ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 11 | November - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

"GROWTH HORMONE AND CRANIOFACIAL DEVELOPMENT"

Orthodontics

Dr. Roulath TR	Post graduate student, Department of Orthodontics, Government Dental college, Kozhikode, Kerala.
Dr. Praveen S	Professor and Head, Department of Orthodontics, Government Dental college, Kozhikode, Kerala.
Dr. Latheef VP	Associate professor, Department of Orthodontics, Government Dental college, Kozhikode, Kerala.
Dr. Sreehari S	Associate professor, Department of Orthodontics, Government Dental college, Kozhikode, Kerala.
Dr. Baby Jisha	Assistant Professor, Department of Orthodontics, Government Dental college, Kozhikode, Kerala.
Dr. Muhammed Shibin P	Assistant Professor, Department of Orthodontics, Government Dental college, Kozhikode, Kerala

ABSTRACT

Growth hormone (GH) is a key regulator of somatic and craniofacial development, exerting its effects directly via GH receptors and indirectly through insulin-like growth factor-I (IGF-I). The GH/IGF-I axis influences bone modelling, remodelling, and soft tissue growth, essential for normal facial morphology. GH also stimulates osteoblast proliferation, enhances osteoclastic activity, and supports periosteal apposition at the cellular level. Secondary cartilage in the mandibular condyle exhibits GH and IGF-I receptor expression, highlighting their role in endochondral ossification and mandibular development. Additionally, GH impacts dental tissues by promoting odontogenic proliferation and facilitating dentin and cementum formation. Growth hormone deficiency (GHD) often presents with distinctive craniofacial anomalies, including reduced cranial base length, mandibular retrognathia, increased gonial angles, and delayed dental maturation. Cephalometric studies reveal smaller maxillary and mandibular dimensions in GHD patients. Recombinant human GH (rhGH) therapy has demonstrated improvements in mandibular growth and facial balance, though complete normalization is rare. In contrast, GH excess, as seen in acromegaly, results in mandibular prognathism, macroglossia, and dental malocclusions due to excessive periosteal bone deposition and soft tissue hypertrophy. Recognizing the pivotal role of GH in craniofacial development is essential for clinicians. Dentists and orthodontists, in particular, can identify early signs of GH dysregulation, facilitating timely diagnosis and intervention to optimize growth outcomes.

KEYWORDS

INTRODUCTION

Human growth from conception to adulthood involves a complex interplay of biological systems regulating cell differentiation, tissue formation, and maturation[1]. Craniofacial growth is similarly shaped by genetic, hormonal, nutritional, and environmental factors. Disruptions in these pathways often result in atypical facial development, as seen in endocrine disorders like growth hormone deficiency , idiopathic short stature , and genetic syndromes. An individual's height is another factor is also under the influence of these hormonal changes.

Growth hormone (GH) which is secreted by the anterior pituitary gland, plays an important role in systemic and craniofacial growth. Acting directly through specific receptors and indirectly through stimulation of insulin-like growth factor I (IGF-I), the GH/IGF-I axis regulates bone metabolism, guides modeling and remodeling, and supports the development of orofacial and cranial structures throughout growth[2–4].

MECHANISM OF ACTION OF GH AT CELLULAR LEVEL

GH is synthesized in anterior pituitary somatotrophs, its secretion being tightly regulated by feedback mechanisms involving GHRH, somatostatin, and ghrelin. GHRH stimulates GH release, while somatostatin inhibits it, particularly during hypoglycemia. Ghrelin, secreted by the gastrointestinal tract, enhances GH secretion in fasting states. IGF-1, produced mainly in the liver in response to GH, contributes to negative feedback by suppressing somatotroph activity and enhancing somatostatin release. Together, these mechanisms generate a pulsatile GH secretion pattern with peak levels during puberty and gradual decline with age.

GH acts directly by binding to its receptors on target tissues and indirectly by stimulating IGF-1 production via the Janus Kinase-Signal Transducer and Activator of Transcription (JAK-STAT) pathway. Activated JAK1/2 recruit STAT1, STAT3, and STAT5, which enters the nucleus to induce IGF-1 gene expression. Circulating IGF-1 then mediates growth and metabolic regulation, underscoring the critical role of the GH/IGF-I axis in systemic and craniofacial growth.

GH/IGF-I axis

GH circulates bound to GHBP, modulating bioavailability. Studies have shown that GH have direct as well as indirect actions on tissues. Initially, the Somatomedin Hypothesis was proposed in 2001 by Le Roith et al which states that GH induces the liver to produce somatomedins (IGFs) which supports osteoblast replication and function, modulated by IGFBPs.[5] Local feedback mechanisms involving IGF-I also may suppress GH action by downregulating GHRs which forms a tightly regulated system for skeletal homeostasis.[6-8]This hypothesis explained the indirect action of GH on tissues while direct action was described by the Dual effector theory.[9,10] This theory highlights independent roles of GH and IGF-I during endochondral ossification. The direct action promotes the differentiation of precursor cells which was demonstrated for two mesenchymal cell types and indirect action via IGFs.GH receptors (GHRs) are identified in hypertrophic cartilage zones and dental tissues, reinforcing GH's direct contribution to skeletal and craniofacial development[11–16]. Immunolocalization of GHRs in osteoblasts and osteoclasts during processes like tooth eruption and orthodontic tooth movement suggests GH's role in regulating bone resorption and remodeling in craniofacial regions[17,18].

EFFECT OF GH ON CRANIOFACIAL STRUCTURES

Growth hormone (GH) plays a crucial role in bone modeling and remodeling, essential for maintaining skeletal integrity under mechanical stress. GH directly stimulates osteoblasts which promotes bone formation and indirectly supports osteoclast activity via stromal cell interactions. Clinical evidence shows that GH therapy elevates bone turnover markers, including serum alkaline phosphatase, procollagen type I C-terminal propeptide, and deoxypyridinoline[19]. Experimental studies in also report enhanced bone density and collagen fiber organization around dental implants when GH is applied post-extraction, leading to improved bone healing and implant stability[20,21].

EFFECT ON MANDIBULAR CONDYLE

The mandibular condyle cartilage, a secondary cartilage of periosteal origin from neural crest cells, differs from primary cartilage in its structure and response to stimuli. Its superficial perichondrium contains pre-chondroblastic cells that produce type I collagen, unlike the type II collagen produced in primary cartilage.

Cartilage formation in the condyle is strongly influenced by mechanical stimuli, such as changes in jaw position, which trigger mesenchymal cell differentiation into chondrocytes[22,23]. These cells proliferate, mature into hypertrophic chondrocytes and contribute to endochondral ossification.[24] Growth hormone (GH) and insulin-like growth factor I (IGF-I) receptors are highly expressed in the chondroprogenitor and chondroblast layers, with IGF-I distribution matching its receptors. This suggests GH primarily acts through IGF-I mediation to induce local proliferation and cartilage development[25]. GH deficiency reduces IGF-I synthesis, impairing condylar growth, while elevated GH enhances IGF-I production and chondrocyte activity[26–28]

Genetic studies have linked GHR polymorphisms to mandibular morphology. The P561T SNP (cytosine-to-adenine transversion) in Japanese individuals leads to a proline-to-threonine substitution, associated with shorter mandibular rami[29]. Additionally, the P561T variant has been identified as a potential negative regulator of mandibular growth in Japanese children with mandibular prognathism.[30,31] In contrast, the I526L variant correlates with increased ramus length in Chinese Han populations, though findings in Japanese and Korean cohorts remain inconclusive.

EFFECT ON DENTAL STRUCTURES

Growth hormone (GH) contributes to the formation of mineralized dental tissues-dentin, cementum, and enamel-similar to the actions of bone morphogenetic proteins (BMPs).[7] GH receptors are identified in hard tissues, especially near the amelodentinal junction suggesting their role in localized growth responses. IGF-I receptors, observed during early molar tooth bud formation in rats, further indicate GH's regulatory influence on early odontogenesis[32]

Experimental studies in Lewis dwarf rats showed reduced number of odontogenic epithelial cells in untreated subjects, while GH-treated dwarfs demonstrated normalized cell numbers in the internal enamel epithelium, the stratum intermedium, and Hertwig's epithelial root sheath (HERS). This indicates that GH enhances cell proliferation which critical for overall development of a tooth[32]. In GH receptor-deprived mice, cellular cementum formation was reduced nearly tenfold, while GH antagonist treatment caused a threefold decrease. Conversely, GH-excess mice exhibited a twofold increase in cementum formation[33,34]. Morphometric analyses revealed dwarf mice had smaller crowns, shorter and narrower roots and reduced width at the cementoenamel junction mesiodistally. Interestingly, GH overexpression elongated roots but did not significantly affect crown width or root dentin thickness.[35,36]

In humans, growth hormone deficiency (GHD) is often associated with delayed dental maturation, microdontia, missing third molars, single maxillary central incisors, smaller premolar crowns, and delayed permanent tooth eruption. While GH therapy in idiopathic short stature and GHD patients enhances skeletal growth, its effect on dental maturation remains limited. [25,36–41]

EFFECTS ON ALVEOLAR BONE AND ORAL MUSCLES

GH contributes to alveolar bone width and strength through periosteal apposition and muscle-mediated skeletal loading. In muscle, GH regulates IGF-1 production, influences myofiber type, and promotes hypertrophy, which indirectly supports bone remodeling. GH-deficient states show impaired muscle mass and reduced periosteal bone thickening, impacting craniofacial morphology[8,14].

FEATURES OF GROWTH HORMONE DEFICIENCY

Craniofacial development in growth hormone deficient children is characterized by disproportionate skeletal growth patterns due to impaired GH-mediated regulation of bone and soft tissue growth. The mandible is particularly affected, presenting as mandibular retrognathia with a retruded chin, steep mandibular plane, and increased gonial angle, leading to a more convex facial profile[28,43] Cephalometric studies consistently demonstrate reduced lengths of anterior and posterior cranial base (N-S), with the posterior base often more severely affected[28]. The mandibular ramus (Cd-Go) and corpus (Pog-Go) are significantly shorter, contributing to decreased posterior facial height. In contrast, the maxilla is relatively less impacted, though mild retrusion and reduced maxillary length (A-Ptm) have been reported[44]. Lower anterior facial height (ANS-Me) is also reduced, giving the face a more juvenile and underdeveloped appearance. Soft tissue features include a youthful facial profile with thicker subcutaneous fat layers.[28,43]Gender differences have been noted; girls tend to have smaller mandibles and posteriorly positioned jaws, while boys often exhibit a flatter cranial base and underdeveloped midface and mandibular structures.[43]

In adults, growth hormone deficiency (GHD) leads to subtle but progressive craniofacial changes. Like diminished bone turnover and periosteal apposition, causing mandibular retrusion, a flatter facial profile and decreased lower facial height[28,43]. Loss of muscle mass and tone in the orofacial region contributes to soft tissue sagging and an aged appearance. These changes, although less pronounced than in children, can impact prosthetic planning, implant stability, and increase orthodontic relapse risk. Recombinant GH therapy in adults improves bone density and soft tissue integrity, offering partial restoration of facial contours and function[45,46]. However, skeletal remodeling potential is limited, emphasizing the need for early diagnosis and intervention.

CRANIOFACIAL CHANGES IN GIGANTISM

In gigantism, excessive secretion of growth hormone (GH) before epiphyseal closure leads to proportional overgrowth of skeletal and soft tissues, including the craniofacial complex. The mandible undergoes pronounced enlargement due to continued endochondral and periosteal growth. This results in prognathism**,** contributing to a skeletal Class III malocclusion and altered occlusal relationships. Cephalometric analyses often reveal elongated mandibular bodies and rami, increased gonial angles, and flattening of the cranial base as a consequence of disproportionate growth between the cranial vault and facial skeleton[47].

Frontal bossing is a notable feature caused by excessive bone deposition in the frontal bone, while hypercementosis of tooth roots has been reported radiographically. The accelerated skeletal growth also leads to increased spacing between teeth (diastema) as the alveolar bone expands more rapidly than the dentition can compensate[47]

Soft tissue overgrowth further accentuates facial changes. The lips become thickened, and macroglossia (enlarged tongue) may develop, contributing to dental flaring and spacing. The combination of skeletal and soft tissue alterations gives patients a coarse facial appearance, with exaggerated features that are often noticed early in life.

ORTHODONTIC CONSIDERATIONS AND CLINICAL RELEVANCE

Orthodontic tooth movement is based on a balanced cycle of bone resorption and apposition in response to forces, chiefly mechanical. GH enhances this process by promoting osteoblast proliferation, osteoclastic activity, facilitating efficient tooth movement under orthodontic forces. In GH deficiency (GHD), delayed skeletal maturation, reduced alveolar bone volume, and diminished muscle strength may prolong treatment time and compromise outcomes.

Optimal timing of orthodontic treatment is crucial. Peak GH secretion during puberty can amplify the response to functional appliances, while excessive GH, as seen in acromegaly, may cause mandibular prognathism and dental malocclusions, requiring careful biomechanical management.

GH also accelerates periodontal ligament recovery and bone turnover, which benefits tooth movement but may increase anchorage loss and relapse risk. Extended retention and individualized force application are recommended for patients with GH abnormalities. Recognizing GH's role in craniofacial adaptation enables orthodontists to optimize treatment strategies, particularly in patients with endocrine disorders.[17,38,39,42]

CONCLUSION

The GH/IGF-I axis is indispensable for craniofacial development, influencing endochondral ossification, bone remodeling, and odontogenesis. Growth hormone deficiency results in distinct craniofacial features, such as a shortened cranial base, hypoplastic

maxilla, and retrognathic mandible, whereas GH excess in conditions like gigantism and acromegaly leads to mandibular prognathism, macroglossia, and dental malocclusions.

These changes have important orthodontic implications, as altered bone metabolism and growth patterns can affect treatment timing, mechanics, and long-term stability. Early recognition of GH-related craniofacial anomalies by dental professionals enables prompt referral for endocrine management. While medical therapy can mitigate progression, orthodontic and surgical interventions remain essential for correcting functional and aesthetic concerns.

Advancing research on GH's role in craniofacial biology will further improve diagnostic precision and treatment strategies, enhancing outcomes and quality of life for affected patients.

Abbreviations:

GH – Growth Hormone; IGF-I – Insulin-like Growth Factor-I; GHD – Growth Hormone Deficiency; rhGH – Recombinant Human Growth Hormone; PDL – Periodontal Ligament; BMP – Bone Morphogenetic Protein, IL-6 – Interleukin-6, IGFBPs – Insulin-like Growth Factor Binding Proteins, GHBP – Growth Hormone Binding Protein ,GHR – Growth Hormone Receptor, JAK-STAT – Janus Kinase-Signal Transducer and Activator of Transcription,ISS – Idiopathic Short Stature, Cd-Go – Condylion to Gonion (Mandibular Ramus Height), Gn-Cd – Gnathion to Condylion (Mandibular Length), Pog-Go – Pogonion to Gonion (Mandibular Corpus Length), A-Ptm – Point A to Pterygomaxillary Fissure (Maxillary Length, N-S – Nasion to Sella (Cranial Base Length), ANS-Me – Anterior Nasal Spine to Menton (Lower Anterior Facial Height), HERS – Hertwig's Epithelial Root Sheath, OSA – Obstructive Sleep Apnea, TMJ – Temporomandibular Joint

REFERENCES

1. Giustina A, Veldhuis JD. Pathophysiology of the neuroregulation of growth hormone secretion in experimental animals and the human. Endocr Rev. 1998 Dec;19(6):717–97.
2. Slootweg MC. Growth hormone and bone. Horm Metab Res Horm Stoffwechselforschung Horm Metab. 1993 Jul;25(7):335–43.
3. Wüster C. Growth hormone and bone metabolism. Acta Endocrinol (Copenh). 1993 Jun;128 Suppl 2:14–8.
4. Giustina A, Mazziotti G, Canalis E. Growth Hormone, Insulin-Like Growth Factors, and the Skeleton. Endocr Rev. 2008 Aug 1;29(5):535–59.
5. Le Roith D, Bondy C, Yakar S, Liu JL, Butler A. The Somatomedin Hypothesis: 2001. Endocr Rev. 2001 Feb 1;22(1):53–74.
6. Tsuji K, Bandyopadhyay A, Harfe BD, Cox K, Kakar S, Gerstenfeld L, et al. BMP2 activity, although dispensable for bone formation, is required for the initiation of fracture healing. Nat Genet. 2006 Dec;38(12):1424–9.
7. Li H, Bartold PM, Young WG, Xiao Y, Waters MJ. Growth Hormone Induces Bone Morphogenetic Proteins and Bone-Related Proteins in the Developing Rat Periodontium. J Bone Miner Res. 2001 Jun 1;16(6):1068–76.
8. Nishiyama K, Sugimoto T, Kaji H, Kanatani M, Kobayashi T, Chihara K. Stimulatory effect of growth hormone on bone resorption and osteoclast differentiation. Endocrinology. 1996 Jan;137(1):35–41.
9. Isaksson OGP, Lindahl A, Nilsson A, Isgaard J. Mechanism of the Stimulatory Effect of Growth Hormone on Longitudinal Bone Growth*. Endocr Rev. 1987 Nov;8(4):426–38.
10. Green H, Morikawa M, Mxon T. A dual effector theory of growth-hormone action. Differentiation. 1985 Jul;29(2):195–8.
11. Werther GA, Haynes K, Edmonson S, Oakes S, Buchanan CJ, Herington AC, et al. Identification of growth hormone receptors on human growth plate chondrocytes. Acta Paediatr Oslo Nor 1992 Suppl. 1993 Sep;82 Suppl 391:50–3.
12. Gevers EF, van der Eerden BCJ, Karperien M, Raap AK, Robinson ICAF, Wit JM. Localization and regulation of the growth hormone receptor and growth hormone-binding protein in the rat growth plate. J Bone Miner Res Off J Am Soc Bone Miner Res. 2002 Aug;17(8):1408–19.
13. Leung DW, Spencer SA, Cachianes G, Hammonds RG, Collins C, Henzel WJ, et al. Growth hormone receptor and serum binding protein: purification, cloning and expression. Nature. 1987 Dec 10;330(6148):537–43.
14. Barnard R, Ng KW, Martin TJ, Waters MJ. Growth hormone (GH) receptors in clonal osteoblast-like cells mediate a mitogenic response to GH. Endocrinology. 1991 Mar;128(3):1459–64.
15. Hogan BL. Bone morphogenetic proteins: multifunctional regulators of vertebrate development. Genes Dev. 1996 Jul 1;10(13):1580–94.
16. Ong CK, Joseph BK, Waters MJ, Symons AL. Growth hormone receptor and IGF-I receptor immunoreactivity during orthodontic tooth movement in the prednisolone-treated rat. Angle Orthod. 2001 Dec;71(6):486–93.
17. Symons AL. Reduced growth hormone receptor immunoreactivity in osteoclasts adjacent to the erupting molar in the incisor-absent (osteopetrotic) rat. Eur J Oral Sci. 2003 Dec;111(6):503–9.
18. Tengku BS, Joseph BK, Harbrow D, Taverne AA, Symons AL. Effect of a static magnetic field on orthodontic tooth movement in the rat. Eur J Orthod. 2000 Oct;22(5):475–87.
19. Baroncelli GI, Saggese G. Effect of GH treatment on bone mass in children with GH deficiency. J Endocrinol Invest. 2005;28(10 Suppl):23–7.
20. Calvo-Guirado JL, Mate-Sanchez J, Delgado-Ruiz R, Ramirez-Fernández MP, Cutando-Soriano A, Peña M. Effects of growth hormone on initial bone formation around dental implants: a dog study. Clin Oral Implants Res. 2011 Jun;22(6):587–93.
21. Hossam Eldein AM, Elghamrawy SH, Osman SM, Elhak AR. Histological evaluation of the effect of using growth hormone around immediate dental implants in fresh extraction sockets: an experimental study. Implant Dent. 2011 Feb;20(1):47–55.
22. Solem RC, Eames BF, Tokita M, Schneider RA. Mesenchymal and mechanical mechanisms of secondary cartilage induction. Dev Biol. 2011 Aug 1;356(1):28–39.
23. Whetten LL, Johnston LE. The control of condylar growth: An experimental evaluation of the role of the lateral pterygoid muscle. Am J Orthod. 1985 Sep;88(3):181–90.
24. Silbermann M, von der Mark K, Heinegard D. An immunohistochemical study of the distribution of matrical proteins in the mandibular condyle of neonatal mice. II. Non-collagenous proteins. J Anat. 1990 Jun;170:23–31.
25. Kjellberg H, Wikland KA. A longitudinal study of craniofacial growth in idiopathic short stature and growth hormone-deficient boys treated with growth hormone. Eur J Orthod. 2007 Jun 1;29(3):243–50.
26. Lewinson D, Bialik GM, Hochberg Z. Differential effects of hypothyroidism on the cartilage and the osteogenic process in the mandibular condyle: recovery by growth hormone and thyroxine. Endocrinology. 1994 Oct;135(4):1504–10.
27. Visnapuu V, Peltomäki T, Rönning O, Vahlberg T, Helenius H. Growth hormone and insulin-like growth factor I receptors in the temporomandibular joint of the rat. J Dent Res. 2001 Oct;80(10):1903–7.
28. Pirinen S. Endocrine regulation of craniofacial growth. Acta Odontol Scand. 1995 Jan;53(3):179–85.
29. Yamaguchi T, Maki K, Shibasaki Y. Growth hormone receptor gene variant and mandibular height in the normal Japanese population. Am J Orthod Dentofac Orthop Off Publ Am Assoc Orthod Its Const Soc Am Board Orthod. 2001 Jun;119(6):650–3.
30. Sasaki Y, Satoh K, Hayasaki H, Fukumoto S, Fujiwara T, Nonaka K. The P561T polymorphism of the growth hormone receptor gene has an inhibitory effect on mandibular growth in young children. Eur J Orthod. 2009 Oct;31(5):536–41.
31. Kang EH, Yamaguchi T, Tajima A, Nakajima T, Tomoyasu Y, Watanabe M, et al. Association of the growth hormone receptor gene polymorphisms with mandibular height in a Korean population. Arch Oral Biol. 2009 Jun;54(6):556–62.
32. Young WG, Zhang CZ, Li H, Osborne P, Waters MJ. The Influence of Growth Hormone on Cell Proliferation in Odontogenic Epithelia by Bromodeoxyuridine Immunocytochemistry and Morphometry in the Lewis Dwarf Rat. J Dent Res. 1992 Nov;71(11):1807–11.
33. Smid JR, Rowland JE, Young WG, Daley TJ, Coschigano KT, Kopchick JJ, et al. Mouse cellular cementum is highly dependent on growth hormone status. J Dent Res. 2004 Jan;83(1):35–9.
34. Tabata MJ, Fujii T, Liu JG, Ohmori T, Abe M, Wakisaka S, et al. Bone morphogenetic protein 4 is involved in cusp formation in molar tooth germ of mice. Eur J Oral Sci. 2002 Apr;110(2):114–20.
35. Litsas G. Growth Hormone and Craniofacial Tissues. An update. Open Dent J. 2015 Jan 30;9(1):1–8.
36. Smid JR, Rowland JE, Young WG, Coschigano KT, Kopchick JJ, Waters MJ. Mouse Molar Dentin Size/Shape is Dependent on Growth Hormone Status. J Dent Res. 2007 May;86(5):463–8.
37. Sarnat H, Kaplan I, Pertzelan A, Laron Z. Comparison of dental findings in patients with isolated growth hormone deficiency treated with human growth hormone (hGH) and in untreated patients with Laron-type dwarfism. Oral Surg Oral Med Oral Pathol. 1988 Nov;66(5):581–6.
38. Bigeard L, Sommermater J. [Dental delay and microdontia in children with somatotropin hormone deficiency]. J Biol Buccale. 1991 Dec;19(4):291–6.
39. Krekmanova L, Carlstedt-Duke J, Brönnegård M, Marcus C, Gröndahl E, Modéer T, et al. Dental maturity in children of short stature, with or without growth hormone deficiency. Eur J Oral Sci. 1997 Dec;105(6):551–6.
40. Krekmanova L, Carlstedt-Duke J, Marcus C, Dahllöf G. Dental maturity in children of short stature--a two-year longitudinal study of growth hormone substitution. Acta Odontol Scand. 1999 Apr;57(2):93–6.
41. Ito RK, Vig KW, Garn SM, Hopwood NJ, Loos PJ, Spalding PM, et al. The influence of growth hormone (rhGH) therapy on tooth formation in idiopathic short statured children. Am J Orthod Dentofac Orthop Off Publ Am Assoc Orthod Its Const Soc Am Board Orthod. 1993 Apr;103(4):358–64.
42. Iglesias L, Yeh JK, Castro-Magana M, Aloia JF. Expression of concern to: Effects of growth hormone on bone modeling and remodeling in hypophysectomized young female rats: a bone histomorphometric study. J Bone Miner Metab. 2022 Jan;40(1):175.
43. Davidopoulou S, Chatzigianni A. Craniofacial morphology and dental maturity in children with reduced somatic growth of different aetiology and the effect of growth hormone treatment. Prog Orthod. 2017 Dec;18(1):10.
44. Bevis RR, Hayles AB, Isaacson RJ, Sather AH. Facial growth response to human growth hormone in hypopituitary dwarfs. Angle Orthod. 1977 Jul;47(3):193–205.
45. Dattani MT, Malhotra N. A review of growth hormone deficiency. Paediatr Child Health. 2019 Jul;29(7):285–92.
46. Yuen KCJ, Johannsson G, Ho KKY, Miller BS, Bergada I, Rogol AD. Diagnosis and testing for growth hormone deficiency across the ages: a global view of the accuracy, caveats, and cut-offs for diagnosis. Endocr Connect. 2023 Jul 1;12(7):e220504.
47. Bogusławska A, Korbonits M. Genetics of Acromegaly and Gigantism. J Clin Med. 2021 Mar 29;10(7):1377.