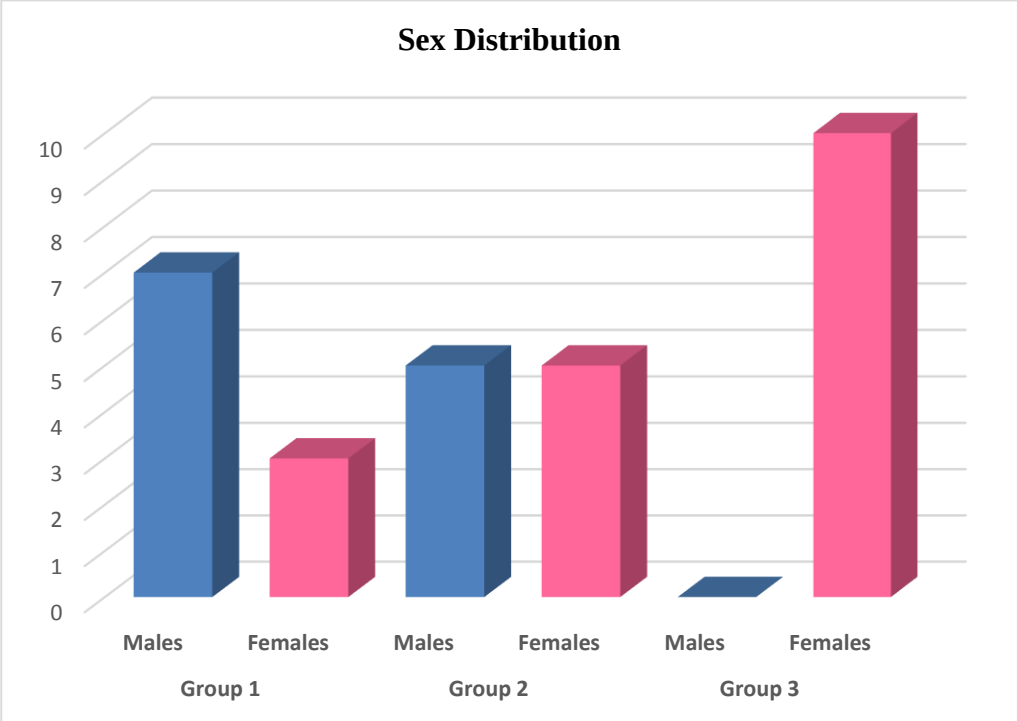
Graph 02: Distribution of Group 2 samples based upon the IGF values



Graph 03: Distribution of Group 3 samples based upon the IGF values



Graph 4: Salivary IGF levels in each group



Graph 05: Sex distribution

DISCUSSION

DISCUSSION

Human growth does not occur at same intervals all the time. There are certain periods during which growth reaches to peak velocities. Maturational status has considerable influence on diagnosis, treatment goals, treatment planning and the eventual outcome of orthodontic treatment. Various methods have been used to identify the stages of growth like sexual maturation characteristics, chronologic age, dental development, height and weight of the individual and skeletal development. One of the important diagnostic tools currently used in determining whether pubertal growth has started, is occurring, or has finished is the hand- wrist radiographic evaluation. However, for assessing skeletal maturation, newer possibilities are provided with biochemical markers which represent the agents that are directly involved in bone growth and remodeling. They could be measured from various biologic fluids such as blood, saliva, and urine, there by overcoming the subjectivity associated with radiographs.[3].

Molecular studies in the last decade have shown various biomarkers that control skeletal and in particular condylar cartilage growth such as IGF-1, Sox-9, Ihh, VEGF, PTHrP and Cbfa-1.[57,58,59,60] In 1957, Salmon and Daughaday discovered insulin- like growth factor – 1 as a mediator of growth hormone (GH) function. IGF-1 is synthesized and secreted in the liver and other organs following stimulation by growth hormone. It accelerates growth as well as differentiation and substrate synthesis activity in osteoblasts and chondroblasts. IGF-1 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. IGF-1 is a useful diagnostic tool for determining growth hormone status as its levels donot fluctuate throughout the day unlike the growth hormone levels. Skeletal growth has been shown to be closely related to growth hormone status. Specifically, the condyle is more sensitive and receptive to Insulin like growth factor-1 than femoral head[62].

Serum IGF-1 has been established as one of the reliable indicator, but the process of collecting serum sample remains an invasive procedure.[6] Though Salivary IGF-1 levels reflects its levels in the plasma, those levels are extremely low, at around 1% of serum levels.[34,61] One problem of using salivary IGF-1 as a predictor of facial growth is the small amount in saliva. In an attempt to quantify salivary IGF-1 levels, Ryan et al.[34,61] used radioimmunoassay, which has high specificity but low sensitivity. Recent advances in assay technology have improved this problem. By using new immunoradiometric assay as low as 1 ng/ml of salivary IGF-1 can be detected. This way sample can be obtained by a noninvasive method as opposed to obtaining it by invasive blood spot collection method.[2]

The objectives of the present study is to assess whether salivary IGF-1 levels can be used as a skeletal maturity indicator and to compare the mean IGF -1 levels at different stages of skeletal maturity using MP3 staging.

This study consisted of 30 patients who were divided into 3 groups, based on the MP3 staging; group 1 consisted of stages MP3F to MP3FG; group 2 comprises MP3G stage and group 3 consisted of stages MP3H to MP3I, including both males and females in the age range between 7-18 years. The exclusion criteria included subjects suffering from any serious illness like growth abnormality, systemic diseases and disorders like liver disorders, bleeding disorders, history of any serious

trauma or injury to the face, hand and wrist region. All the patients were subjected to dental periapical radiographs.

The radiograph of middle phalanx of third finger (MP3) of right hand was taken. MP3 radiograph used IOPA film which would suspend the patient to minimal radiation exposure. Tanner and colleagues devised a method called TW2 to classify many of the ossification centers of the hand and wrist. Development of the radius, metacarpals, phalanges, and trapezium were each divided into nine stages (A-I), and that of the ulna and the rest of the carpals into eight stages (A-H). Houston WLB, Miller JC and Tanner JJM identified the four stages of MP3 bone development (F-I) that occur within a few years of the onset of puberty.[23] Hagg U and Taranger J recommended using five distinct stages of MP3 development (adapted from Tanner's classification) as a reliable biological indicator. Chapman SM was the first to use periapical X-ray film to evaluate ossification of the ulnar sesamoid bone as a skeletal maturity marker.[56] Abdel- Kader applied this idea to recording MP3 stages. As the present study confirms, assessment of remaining pubertal growth can be reliably performed throughout treatment using the modified MP3 stages by taking simple periapical X-rays, without the need for extra lateral cephalograms or hand-wrist X-rays.

All MP3 radiographs would be classified according to Modified MP3 staging criteria by Rajagopal R, Kansal S by two authors. Two independent examiner (senior lecturer from department of oral medicine and orthodontics) would be blinded about the patient's age, pubertal status and IGF-1 levels during the staging of MP3 radiograph to avoid errors. This method is a modification of the method described by Hagg U and Taranger I , an additional bone stage was given between

MP3-H (deceleration of the curve of the pubertal growth spurt) and MP3-I (end of the pubertal growth spurt), which was called the MP3-HI stage, resulting in a total of six stages of MP3 growth. The advantage of this method was the high degree of clarity on the radiographs, with no superimposition of bones or variations in posture as in evaluation of the cervical vertebrae. Discrete, easily identifiable stages of development, unlike the more subtle changes in CVMI stages. Close correlation to the six stages of CVMI. No need to obtain equipment beyond the standard periapical x-ray film and dental x-ray machine.[14]

Mixed saliva from patients would be aspirated from the floor of mouth by use of gentle suction and then it would be transferred to individual centrifugable collector. The samples from each patient is collected and transferred to a standard thermal box with icepacks maintained at temperatures between 2˚-8˚ C, which were then send to the Biogenix Research centre at Trivandrum on the collection day itself.

Mixed saliva could be stored at room temperature for upto 24 hours without altering its IGF concentration.[3] According to a study by Costigan D et al 1988 mixed saliva samples stored and analysed after 24 hours in normal room temperature did not show any damage or loss of structural stability. Salivary IGF – 1 concentration was not influenced by flow rate. Also salivary IGF-1 concentration was not affected by day, time and food intake as opposed to diurinal variation in serum growth hormone concentration.

The samples would then be analyzed by human IGF-1 Enzyme-Linked Immunosorbent Assay kits (ELISA) specific for salivary IGF-1 protein structure; no functional assessment of the enzyme was done hence the risk of protein denaturement not affected the study.

The advantage of this study is that the saliva collection is a simple noninvasive procedure, which eliminates the risk of infection for the healthcare worker, avoidance of needle stick injuries, acceptable to those with needle phobias and furthermore transmission of HIV via saliva is unlikely. The present study maybe of great importance because it allows skeletal age to be estimated in an objective manner.

Descriptive analysis, which includes mean and standard deviation are calculated for each group. ANOVA and Post hoc test is employed to determine the correlation between the modified MP3 stages and the IGF-1 values.

- In this study the mean of IGF values of group 2 (pubertal) is significantly higher than that of group 3(post pubertal) and group 1(prepubertal), ($p < .05$). Therefore showing that there is correlation between mean IGF levels to that of skeletal maturity assessment using MP3 in the study. These findings are consistent with the study conducted by Sinha P et al for the assessment of skeletal maturity by correlating insulin like growth factor-1 in serum with hand – wrist radiographs. They concluded that IGF-1 levels at the pubertal stage were significantly higher than the prepubertal and postpubertal stages. The levels in post pubertal stage declined to almost the same level as the prepubertal stage. IGF-1 levels might prove to be a valuable skeletal maturity indicator. These findings showed that there is correlation between MP3 radiographs and serum IGF-1 levels in pubertal phase.

- Also in this study the comparison between prepubertal and pubertal group showed statistically significant higher mean of pubertal group as compared to prepubertal group.($p<0.05$)

- Comparison between prepubertal and post pubertal group showed statistically significant higher mean of postpubertal group as compared to pre pubertal group.
- But in the current study when comparing pubertal and postpubertal group no statistically significant difference between the two groups was found. This is in agreement with previous study done by Masoud et al to show the relationship between blood spot insulin like growth factor-1 levels and hand wrist assessment of skeletal maturity. A marked positive correlation was observed between IGF- 1 levels and hand- wrist stages from pre- pubertal stages to the stages of highest velocity of mandibular growth, whereas there was a moderate negative correlation between IGF-1 levels and hand – wrist radiograph stages from the levels associated with peak mandibular growth to the final hand-wrist stages. The findings showed that IGF-1 levels were still relatively high in many post-pubertal patients, and that, in the post pubertal group, IGF-1 levels tended to decline as the subjects aged. The study concluded the pattern that mean IGF-1 levels followed at various skeletal stages mirrored the mandibular growth velocity pattern that Fishman observed, with a sharp acceleration to the peak late in puberty and a more gradual decline thereafter. In the post- pubertal stage, IGF-1 levels were higher in the younger subjects and decreased as they aged.
- In this study, a high standard deviation was observed. This could be a reflection of great individual variations with regard to skeletal maturation. Similar wide variation in IGF-1 levels has also been noted in other body fluids.[6] This variation could be a reflection of errors associated with the use of cross-sectional study of growth and using a technique that relies on prediction of growth velocity based on other ethnic groups. Evidence has shown that environmental and

socioeconomic factors can greatly influence timing and pattern of growth in a particular ethnic group.[63,64]

Along with additional radiation exposure one inherent drawback of present skeletal indicators is lack of prediction of residual mandibular growth. Residual facial growth is of particular importance to relapse from orthopaedic and orthognathic surgical corrections, as well as implant placement procedures. Similar to a study on serum IGF-1 levels by Masoud et al[4,6], the present study also observed relatively high salivary IGF-1 levels and its secretion rate in many subjects who were in decelerating velocity stage. Thus, salivary IGF-1 levels and its secretion rate follow similar pattern of serum IGF-1 and might be a reliable indicator of residual mandibular growth.

In the study by Masoud et al the results showed that IGF-1 levels were still relatively high in many subjects who were at CS6 and had supposedly completed their growth. In that stage, it was found that IGF-1 levels were negatively correlated with time since the onset of puberty. In this study also there was no statistically significant difference between the mean values of salivary IGF-1 in groups 2 (pubertal) and Group 3 (Post Pubertal), which suggests that second objective of this study to prove IGF-1 can be reliably used as a skeletal maturity indicator is not possible. This study concludes that IGF-1 levels are low in the prepubertal cervical skeletal stages, rise sharply to their peak in late puberty, and decline to approach prepubertal levels after puberty not at immediate postpubertal phase.

To support the above mentioned decrease decline in IGF-1 levels in postpubertal phase there is another study by Jain N et al which was to assess the reliability of serum IGF-1, IGFBP-3 and their ratio as potential biochemical growth

maturity indicators. Even though a sharp increase was observed from CVMI2 to CVMI3. A progressive decline in mean serum IGF- 1 levels was only observed from CVMI3 to CVMI6. It was observed that mean serum IGF-1 levels at CVMI6 or at skeletal stage of growth completion was relatively high than at CVMI1. It was concluded in the study that mean serum IGF-1 levels were found to be highest at CVMI3 stage of CVMI and there the decline is completed only by CVMI6. [5] This study that we conducted showed similar and comparable results to the above mentioned study.

At present scenario there are multitude of studies undergoing at various institutions around the world looking at the implications of IGF-1 levels in humans not only as skeletal maturity indicator but also in various other roles.

According to present study, pubertal group showed higher IGF-1 values than the pre and post pubertal group but a significant difference in pubertal and post pubertal group was not found. Although saliva collection can be simplified using the presented technique, routine availability of specialized assays is questionable. Hence, these types of additional skeletal growth markers can be reserved for patients with disparity between skeletal maturation and conventional skeletal maturity indicators. Additionally it can provide an estimate of any residual mandibular growth, whenever required. Present study results showed that IGF-1 levels were still relatively high in many subjects who are in MP3H -I stage and had supposedly completed their growth. In that stage it was found that IGF-1 levels were negatively correlated with time since the onset of puberty. Thus IGF-1 might be a good indicator of residual mandibular growth. Hence further longitudinal studies are

necessary to evaluate whether salivary IGF-1 can be used as a marker for growth prediction.

Scope for future research:

Longitudinal data are needed to confirm the usefulness of this technique to accurately determine the timing, and possibly the intensity, of a patient's growth spurt and to determine whether IGF-1 levels are good predictors of residual facial growth.

SUMMARY

SUMMARY

Orthodontic diagnosis and treatment planning is influenced by the developmental status of the child and has periods of acceleration to a peak velocity and deceleration. In a growing child, many abnormal skeletal discrepancies can be confronted that need intervention by growth modification.

Various biologic indicators have been used which include the assessments by chronologic age, skeletal age, skeletal maturation, mandibular growth, standing height, menarche, voice changes and cervical vertebral maturation (CVM). Skeletal maturity can be assessed by visually inspecting the developing bones, their initial appearance, sequential ossification, and changes in size and shape of bones of the hand, wrist, and elbow on radiographs. The ossification of bones of the hand and wrist is considered the most accurate method. However, they require an additional exposure of radiation, leading to ethical limitations.

To reduce this radiation exposure, and subjectivity of staging hormonal biomarkers such as IGF-1 were found reliable for assessing skeletal age. However it carries certain limitations like; small amount found in saliva. IGF-1 is a circulating growth hormone dependent factor whose levels correlate with sexual maturity.

The Aim of the study was to assess skeletal maturity by measuring salivary IGF-1 levels. The Objectives were i) To assess whether salivary IGF-1 levels can be used as a skeletal maturity indicator. ii) To compare the mean IGF -1 levels at different stages of skeletal maturity using MP3 staging.

For this study, MP3 radiographs and saliva samples of 30 patients between the age range 7-18 yrs were collected. The saliva samples would then be analyzed

and the absolute concentration of IGF-1 in unit sample(pg/ml) would be found out and recorded. All MP3 radiographs would be classified according to Modified MP3 staging criteria by R. Rajagopal, Sudhanshu Kansal by two independent blindfolded examiners.

Distinct advantages of the salivary IGF- 1 skeletal maturity assessment includes: avoidance of unnecessary radiation exposure, high degree of clarity, with no superimposition of bones, noninvasive, eliminates risk of infection, also detection of residual mandibular growth.

The study results showed that the mean of IGF values of group 2 (pubertal) was significantly higher than that of group 3(post pubertal) and group 1(prepubertal). Therefore showing that there is correlation between mean IGF levels to that of skeletal maturity assessment using MP3. Also Post HOC test values showed that the comparison between prepubertal and pubertal group showed statistically significant higher mean of pubertal group as compared to prepubertal group. Comparison between prepubertal and post pubertal group showed statistically significant higher mean of postpubertal group as compared to pre pubertal group. But when comparing pubertal and postpubertal group no statistically significant difference between the two groups was found.

CONCLUSION

CONCLUSION

i) The salivary IGF-1 levels follow the same pattern of a sharp acceleration to a peak in puberty and a more gradual fall thereafter.

ii) IgF-1 levels at the pubertal stage were significantly higher than the prepubertal and post pubertal stages. The levels obtained in prepubertal stage was lowest, and in pubertal group was highest. Whereas the levels at post pubertal stages showed almost same value as pubertal.

iii) Salivary IGF-1 can be used as a marker of residual mandibular growth.

iv) Estimation of salivary IGF-1 should be reserved for patients with disparity between skeletal maturation and conventional skeletal maturity indicators.

v) Longitudinal data is necessary to confirm salivary IGF-1 as a marker for skeletal growth prediction and residual mandibular growth.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Sinha P, Trehan M, Sharma S. Assessment of skeletal maturity by correlating Insulin like growth factor-1 with hand-wrist radiographs: an invivo study. J Ind Orthod Soc 2014; 48(1):22-6.
2. Nayak S, Bhad Patil WA, Doshi UH. The relationship between salivary insulin-like growth factor I and quantitative cervical maturational stages of skeletal maturity. J Orthod 2014; 41(3):170-4.
3. Costigan DC, Guyda HJ, Posner BI. Free insulin-like Growth factor I (IGF-I) and IGF-II in Human saliva. J Clin Endocrinol Metab 1988; 66(5):1014-8.
4. Masoud M, Masoud I, Kent RL Jr, Gowharji N, Cohen LE. Assessing skeletal maturity by using blood spot insulin-like growth factor I (IGF-I) testing. Am J Orthod Dentofacial Orthop 2008; 134(2):209-16.
5. Jain N, Tripathi T, Gupta SK, Rai P, Kanase A, Kalra S. Serum IGF-1, IGFBP-3 and their ratio: potential biochemical growth maturity indicators. Prog Orthod 2017;18 (1):11-8
6. Masoud MI, Masoud I, Kent RL Jr, Gowharji N, Hassan AH, Cohen LE. Relationship between blood-spot insulin-like growth factor 1 levels and hand-wrist assessment of skeletal maturity. Am J Orthod Dentofacial Orthop 2009; 136(1):59-64.
7. Suzuki S, Itoh K, Ohyama K. Local administration of IGF-I stimulates the growth of mandibular condyle in mature rats. J Orthod 2004; 31(2):138-43.
8. Proffit WR, Fields HW, Sarver DM. Later stages of development In:Contemporary Orthodontics. 4th ed. St. Louis: Elsevier; 2007. pp:92-113.

9. Flores-Mir C, Nebbe B, Major PW. Use of Skeletal Maturation Based on Hand-Wrist Radiographic Analysis as a Predictor of Facial Growth: A Systematic Review. Angle Orthod 2004; 74(1):118-24.
10. Madhu S, Hedge AM, Munshi AK. The developmental stages of the middle phalanx of the third finger (MP3): a sole indicator in assessing the skeletal maturity? J Clin Pediatr Dent. 2003; 27(2):149-56.
11. Gabriel DB, Southard KA, Qian F, Marshall SD, Franciscus RG, Southard TE. Cervical vertebrae maturation method: poor reproducibility. Am J Orthod Dentofacial Orthop 2009; 136(4):478.e1-7.
12. Riad-Fahmy D, Read GF, Walker RF, Griffiths K. Steroids in Saliva for Assessing Endocrine Function. Endocr Rev 1982; 3(4):367-95.
13. Patrikar S. Textbook on public health and community medicine. 1st ed; Newdelhi:AFMC Pune and WHO; 2009. Pp:1196-98
14. Rajagopal R, Kansal S. A Comparison of Modified MP3 Stages and the Cervical Vertebrae as Growth Indicators. J Clin Orthod 2002; 36(7):398-406.
15. Argente J, Barrios V, Pozo J, Munoz MT, Hervas F, Stene M et al. Normative data for insulin-like growth factors (IGFs), IGF-binding proteins, and growth hormone-binding protein in a healthy Spanish pediatric population: age and sex related changes. J Clin Endocrinol Metab 1993; 77(6):1522-8.
16. Guler HP, Zapf J, Schmid C and Froesch ER. Insulin-like growth factors I and II in healthy man. Estimations of half-lives and production rates. Acta Endocrinol(Copenh) 1989; 121(6):753-8.
17. Abdel-Kader HM. The reliability of dental x-ray film in assessment of MP3 stages of the pubertal growth spurt. Am J Orthod Dentofacial Orthop 1998; 114(4):427-9.

18. Jain S, Jain S, Deoskar A, Prasad VS. Serum IGF-1 levels as a clinical tool for optimizing orthodontic treatment timing. Prog Orthod 2013; 14(1):46

19. Ishaq RAR, Soliman SAZ, Foda MY, Fayed MMS. Insulin-like growth factor I: A biologic maturation indicator. Am J Orthod Dentofacial Orthop 2012; 142(5):654-61.

20. Masoud MI, Marghalani HYA, Bamashmous M, Alamoudi NM, Derwi DE, Masoud IM et al. Predicting changes in mandibular length and total anterior facial height using IGF-1, cervical stage, skeletal classification, and gender. Progress in Orthod 2015; 16(1):7.

21. Gupta S, Jain S, Gupta P, Deoskar A. Determining skeletal maturation using insulin-like growth factor I (IGF-I) test. Prog Orthod 2012; 13(3):288-95.

22. Singh S, Singh M, Saini A, Misra V, Sharma VP, Singh GK. Timing of Myofunctional Appliance Therapy. J Clin Pediatr Dent 2010; 35(2):233-40.

23. Houston WLB, Miller JC, Tanner JJM. Prediction of the timing of adolescent growth spurt from ossification events in hand-wrist films. Br J Orthod 1979; 6(3):145-52.

24. Clemmons DR. IGF binding proteins: regulation of cellular actions. Growth Regul. 1992 Jun; 2(2):80-7.

25. Fielder PJ, Mortensen DL, Mallet P, Carlsson B, Baxter RC, Clark RG. Differential long-term effects of insulin-like growth factor-I (IGF-I) growth hormone (GH), and IGF-I plus GH on body growth and IGF binding proteins in hypophysectomized rats. Endocrinology. 1996 May; 137(5):1913–20.

26. Yeung HY , Tang NL , Lee KM, Ng BK, Hung VW, Kwok R et al. Genetic association study of insulin-like growth factor-I (IGF-I) gene with curve severity and osteopenia in adolescent idiopathic scoliosis. Stud Health Technol Inform 2006; 123:18-24.

27. Hauspie R, Bielicki T, Koniarek J. Skeletal maturity at onset of the adolescent growth spurt and at peak velocity for growth in height: a threshold effect? Ann Hum Biol 1991; 18(1):23-9.

28. Darendeliler F, Hindmarsh PC, Preece MA, Cox L, Brook CG. Growth hormone increases rate of pubertal maturation. Acta Endocrinol(Copenh) 1990; 122(3):414-6 .

29. Kaur N, Kumar RR, Miglani A. IGF - I: A legitimete skeletal maturity indicator. J Indian Orthod Soc 2010; 44(2):25-32.

30. Rogol AD, Roemmich JN, Clark PA. Growth at puberty. J Adolesc Health 2002; 31(6):192-200.

31. Morris JM, Park JH. Correlation of Dental Maturity with Skeletal Maturity from Radiographic Assessment: a review. J Clin Pediatr Dent 2012; 36(3):309-14.

32. Bonjour JP. The dietary protein, IGF-I, skeletal health axis. Horm Mol Biol Clin Investig 2016; 28(1):39-53.

33. Wikland KA. Growth Hormone Treatment in Short Children. Acta Paediatrica 1986; 75(s325):64-70.

34. Ryan J, Mantle T, Costigan DC. A normal population study of human salivary insulin-like growth factor-I concentrations from birth through puberty. J Clin Endocrinol Metab.1992; 74(4):774–8.

35. Juul A , Flyvbjerg A , Frystyk J, Muller J, Skakkebaek NE. Serum concentrations of free and total insulin-like growth factor-I, IGF binding proteins -1 and-3 and IGFBP-3 protease activity in boys with normal or precocious puberty. Clin Endocrinol (oxf) 1996; 44(5):515-23.

36. Krailassiri S, Anuwongnukroh N, Dechkunakorn S. Relationships between Dental Calcification Stages and Skeletal Maturity Indicators in Thai Individuals. Angle Orthod 2002; 72(2):155-66.

37. Sierra AM. Assessment of Dental and Skeletal Maturity A New Approach. Angle Orthod 1987; 57(3):194-208.

38. Hägg U, Taranger J. Skeletal stages of the hand and wrist as indicators of the pubertal growth spurt. Acta Odontol Scand 1980; 38(3):187-200.

39. Uysal T, Ramoglu SI, Basciftci FA et al. Chronologic age and skeletal maturation of the cervical vertebrae and hand-wrist: Is there a relationship? American Journal of Orthodontics and Dentofacial Orthopedics 2006; 130(5):622-628.

40. Grave KC, Brown T et al. Skeletal ossification and the adolescent growth spurt. Am J Orthod 1976; 69(6):611-9.

41. Vogelsang F, Kohnen M, Schneider H, Weiler F, Kilbinger MW, Wein BB, Guenther RW. Skeletal maturity determination from hand radiograph by model-based analysis. InMedical Imaging: Image Processing 2000;3979:294-306.

42. Sato K, Mito T, Mitani H et al. An accurate method of predicting mandibular growth potential based on bone maturity. Am J Orthod Dentofacial Orthop 2001; 120(3):286-93.

43. So LL. Skeletal maturation of the hand and wrist and its correlation with dental development. Aust Orthod J 1997; 15(1):1-9.

44. Houston WJB. Relationships between skeletal maturity estimated from hand-wrist radiographs and the timing of the adolescent growth spurt. Eur J Orthod 1980; 2(2):81-93.

45. Bowden BD. Epiphysial changes in the hand/wrist areas as indicators of adolescent stage**.** Aust Orthod J 1976; 4(3):87-104.

46. Hegde DY, Baliga S, Yeluri R, Munshi AK. Digital radiograph of the middle phalanx of the third finger (MP3) region as a tool for skeletal maturity assessment. Indian J Dent Res 2012; 23(4):447-53.

47. Bala M, Pathak A, Jain RL. Assessment of skeletal age using MP_3 and hand-wrist radiographs and its correlation with dental and chronological ages in children. J Indian Soc Pedod Prev Dent 2010; 28(2):95-9.

48. Moore RN, Moyer BA, DuBois LM. Skeletal maturation and craniofacial growth. Am J Orthod Dentofacial Orthop 1990; 98(1):33-40.

49. Houston WJB, Miller JC, Tanner JM. Prediction of the Timing of the Adolescent Growth Spurt from Ossification Events in Hand-Wrist Films. Br J Orthod 1979; 6(3):145-52.

50. Roche AF, Davila GH. The Reliability of Assessments of the Maturity of Individual Hand-Wrist Bones. Hum Biol 1976; 48(31):585-97.

51. Tripathi T, Gupta P, Rai P. Biochemical markers as skeletal maturity indicators. Int J Orthod Rehabil 2017; 8(2):60-6.

52. Chen LL, Xu TM, Jiang JH, Zhang XZ, Lin JX. Quantitative cervical vertebral maturation assessment in adolescents with normal occlusion: A mixed longitudinal study. Am J Orthod Dentofacial Orthop 2008; 134(6):720e1-e7.

53. Baccetti T, Franchi L, McNamara JA. An Improved Version of the Cervical Vertebral Maturation (CVM) Method for the Assessment of Mandibular Growth. Angle Orthod 2002; 72(4):316-23.
54. Baccetti T, Franchi L, and McNamara J A. The Cervical Vertebral Maturation (CVM) Method for the Assessment of Optimal Treatment Timing in Dentofacial Orthopedics. Semin Orthod 2005; 11(3):119-29.
55. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child 1969; 44(235):291-303.
56. Chapman SM. Ossification of the adductor sesamoid and the adolescent growth spurt. Angle Orthod 1972; 42(3):236-44.
57. Akiyama H, Chaboissier MC, Martin JF, Schedl A, De Crombrugghe B. The transcription factor Sox-9 has essential roles in successive steps of the chondrocyte differentiation pathway and is required for expression of Sox5 and Sox6. Genes Dev 2002; 16(21):2813-28.
58. Minina E, Wenzel HM, Kreschel C, Karp S, Gaffield W, McMahon AP, et al. BMP and Ihh/PTHrP signaling interavt to coordinate chondrocyte proliferation and diiferentiation. Development 2001; 128(22):4523–34.
59. Van der Eerden BC, Karperien M,Wit JM. Systemic and local regulation of the growth plate. Endocr Rev 2003; 24(6):782–801.
60. Zelzer E, Glotzer DJ, Hartmann C, Thomas D, Fukaim N, Soker S, et al. Tissue specific regulation of VEGF expression during bone development requires Cbfa1/Runx2. Mech Dev 2001; 106(1-2):97–106.
61. Ryan J, Mantle T, McQuaid S, Costigan DC. Salivary insulin like growth factor-I originates from local synthesis. J Endocrinol 1992; 135(1):85-90.

62. Delatte M, Von den Hoff JW, Maltha JC, Kuijpers-Jagtman AM. Growth stimulation of mandibular condyles and femoral heads of newborn rats by IGF-I. Arch Oral Biol 2004; 49(3):165-75.
63. Floyd B. Can socioeconomic factors account for 'atypical' correlations between timing, peak velocity, and intensity of adolescent growth in Taiwanese girls? Am J Hum Biol 2000; 12(1):102-17.
64. Floyd B. Patrilineal family values, family planning and variation in stature among Taiwanese six-year-olds. J Biosoc Sci 2003; 35(3):369-84.

ANNEXURE

INSTITUTIONAL HUMAN ETHICS COMMITTEE

SREE MOOKAMBIKA INSTITUTE OF MEDICAL SCIENCES,
KULASEKHARAM, TAMILNADU

Communication of Decision of the Institutional Human Ethics Committee(IHEC)

SMIMS/IHEC No: 2 / Protocol no: 19 / 2017

Protocol title: SKELETAL MATURITY ASSESSMENT BY CORRELATING SALIVARY INSULIN LIKE GROWTH FACTOR-1 WITH MIDDLE PHALANX OF THIRD FINGER STAGING
Principal Investigator: Dr.Shreevidhya Vijayan
Name& Address of Institution: Department of Orthodontics and Dentofacial Orthopaedics Sree Mookambika Institute of Dental Sciences ☑ New review ☐ Revised review ☐ Expedited review
Date of review (D/M/Y): 05-12-2017 Date of previous review , if revised application:
Decision of the IHEC: ☑ Recommended ☐ Recommended with suggestions ☐ Revision ☐ Rejected
Suggestions/ Reasons/ Remarks:
Recommended for a period of :One year

Please note*

- Inform IHEC immediately in case of any Adverse events and Serious adverse events.
- Inform IHEC in case of any change of study procedure, site and investigator
- This permission is only for period mentioned above. Annual report to be submitted to IHEC.
- Members of IHEC have right to monitor the trial with prior intimation.

Reneegalyangadkar

Signature of Member Secretary (IHEC)

SREE MOOKAMBIKA INSTITUTE OF MEDICAL SCIENCES
IHEC
Date. 5/12/17

SREE MOOKAMBIKA INSTITUTE OF DENTAL SCIENCES

KULASEKHARAM, KANYAKUMARI DIST., TAMIL NADU, INDIA.

INSTITUTIONAL RESEARCH COMMITTEE

Certificate

This is to certify that the research project protocol, ***Ref no. 09/09/2017*** titled, ***"Skeletal maturity assessment by correlating salivary Insulin like Growth Factor-1 with Middle phalanx of third finger staging"*** submitted by ***Dr. Shreevidhya Vijayan, II Year MDS, Department of Orthodontics and Dentofacial Orthopaedics*** has been approved by the Institutional Research Committee at its meeting held on ***26th September 2017.***

Convener
Dr. T. Sreelal

Secretary
Dr. Pradeesh Sathyan

BIOGENIX RESEARCH CENTER
CENTER FOR MOLECULAR BIOLOGY AND APPLIED SCIENCE
KRRA 31 - KESHAVADEV ROAD - POOJAPPURA - THIRUVANANTHAPURAM

Phone : 0471 - 3229192
E-mail : info@biogenixresearchcenter.com
Web : www.biogenixresearchcenter.com

REG NO : 2427/14

BRMAS/Res./Consent Lett./2017/008

18th September 2017

To
Dr. Anil Kumar. P.,
Professor & Head,
Department of Orthodontics,
Sree Mookambika Institute of Dental Sciences,
Kulasekharam.

Dear Sir,

Sub: Permission letter for doing research regarding reference letter dated 11-09-2017

As per your reference letter we would like to inform you that **Dr. Shreevidhya Vijayan** (2nd year Post Graduation student) has been permitted for carrying out her research work entitled as "**Skeletal maturity assessment by correlating salivary IGF-1 with MP3 staging**" in our research labs.

BIOGENIX RESEARCH CENTRE
BGRC
Reg. No. 594/07
THIRUVANANTHAPURAM

DIRECTOR
BRMAS

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Report of Human IGF-1 ELISA

Sample Number 30 Nos
Samples submitted by Dr. Shreevidhya Vijayan, Dept. of Orthodontics and Dentofocal Orthopedics, Sree Mookambika Institute of Dental Science, Kulasekharam, Tamilnadu.
Experiment details Estimation of Skeletal Maturity indicator using Human IGF-1 ELISA kit (Catalogue No: ITEH0165)

Sample Code	IGF 1 content in sample (pg/ml)
1	195.5
2	73.3
3	36.65
4	29.32
5	73.3
8	73.3
9	219.95
10	240
11	953.29
12	733.3
13	659.985
14	322.636
15	659.98

Sample Code	IGF 1 content in sample (pg/ml)
16	1319.94
17	615.972
19	620.2
20	615.972
21	659.98
22	620.2
23	366.64
24	615.972
25	1319.94
26	366.64
27	293.3
28	620.2
29	620.2
30	293.3
31	219.95
32	733.3
33	73.3

For Biogenix Research Center,

Authorized signatory

BIOGENIX RESEARCH CENTRE BGRC Reg. No. 594/07 THIRUVANANTHAPURAM

Dr Shrikanth Muralidharan

Statistician

Email : shrikanthmuralidharan23@gmail.com

TO WHOMSOEVER IT MAY CONCERN

This is to certify that the statistical analysis of data submitted by Dr Shreevidhya Vijayan, Post graduate student of Department of Orthodontics and Dentofacial Orthopaedics, Sree Mookambika Institute of Dental Sciences, Kulasekharam, Kanyakumari District, Tamil Nadu was done by me. Statistical Package for the Social Sciences (SPSS) 22.0, IBM Analytics, New York, U.S.A was used to carry out the statistical analysis. The statistics was done for her thesis work entitled **"Skeletal maturity assessment by correlating salivary insulin like growth factor – 1 with middle phalanx of third finger staging."**

Dr Shrikanth Muralidharan

(8308008831)

CONSENT FORM

PART 1 OF 2

INFORMATION FOR PARTICIPANTS OF THE STUDY

Dear Volunteers,

We welcome you and thank you for your keen interest in participation in this research project. Before you participate in this study, it is important for you to understand why this research is being carried out. This form will provide you all the relevant details of this research. It will explain the nature, the purpose, the benefits, the risks, the discomforts, the precautions and the information about how this project will be carried out. It is important that you read and understand the contents of the form carefully. This form may contain certain scientific terms and hence, if you have any doubts or if you want more information, you are free to ask the study personnel or the contact person mentioned below before you give your consent and also at any time during the entire course of the project.

1. **Name of the Principal Investigator:** Shreevidhya Vijayan
   Second Year Post Graduate student
   Department of Orthodontics
   Sree Mookambika Institute of Dental Sciences,
   Kulasekharam

2. **Name of the Guide:** Dr. Anilkumar P. MDS
   Professor and Head
   Department of Orthodontics
   Sree Mookambika Institute of Dental
   Sciences
   Kulasekharam, KanyaKumari District-629161

3. **Name of the Co-Guide:** Dr Amal S Nair. MDS
   Professor
   Department of Orthodontics.
   Sree Mookambika Institute of Dental Sciences.
   KanyaKumari District-629161

4. **Institute:** Sree Mookambika Institute of Dental Sciences,
   V.P.M Hospital complex,
   Padanilam, Kulasekharam,
   Kanyakumari – 629161
   Tamilnadu

5. **Title of the study:** "Skeletal maturity assessment by correlating salivary igf-1 with MP3 staging."

6. **Background information:**

X- rays of various parts of body mainly hand – wrist region was used to assess skeletal growth/maturity. This was very complex and stippled with many inter and intra observer variation. The radiation exposure involved with x-rays makes it a risk.IGF-1 stimulates growth locally as well as systemically. IGF (insulin like growth factor) has been found to be associated with levels of serum Growth hormone. An increase in level of IGF-1 has been correlated with pubertal growth spurt. IGF-1 levels have been proposed as an alternative method to detect pubertal growth spurt timing. In this study we evaluate the MP3 radiographs and IGF-1 levels in patients who have come for orthodontic treatment to find if any correlation is present.

7. **Aims and Objectives**

- To compare the mean IGF -1 levels at different stages of skeletal maturity using MP3 radiographs.
- To assess whether salivary IGF-1 levels can be used as a skeletal maturity indicator.

8. **Scientific justification of the study:**

- IGF-I is a useful diagnostic tool for determining GH status as its levels do not fluctuate throughout the day unlike the GH levels.
- Skeletal growth has been shown to be closely related to GH status.
- IGF- 1 has been reported to play an important role in growth of long bone as well as growth of mandibular condyle.
- Hormonal biomarkers provide an edge over radiographic skeletal maturity assessment methods.

9. **Procedure for the study:**

i. The parents and subjects are explained about the research and their informed consent obtained for using saliva sample and their MP3 radiograph (which were taken for routine orthodontic examination) for the study.
ii. Saliva samples are to be collected after obtaining MP3 radiographs from the subjects.
iii. Saliva is to be collected in a simple plastic collector.
iv. Saliva samples send on the same day to Biogenix Research Centre, Karamana, Trivandrum a Kerala Govt. Affliated Centre for Research.
v. No Personal Information shared.

10. Expected **risks** for **the participants:** NIL

11. Expected benefits of research for the participants:

- The study will help health care practitioners understand the role of biomarkers in determining the growth status of the patient and in due course improve health care for the patients at large.
- Card based skeletal growth tests can be devised
- Avoids X-ray exposure and thereby the associated health hazards.
- Ease of use and readily available non-invasive test for the clinician

12. Maintenance of confidentiality:

a. You have the right to confidentiality regarding the privacy of your medical information (Personal details, results of physical examinations, investigations, and your medical history).

b. By signing this document, you will be allowing the research team investigators, other study Personnel, sponsors, institutional ethics committee and any person or agency required by law to view your data, if required.

c. The results of study performed as part of this research may be included in your medical record.

d. The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

13. Why have I been chosen to be in this study?

a. Chosen because of grouping under the inclusion and exclusion criteria
b. Need of good sampling size
c. No invasive procedure that harm your health and it helps in diagnosis and helpful for the society

14. How many people will be in the study?

30 minimum

15. Agreement of compensation to the participants (In case of a study related injury):

No related injury anticipated. Patient will be taken care in case of complication and medical treatment will be provided.

16. Anticipated prorated payment, if any, to the participant(s) of the study: Not applicable.

17. Can I withdraw from the study at any time during the study period?

- The participation in this research is purely voluntary and you have the right to withdraw from this study at any time during the course of the study without giving any reasons.
- However, it is advisable that you talk to the research team prior to stopping information.

18. If there is any new findings/information, would I be informed? Yes

19. Expected duration of the participant's participation in the study?

1 day

20. Any other pertinent information?

No other information

21. Whom do I contact for further information?

For any study related queries, you are free to contact:

Dr.Shreevidhya Vijayan,
Post graduate student,
Department of Orthodontics
Sree Mookambika Institute of DentalSciences
Kulasekharam, KanyaKumari District-629161
7708787894
Shreevidhya193@gmail.com

Place:

Date: Signature of Principal Investigator

Signature of the participant

CONSENT FORM

PART 2 OF 2

PARTICIPANTS CONSENT FORM

The details of the study have been explained to me in writing and the details have been fully explained to me. I confirm that I have understood the study and had the opportunity to ask questions. I understand that my participation in the study is voluntary and that I am free **to** withdraw at any time, without giving any reason, without the medical care that will **normally** be provided by the hospital being affected. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). I have been given an information sheet giving details of the study. I fully consent to participate in the study titled: **"Skeletal maturity assessment by correlating salivary igf-1 with MP3 staging."**

Serial no / Reference no:

Name of the participant:

Address of the participant:

Contact number of the participant:

Signature / thumb impression of the Parent / Legal guardian

Witnesses:

1.

2.

Date:

Place:

സമ്മത പത്രം - ഭാഗം - 1

പഠനവുമായിസഹകരിക്കുന്ന വ്യക്തികളുടെഅറിവിലേയ്ക്ക്

പ്രിയപ്പെട്ട സന്നദ്ധ സേവകരേ,

ഞങ്ങൾ നിങ്ങളെ സ്വാഗതം ചെയ്യുന്നു. അതോടൊപ്പം ഈ പഠനവുമായി സഹകരിക്കാനുള്ള സന്നദ്ധതയോട് നന്ദി രേഖപ്പെടുത്തുന്നു. നിങ്ങൾഈ പഠനത്തിൽ പങ്കെടുക്കുന്നതിനു മുൻപ് ഈ പഠനം എന്തിനാണ് നടത്തപ്പെടുന്നത് എന്ന് അറിയേ□തു□്. അതിനാൽ ഈ ഫോറത്തചന്റ് ഗവേഷണ പഠനത്തിന്റെ വിവരങ്ങളും മറ്റും വിശദമായി രേഖപ്പെടുത്തിയിരിക്കുന്നു. ഈ പഠനത്തിന്റെ രീതി, ഉദ്ദേശം, പ്രയോജനം, അപകടസാദ്ധ്യത, ക്ലേശം, മുൻകരുതൽ, എങ്ങനെ ഈ പഠനം മുൻപോട്ടു കൊ□ുപോകുന്നു എന്നിങ്ങനെ എല്ലാവിവരങ്ങളും ഫോറത്തിൽ രേഖപ്പെടുത്തിയിരിക്കുന്നു. സദയം ഈ വിവരങ്ങൾ വായിച്ചു മനസ്സിലാക്കുവാൻ അഭ്യർത്ഥിക്കുന്നു. ഈ വിവരങ്ങളിൽ ശാസ്ത്രപരമായ പദങ്ങൾ ഉള്ളതിനാൽ സംശയനിവാരണത്തിനു പ്രധാന പഠനകർത്താവിനോടോ താഴെ രേഖപ്പെടുത്തിയിരിക്കുന്ന വ്യക്തികളോടോ ഫോറം ഒപ്പിടുന്നതിനു മുൻപോ അല്ലെങ്കിൽ ഈ പഠനത്തിന്റെ കാലാവധി തീരുന്നതുവരേയോ സമീപിക്കാവുന്നതാണ്.

1. മുഖ്യ ഗവേഷകൻ : ഡോ. ശ്രീവിദ്യ വിജയൻ
ര□ാംവർഷം പോസ്റ്റുഗ്രാജുവേറ്റ്
ഡിപ്പാർട്ട്മെന്റ്ഓഫ ഓർത്തോഡോന്റിക്സ്
ശ്രീമൂകാംബിക ഇൻസ്റ്റിറ്റ്യൂട്ട് ഓഫ്ഡെന്റൽ സയൻസ്,
കുലശേഖരം - 629 161.

2.പ്രധാന മാർഗ്ഗദർശി : ഡോ.അനിൽകുമാർപി. എം ഡി എസ്
പ്രൊഫസർ&ഹെഡ്ഓഫ് ദി ഡിപ്പാർട്ടുമെന്റ്,
ഡിപ്പാർട്ട്മെന്റ് ഓഫ് ഓർത്തോഡോന്റിക്സ്
ശ്രീമൂകാംബിക ഇൻസ്റ്റിറ്റ്യൂട്ട് ഓഫ്ഡെന്റൽ സയൻസസ്,
കുലശേഖരം.

3.സഹമാർഗ്ഗ ദർശി : ഡോ.അമൽ എസ്. നായർ. , എം.ഡി.എസ്.
പ്രൊഫസർ
ഡിപ്പാർട്ട്മെന്റ്ഓഫ് ഓർത്തോഡോന്റിക്സ്
ശ്രീമൂകാംബിക ഇൻസ്റ്റിറ്റ്യൂട്ട് ഓഫ്ഡെന്റൽ സയൻസസ്,
കുലശേഖരം.

4. ഇൻസ്റ്റിറ്റ്യൂട്ട് : ശ്രീ. മൂകാംബിക ഇൻസ്റ്റിറ്റ്യൂട്ട് ഓഫ്ഡെന്റൽ സയൻസസ്
പടനിലം, കുലശേഖരം, കന്യാകുമാരി - 629 161.
തമിഴ്നാട്.

5. പഠന ശീർഷകം

കൈവിരൽ(MP3) റേഡിയൊഗ്രാഫുകൾ ഉപയോഗിച്ച് ഉമിനീർ IGF-1 പരസ്പരം ബന്ധപ്പെടുത്തി എല്ലിൻറെ മെച്യൂരിറ്റി വിലയിരുത്തൽ

6. പശ്ചാത്തല വിവരം?

Xray പ്രധാനമായിട്ടു ഉപയോഗിക്കുന്ന തമനുഷ്യ ശരീരത്തിലെ അസ്ഥികളുടെ വളർച്ചയും പ്രായവും മനസിലാകുന്നതിന് ആണ്. ഈ പരിശോധന വളരെ കൃത്യതയോടെ ശ്രദ്ദിച്ചു ചെയേണ്ടത് ആണ്. പരിശോധന സമയങ്ങളിൽ x-ray കിരണങ്ങൾ പരിശോധകന്റെ ശരീരത്തിൽ പതിയാതെ സുരക്ഷാ കവചങ്ങൾ ഉപയോഗിക്കേണ്ടതാണ്. ഇസ്സുലിന്റ്രോവത്സാകൂർ (IGF -1) സാധാരണയായി സെറം ജിറൗത്ഹോർമോണും ആയി ബന്ധപ്പെട്ട ആണ്ടുണ്ടുവരുന്നത്. IGF -1 ഇന്റെ ഉയർച്ച രീതി പുബെർട്ടൽ ജിറൗത്സ്പുർട്ടുമായി ബന്ധപ്പെട്ടുള്ളതാണ്. IGF ലെവൽ മനസിലാകുന്നതിലൂടെ പുബെർട്ടൽ ഗ്രോവത്സ്പുർട്ടൈമിംഗ്ണ്ടു പിടിക്കാൻ കഴിയും .കൈവിരലിന്റെ (MP3) xray ചിത്രങ്ങൾ നോക്കിയും IGF - 1 ഇന്റെ ലെവൽ നോക്കിയും ഉള്ള താരതമ്യ പഠനത്തിന് ഓർത്തോഡോന്റിക് സ്ചികത്സ ക്കവരുന്ന രോഗികളെ വിദേയമാകുന്നു .

7. പഠനോദ്ദേശ്യം.

- ഗ്രോവത്ഹോർമോന്റെ നിലവാരം കണ്ടെത്താൻ IGF - 1 ഉപയോഗിക്കുക വഴി രോഗിയുടെ പല കാലഘട്ടങ്ങളിൽ എടുക്കുന്ന കൈവിരൽ റേഡിയോ ഗ്രാഫിക്ചിത്രങ്ങൾ എലിന്റെ അവസ്ഥ വെളിപ്പെടുത്തുന്നു. ഈ കണ്ടത്തലുകളെ IGF - 1 ഇന്റെ അവസ്ഥയുമായി ചേർത്തുപഠന വിദേയമാകുന്നു.
- അസ്ഥികളുടെ പ്രായം കണ്ടെത്തുന്നതിന് ഉമിനീരിലെ IGF -1 ലെവൽ ഉപയോഗിക്കാൻ കഴിയുമോ എന്നുപഠന വിദേയമാകുന്നു .

8. പഠനത്തെക്കുറിച്ചുള്ളശാസ്ത്രീയ ന്യായീകരണം

- വളർച്ച ഹോർമോണിന്റെ അളവ്വിവസവും സമയബന്ധി തമായിമാറ്റം സംഭവിക്കുന്നത് ആണ്, പക്ഷെ IGF - 1 ഇന്റെ അളവ്വിവസം മുഴുവൻ മാറാതെ നില്ക്കുന്നത് ആണ്.
- അസ്ഥികളുടെ വളർച്ചക്കായി വളർച്ചഹോർമോണിന്റെ സാന്നിധ്യം അനിവാര്യം ആണ് .
- ഇതിൽ IGF-1 ഇന്മനുഷ്യ ശരീരത്തിലെ പ്രധാനപ്പെട്ട എല്ലുകളുടെയും പ്രത്യേകിച്ച്താടി എല്ലുകളുടെ പൂർണ വളർച്ചെക്കു പ്രധാനപ്പെട്ട ഒരു പങ്ക് ഉണ്ട് .
- മേല്പറഞ്ഞ കാരണങ്ങളാൽ എന്തുകൊണ്ടും വളർച്ചഹോർമോണുകൾ അടിസ്ഥാനമാക്കിയുള പരിശോധനകൾ x-ray യുടെ സഹായത്തോടുള്ള പരിശോധനകളെക്കാൾ വളരെ അധികം മെച്ചപ്പെട്ടതാകുന്നു .

9.പഠനരീതി

i. ഈ പഠനത്തിനവിദേയമാകുന്ന രോഗികളിൽ നിന്നും അവരുടെ ഉമിനീരിന്റെ സാംപിളും കൈവിരലുകളുടെയും Xray ഉം എടുക്കുന്നതിനുള്ള ആവശ്യമായ സമാധാപത്രം ഉറപ്പാരുത്തേണ്ടാതാണ് .

ii. ഉമിനീരിന്റെ സാംപിളുകൾ അണുവിമുക്ത മാക്കിയ കുപ്പികളിൽ ശേഖരിച്ച കേരളം ഗവണ്മെന്റ്സ്ഥാപനമായ Biogenix Research Center, Trivandrum ആയിക്കുന്നു .

iii. ഈ പഠനത്തിനവിദേയമാകുന്നവരുടെപേരവിവരങ്ങൾവെളിപ്പെടുത്തുന്നത്അല്ല .

10. പഠനം മൂലം പങ്കെടുക്കുന്ന ആൾക്ക് ഉ□ാകാൻ ഇടയുള്ള അപകട സാദ്ധ്യത

അപകട സാധ്യത ഇല്ല

11. രോഗികൾക്ക് പ്രതീക്ഷിക്കാവുന്ന ഗുണങ്ങൾ ?

- ഈപഠനംഈമേഖലയിൽപ്രവർത്തിക്കുന്നഭിഷ്വഗരമാർക്കുംരോഗികൾക്കുംഒരേപോലെപൂർണസുരക്ഷിതമായരോഗനിർണായരീതിസഫലമാകുന്നുXrayയുടെഉപയോഗമിലാതെ .
- കാർഡ് അടിസ്ഥാന അസ്ഥിരമായ വളർച്ചാ പരിശോധനകൾ നിർമ്മിക്കാവുന്നതാണ്
- Xray എക്സ്പോഷർ ഒഴിവാക്കുകയും അതുവഴി ബന്ധപ്പെട്ട ആരോഗ്യപ്രശ്നങ്ങൾ ഒഴിവാക്കുകയും ചെയ്യുന്നു.

12. വിവരങ്ങൾരഹസ്യമായിസൂക്ഷിക്കുമോ ? അതെ

13. എന്നെ എന്തുകൊ□ ്ഈ പഠനത്തിൽഉൾപ്പെടുത്തി ?

നിങ്ങൾഞങ്ങളുടെ പഠനത്തിന് അനുയോജ്യമായ ഘടകങ്ങൾ പാലിക്കപ്പെടുന്ന മാതൃകാപരമായഉദാഹരണമാകുന്നു. ഈ പഠനം മൂലംരോഗനിർണ്ണയത്തിന് സഹായവുംസമൂഹത്തിന് നന്മയും പ്രധാനം ചെയ്യുന്നു.

14. എത്ര ആളുകൾ ഈ പഠനത്തിൽഉൾപ്പെടുന്നു ? 30

15. പഠനം മൂലമു□ ാകുന്ന ക്ഷതങ്ങൾക്ക് നഷ്ടപരിഹാരത്തിനുള്ള സമ്മതം

പഠനകർത്താവ്ചികിത്സാചെലവ്വഹിക്കുന്നതാണ്.

16. ഏതെങ്കിലുംവിധത്തിൽവേദനം ലഭിക്കുമോ? ഇല്ല

17. എപ്പോൾവേണമെങ്കിലും എനിക്ക്ഈ പഠനത്തിൽ നിന്ന് പന്മാറാമോ ?

സ്വന്തംതാൽപര്യപ്രകാരംകാരണങ്ങൾ നൽകാതെതന്നെ ഈ പഠനത്തിൽ നിന്ന്എപ്പോൾവേണമെങ്കിലും പിന്മാറാവുന്നതാണ്. എന്നിരുന്നാലുംഗവേഷണസംഘത്തോട് പിന്മാറുന്നതിനു മുൻപ് സംസാരിക്കുവാൻ ഞങ്ങൾ നിങ്ങളോട്അഭ്യർത്ഥിക്കുന്നു.

18. ഈ ഗവേഷണത്തിന്റെ ഫലമായി പുതിയ എന്തെങ്കിലും ക□ ത്തലുകളു□ ങ്കിൽഅത് എന്നെ അിറയിക്കുമോ? അതെ

19. ഈ പഠനത്തിന്റെസമയദൈർഘ്യം എത്രയാണ് ? ഒരുദിവസം

22. ഇതിന്റെ ഭാഗമായിഎന്തെങ്കിലുംകൂടുതൽവിവരങ്ങൾ ?ഇല്ല

21. കൂടുതൽവിവരങ്ങൾക്കായിതാഴെ പറയുന്നവരെ നിങ്ങൾക്ക് ബന്ധപ്പെടാവുന്നതാണ്.

ഡോ .ശ്രീവിദ്യ വിജയൻ

ര□ ാംവർഷം പോസ്റ്റ്ഗ്രാജുവേറ്റ്

ഡിപ്പാർട്ട്മെന്റ്ഓഫ്ഓർത്തോഡോന്റിക്സ്

ശ്രീമൂകാംബിക ഇൻസ്റ്റിറ്റ്യൂട്ട് ഓഫ്ഡെന്റൽ സയൻസ്,

കുലശേഖരം - 629 161.

മൊബൈൽ നമ്പർ :7708787894

ഇ-മെയിൽ ഐ ഡി. : shreevidhya193@gmail.com

സ്ഥലം: പ്രഥമ അന്വേഷകന്റെഒപ്പ്

തീയതി : പങ്കെടുക്കുന്ന ആളിന്റെഒപ്പ്

സമ്മതപത്രം (7-18വയസ്സ്)

ഭാഗം - 2

ഈ പഠനത്തെ പറ്റിയുള്ളഎല്ലാകാര്യങ്ങളും എനിക്ക് പറഞ്ഞ് മനസ്സിലാക്കിതരികയുംഅതിന്റെ ഒരു പകർപ്പ് എനിക്കു നൽകുകയുംചെയ്തിട്ടു□്. ഈ പഠനം ഗവേഷണത്തിനായിഉള്ളതാണെന്നും എനിക്ക്ഇതിൽ നിന്ന് നേരിട്ട് ഒരു ഫലവുംഉ□ാകില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. ഈ പഠനത്തിന്റെരീതിയുംഉദ്ദേശവും എനിക്ക് മനസ്സിലാക്കിതന്നിട്ടു□്. അതു പോലെ എനിക്ക്സംശയങ്ങൾ ചോദിക്കാൻ അവസരങ്ങൾലഭിച്ചിട്ടുമു□്. ഇതിൽ പങ്കെടുക്കാനും പങ്കെടുക്കാതിരിക്കാനും ഉള്ള അവകാശം എനിക്കു□ുംഅതുപോലെ പഠനത്തിന്റെഏതു ഘട്ടത്തിലുംഇതിൽ നിന്ന് പിൻവങ്ങാനുള്ളസ്വാതന്ത്ര്യവും എനിക്കു□ുന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. ഈ പഠനത്തിൽ പങ്കെടുക്കുന്നതുകൊ□ാ, പങ്കെടുക്കാത്തതുകൊ□ാഎന്റെമറ്റുചികിത്സകളെ ബാധിക്കുന്നതല്ലെന്ന് ഞാൻ അിറയുന്നു.

"കൈവിരൽ(MP3) റേഡിയൊഗ്രാഫുകൾ ഉപയോഗിച്ച് ഉമിനീർ igf-1 പരസ്പരം ബന്ധപ്പെടുത്തി എല്ലിൻറെ മെച്യൂരിറ്റി വിലയിരുത്തൽ."എന്ന ഗവേഷണത്തിൽ പങ്കെടുക്കുന്നതിനും ഇതിന്റെ ഫലങ്ങൾശാസ്ത്രലേഖനത്തിൽ പ്രസിദ്ധീകരിക്കുന്നതിനും എനിക്ക് സമ്മതമാണെന്ന് ഞാൻ ഇതിനാൽഅിറയിച്ചുകൊള്ളുന്നു.

സീരിയൽനമ്പർ / റഫറൻസ്നമ്പർ

പങ്കെടുക്കുന്ന ആളിന്റെ പേര് :

അച്ഛൻ / അമ്മയുടെ പേര്

മേൽവിലാസം :

ഫോൺ നമ്പർ :

പങ്കെടുക്കുന്ന

കുട്ടിയുടെ പേര്

സാക്ഷി : അച്ഛൻ /

അമ്മയുടെ ഒപ്പ്

സ്ഥലം :

തീയതി

ஒப்புதல் வாக்கு மூலம்

முதல் பாகம்
ஆராய்ச்சியில் பங்குபெறுவோருக்கான தகவல் குறிப்பு

அன்பார்ந்த பங்கேற்பாளர்களே,

இந்த ஆராய்ச்சியில் தங்களை ஈடுபடுத்திக்கொள்ள மிகுந்த ஆர்வத்துடன் முழுமனதுடன்கலந்துகொள்ள வந்த வரவேற்பாளர்களை வரவேற்கிறேன். நீங்கள் இந்த ஆராய்ச்சியில் பங்கெடுத்துக்கொள் வதற்கு முன் இந்த ஆராய்ச்சி எதற்காக நடத்தப்படுகிறது என்பதை தெளிவாகபுரிந்துகொள்ளவேண்டும். உங்களுக்கு தேவையான அனைத்து விபரங்களும் கீழேகொடுக்கப்பட்டுள்ளது

இந்த ஆராய்ச்சியின் மூலம் ஏற்படும் நன்மைகள், ஏதேனும் ஆபத்துகள் மற்றும் அதற்காகமற்றும் எவ்வாறு இந்த ஆராய்ச்சி மேற்கொள்ளப்படும் முறைகளையும் தெரிவிக்கப்பட்டுள்ளது.இதில் கொடுக்கப்பட்டுள்ள விபரங்களை தெளிவாக படித்து புரிந்து கொள்ளவேண்டும். நீங்கள் ஆராய்ச்சியில் பங்கேற்பாளர்களாக ஒப்புதல் வழங்குவதற்கு முன்பு உங்களுக்கு ஏற்படும் அறிவியல் சார்ந்த சந்தேகங்கள் மற்றும் ஆராய்ச்சி சம்பந்தப்பட்ட சந்தேகங்கள் அனைத்தும் இந்த ஆராய்ச்சியின் எந்த காலகட்டத்திலும் நீங்கள் படிவத்தில்குறிப்பிட்ட நபரிடம் கேட்டு தெளிவுபடுத்திக்கொள்ளலாம்.

1. தலைமை ஆய்வாளர் : டாக்டர். ஸ்ரீவித்யா விஜயன்
   தகுதி : முதுகலை மாணவி
   பிரிவு : ஓர்தொடோன்டிக்ஸ் துறை
   நிறுவனம் :
   ஸ்ரீ மூகாம்பிகா இன்ஸ்டிட்யூட் ஆப் டென்டல் சயன்ஸஸ்,
   இடம் : குலசேகரம் - 629 161.

2. வழிகாட்டி : டாக்டர். அனில்குமார் பி . MDS
   தகுதி : தலைமையாளர், பேராசிரியர்
   பிரிவு : ஓர்தொடோன்டிக்ஸ் துறை
   நிறுவனம் :
   ஸ்ரீ மூகாம்பிகா இன்ஸ்டிட்யூட் ஆப் டென்டல் சயன்ஸஸ்,
   இடம் : குலசேகரம் - 629 161

3. இணைவழிகாட்டி : டாக்டர்அமல்ஸ்நாயர் MDS
   தகுதி : ரீடர்
   பிரிவு : ஓர்தொடோன்டிக்ஸ் துறை
   நிறுவனம் :
   ஸ்ரீ மூகாம்பிகா இன்ஸ்டிட்யூட் ஆப் டென்டல் சயன்ஸஸ்,
   இடம் : குலசேகரம் - 629 161.

4. கல்லூரி :

ஸ்ரீ மூகாம்பிகா இன்ஸ்டிட்யூட் ஆப் டென்டல் சயன்ஸஸ்,
படநிலம் குலசேகரம்- 629 161.

5. ஆராய்ச்சியின் தலைப்பு

மனித எலும்பு கூட்டின் முதிர்ச்சியின் அளவை உமிழ்நீரிலுள்ள இஃப் 1 மதிப்பை கை - MP3 நிலைகள்ஸலம் ஒப்பிட்டு மதிப்பிடுதல்

6 . பின்னணி தகவல்கள்

முக்கிய புள்ளிகளை கண்டுபிடிப்பது மற்றும் x-ரயின் நிலைப்பாடு பற்றி அளவிடுவது கர்ப்பப்பை வாய் முதுகலெும்பு முதிர்வு (சி.வி.எம்) மற்றும் MP3 உள்ளார்ந்த சுறபைாடு ஆகும் மலேும், இந்த இரண்டு வழிமுறைகளைோடு தைொடர்புடையை கதிர்வீச்சு வளிைப்பாடு காரணமாக, x-கதிர்கள் ஒரு வரடத்திற்கு ஒரு முறைக்கு மலே சயெ்ய முடியாது. இஃப்1அந்த இடத்தில் மற்றும் வறே எல்லா எடத்திலுமுள்ள வளர்ச்சியை துண்டுகிகிறது. IGF-1 அளவை அதிகரிப்பது பரவவளர்ச்சி வளர்ச்சியுடன் தைொடர்புடையை. IGF-1 அளவுகள் பரப்பு வளர்ச்சி வளர்ச்சியைக் கண்டறிவதற்கான மாற்ற வழிமுறையாக முன்மைொழியப்பட்டது. கை-மணிக்கட்டு கதிர்வரைப்படம் மற்றும் IGF-1 இங்குபல் கட்டவரும் நோயாளிகளிடம் தைொடர்பு இரக்கிறதாஎன்பதை கண்டறிவதே எனது ஆய்வின் நோக்கமாகும்.

7. குறிக்கோள் மற்றும் நோக்கம் :

- MP3 பயன்படுத்தி எலும்பு முதிர்ச்சியின் பல்வறே கட்டங்களில் சராசரி IGF -1 அளவை ஒப்பிட்டு பார்க்க
- உயிர்ச்சத்து IGF-1 அளவுகள் எலும்பு முதிர்வு அடையாள அட்டையைப் பயன்படுத்த முடியுமா என்பதை மதிப்பிடுவதற்கு
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8. ஆய்வின் அறிவியல் நியாயப்படுத்துதல்

GH நிலைகளைப் பாலல்லாமல், அதன் நிலைகள் நாள் முழுவதும் மாறா நிலையில் இல்லாததால், GH நிலையை நிர்ணயிக்கும் ஒரு பயனுள்ள கண்டறியும் கருவி IGF-I ஆகும். எலும்பு வளர்ச்சியானது GH நிலைக்கு மிக நரெ்கமாக தைொடர்புடையைதாகக் காட்டப்பட்டுள்ளது IGF- 1 நீண்ட எலும்பு வளர்ச்சியில் ஒரு முக்கிய பங்கு வகிக்கிறது, அதே போல் கீழ்தாடையின் தடித்த எலும்பு முனை வளர்ச்சி கண்டுள்ளது. தரிதமான தாடை வளர்ச்சி, கதிரியக்க எலும்பு முதிர்வு வளர்ச்சியுள்ள சில மனிதர்களில் உள்ளது. அதனை நாம் ரசெிடுவாள் மண்டி புலர்கரோவ்த் என்கிறோம். மலேும் சில கறிப்பிட்ட விஷயங்களில் ரடேியோகிராஃபிக் பபலெ்ட் வளர்ச்சி நிலைக்கு முன், சிறுவயது முடுக்கம் என அழைக்கப்படும் நிகழ்வு உள்ளது. இத்தகயை சந்தர்ப்பங்களில், ஹார்மானே் உயிரிகள், கதிரியக்க எலும்பு முதிர்வு மதிப்பீட்டு முறைகள் மீது நல்ல பயன்களை தருகின்றன.

9. ஆய்வின் நடைமுறை

i. பறெ்றோர் மற்றும் நோயாளிகளிடம், ஆய்வு பற்றி விளக்கி அவர்களது உமிழுநீர் மற்றும் MP3 கதிரவரை படம் ((வழக்கமான orthodontic பரிசோதனைக்கு எடுத்த அவை) தகவல் ஒப்புதல் பறெ்ற பின்னரே இந்த ஆய்வில் பயன்படுத்தப்பட்டது .
ii. நோயாளிகளின் உமிழ்நீரகை - மணிக்கட்டு கதிர்வரை படம் எடுத்த ஒரு வாரத்திற்குள் எடுக்கப்பட வண்டும்
iii. ஒரு சறெிவூட்டப்பட்ட பிளாஸ்டிக் சகேரிப்பில் உமிழ்நீர் சகேரிக்கப்பட்டது. உமிழ் நீரை உட்சவெ்தித்திய IGF-1 அளவை ஆய்வு சயெ்ய அதே நாளில் ஆய்வகத்திற்கு அனுப்பப்பட்டது.

iv. அனைத்து கை – மணிக்கட்டு கதிர்படம், இரு நபர்களால் பிஜோர்க் , க்ராவ் அண்ட் பிரவுன் அடிப்படைகளை வைத்து பிரித்து பார்க்கப்படுகிறது.

v. Bjork, க்ரவே மற்றும் பிரவுன்ஸ்டஜேங் அடிப்படையில், 9 நிலைகள் 3 கட்டங்களாக (Prepubertal, Pubertal & Postpubertal) மீண்டும் இணைக்கப்பட்டன.

vi. எலும்பு முதிர்வு காட்டி (SMI) மதிப்பெண்கள் காலவரிசை வயது மற்றும் பாலியல் முறிப்புடன் பகுப்பாய்வு செய்யப்பட்டன.

10. ஆய்வில் கலந்து கொள்பவர்களுக்கு எதிர்பார்க்கப்படும் ஆபத்துகள் ?

ஒன்றும் இல்லை

11 . பங்கேற்பாளர்களுக்கு எதிர்பார்க்கப்படும் பயன்கள்?

இந்த ஆய்வு சுகாதார பராமரிப்பு பயிற்சியாளர்களுக்கு உயிரிகளின் முக்கியத்துவத்தின் மூலம் நோயாளிகளின் உடல் நலபராமரிப்பு அதிகரிக்கபடுவதிலும் மற்றும் வளர்ச்சியை தீர்மானிக்கப்படுவதிலும் பெரிதும் உதவுகிறது .

12 இரகசியத்தன்மை காத்தல் ?

உங்களிடம் இருந்து சேகரித்த எந்த விபரமும் இரகசியமாக வைக்கப்படும். இதன்மூலம் கிடைக்கும் புள்ளிவிபரம் மட்டும் வெளியிடப்படும். மற்றபடி தனிநபரின் சொந்த விபரங்கள் வெளியிடப்படமாட்டாது.

13. . எதனால் இந்த ஆய்வில் நான் பங்கேற்க தேர்ந்தெடுக்கப்பட்டேன் ?

அ, எனது கல்வி நிறுவனத்தின் நிபந்தனைகளுக்கு இது உட்பட்டது.

ஆ. நோய்களின் ஆய்வு

இ. எந்த வகையிலும் நோயாளிகளை மிகுந்த சிரமத்திற்கு உட்படுத்தாது.

14. இந்த ஆய்வில் எத்தனைபேர் பங்கேற்கிறார்கள் ? 30

15. இந்த ஆய்வின் மூலம் ஏதேனும் பின்விளைவுகள் ஏற்பட்டால் ஆராய்ச்சியாளர் பொறுப்பு ஏற்பாரா? பொருத்தமல்லை

16. இந்த ஆராய்ச்சியில் பங்குபெறுவோருக்கு எவ்வித தொகையும் வழங்கப்படுமா ? இல்லை

17. நான் இந்த ஆராய்ச்சியிலிருந்து விருப்பப்பட்டால் எந்த காலகட்டத்திலும் விலகலாமா ?

நோயாளியின் எந்த ஒரு கட்டுப்பாடு / நிபந்தனைகளின் கீழ் இந்த ஆய்விற்கு உட்படுத்தப்படவில்லை. அவர்களின் முழு ஒத்துழைப்பு மற்றும் சம்மதத்தின் பேரில் மட்டுமே பங்கெடுத்துள்ளனர்

18. ஏதேனும் புதிய செய்தி, புதிய கண்டுபிடிப்பு பற்றி நான் அறிவிக்கப்படுவேனா ? ஆம்

19. ஆராய்ச்சியின் எதிர்பார்க்கப்படும் பங்குகால அளவு ? ஆறு மாதம்

20. வேறு ஏதேனும் பொருத்தமான விபரங்கள் உண்டா ? இல்லை

21. இவ்வாராய்ச்சியைப் பற்றிய விவரங்களை யாரிடம் கேட்டு தெரிந்துக்கொள்வது ?

தலைமை ஆய்வாளர் : டாக்டர். ஸ்ரீவித்யா விஜயன்
தகுதி : முதுகலை மாணவி
பிரிவு : ஓர்தொடோன்டிக்ஸ் துறை
நிறுவனம் : ஸ்ரீ மூகாம்பிகா இன்ஸ்டிட்யூட் ஆப் டென்டல் சயன்ஸஸ்,
இடம் : குலசேகரம் - 629 161.
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இடம் :
தேதி :

முதன்மை ஆராய்ச்சியாளரின் கையொப்பம்

ஒப்புதல் படிவம்

பாகம் 2

இந்த ஆராய்ச்சியின் தகவல்கள் அனைத்தும் என்னிடம் தெளிவாக எழுத்துமூலம் விளக்கப்பட்டுள்ளது. இந்த ஆராய்ச்சியின் முடிவுகள் எனக்கு நேரடியாக பயன்பராவிட்டாலும் மருத்துவத்துறையின் முன்னேற்றத்திற்கு பயன்படும் என்பதை அறிவேன். இவ்வாராய்சியைப் பற்றி நான் தெளிவாக புரிந்துக் கொண்டுள்ளேன். நான் தானாக முன்வந்து இதில் பங்குப் பெறுகிறேன்என்பதை அறிவேன். இதிலிருந்து எந்த நேரமும் எக்காரணமும் கூறாமல் வந்த ாலும் இந்த மருத்துவமனையில் எனக்கு கிடைக்கும் மருத்துவ உதவி எவ்விதத்திலும் பாதிக்க ப்படாது என்பதையும் அறிவேன். இவ்வாராய்ச்சியின் மூலம் வரும் முடிவுகள் மற்றும் தகவ ல்களை அறிவியல்துறையின் பயன்பாடுகளுக்கு (மட்டுமே) உபயோகப்பட்டிக்கொள்ள சம்மதிக்கி றேன். எனக்குஇவ்வாராய்ச்சியைப் பற்றிய விரிவான தகவல்கள் அடங்கிய படிவம் தரப்பட்டு ள்ளது.

மனித எலும்பு தூட்டின் முதிர்ச்சியின் அளவை உமிழ்நீரிலுள்ள IGF-1 மதிப்பை MP3 நிலைகள் மூலம் ஒப்பிட்டு மதிப்பிடுதல் என்கிற ஆராய்ச்சியில் நான் பங்கேற்க முழுமனதுடன் சம்மதிக்கிறேன்.

பங்கு கொள்பவரின் தொடர், மருத்துவ எண் :
பங்கு கொள்பவரின் பெயர் :

18 வயதிற்கு கீழ் உள்ளவர்களுக்கு பாதுகாவலரின் கையொப்பம்:

முகவரி

தொலை தொடர்பு எண் :

பங்கு கொள்பவர் பராமரிப்பவர் கையொப்பம்/பெருவிரல் சுவடு :

சாட்சி 1

சாட்சி 2

தேதி:

இடம்: குலசேகரம்

DATA ENTRY SHEET

Group I (MP3F – MP3FG)

S.No	NAME	AGE	SEX	IGF VALUE (pg/ml)	MP3 STAGE
1.					
2.					
3.					
4.					
5.					
6.					
7.					
8.					
9.					
10.					

Group II (MP3G)

S.No	NAME	AGE	SEX	IGF VALUE (pg/ml)	MP3 STAGE
1.					
2.					
3.					
4.					
5.					
6.					
7.					
8.					
9.					
10.					

Group III (MP3H- MP3I)

S.No	NAME	AGE	SEX	IGF VALUE (pg/ml)	MP3 STAGE
1.					
2.					
3.					
4.					
5.					
6.					
7.					
8.					
9.					
10.					

INDIVIDUAL DATA SHEET

“SKELETAL MATURITY ASSESSMENT BY CORRELATING SALIVARY IGF-1 WITH MP 3 STAGING.”

S.**NO :**

DATE :

NAME :

D.O.B:

AGE/ SEX :

FATHER’S/ GUARDIAN’S NAME :

ADDRESS :

PHONE NO :

OCCUPATION :

GENERAL HEALTH :

FAMILIAL DISEASES :

H/O ACCIDENT /TRAUMA :

MILESTONES OF DEVELOPMENT :

PAST MEDICAL HISTORY :

MP3 RADIOGRAPH STAGE :

IGF VALUE :

DATA ANALYSIS CHART

Group I (MP3F- MP3FG)

S.NO	NAME	AGE	SEX	IGF VALUE(Pg/ml)	MP3 STAGE
1.	GANESWARAN	11	M	195.5	MP3F
2.	SANJAY	1	M	73.3	MP3F
3.	MARLYN	8	F	36.65	MP3F
4.	MAHAS	10	M	29.32	MP3F
5.	VISHAL	10	M	73.3	MP3F
6.	VARSHINI	9	F	219.9	MP3F
7.	VINOD	9	M	240	MP3F
8.	AUSTRICRAVIN	11	M	73.3	MP3FG
9.	PAVITHRA	9	F	293.3	MP3F
10.	BEVIN	11	M	73.3	MP3FG

Group II (MP3G)

S.NO	NAME	AGE	SEX	IGF VALUE(Pg/ml)	MP3 STAGE
1.	ISWARYA	12	F	953.29	MP3G
2.	LIJO	14	M	659.98	MP3G
3.	BJ BABISHA	12	F	659.98	MP3G
4.	LIBIN	13	M	1319.94	MP3G
5.	SHRUTHI	12	F	1319.94	MP3G
6.	DHARSINI	12	F	620.2	MP3G
7.	BABIN	14	M	293.3	MP3G
8.	SAJAN	14	M	219.95	MP3G
9.	PRADEEP	14	M	322.636	MP3G
10.	ANISHIYA	12	F	366.64	MP3G

Group III (MP3H- MP3I)

S.NO	NAME	AGE	SEX	IGF VALUE (Pg/ml)	MP3 STAGE
1.	SUBALEKSHMI	19	F	733.3	MP3H
2.	BENITHA	15	F	615.972	MP3H
3.	JACQULINE	16	F	615.972	MP3H
4.	VARSHA	17	F	659.98	MP3H
5.	SAMYUKTHA	20	F	620.2	MP3H
6.	KARTHIKA	18	F	620.2	MP3H
7.	AATHIRA	20	F	620.2	MP3I
8.	LAVANYA	19	F	733.3	MP3I
9.	NISHANA	15	F	366.64	MP3H
10.	APARNA	16	F	615.972	MP3I