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# Customizing dental solutions: How floating harbor syndrome shapes pediatric dental innovation

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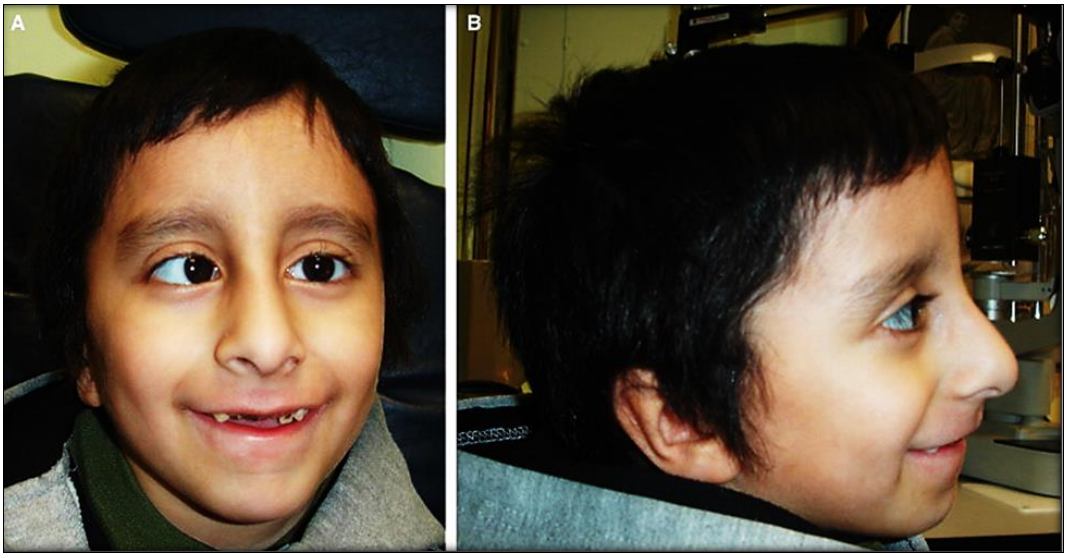
**Abstract**
Floating-Harbor Syndrome (FHS) is an extremely rare genetic disorder marked by a distinctive triad: short stature, speech delay, and unique facial features such as a triangular face, bulbous nose, wide columella, deep-set eyes, long eyelashes, thin lips, short philtrum, and broad mouth. With approximately 50 documented cases, FHS poses significant diagnostic challenges due to its unfamiliar clinical presentation, often leading to delays in diagnosis. Although the syndrome affects both sexes, it is more prevalent in females, and no known cure exists—treatment remains symptomatic and supportive. Early diagnosis is crucial for prompt intervention and comprehensive management. Oral manifestation of FHS often involves oligodontia, ankyloglossia, and delayed tooth eruption, which can significantly impact oral function, appearance, and quality of life. The syndrome's characteristic facial features may complicate orthodontic evaluations and treatments. Effective management requires a multidisciplinary approach, integrating paediatric dentistry, orthodontics, prosthodontics, and surgical interventions tailored to the individual's needs. Paediatric dentists & oral radiologists play a key role in early detection and management, employing thorough dental evaluations and panoramic radiographs for timely intervention. A deep understanding of the syndrome's dental manifestations and potential complications is essential for optimal treatment planning and patient outcomes. Continued research and collaboration with geneticists and other healthcare providers are vital for enhancing care strategies and improving the quality of life for children with FHS.

**Keywords:** Floating harbor syndrome, pediatric dentistry, oligodontia, ankyloglossia, orthodontics, early diagnosis

## Introduction
Floating-Harbor Syndrome (FHS) is an exceptionally rare genetic disorder characterized by a unique constellation of mental, physical, developmental, and oral features. This complex syndrome profoundly affects individuals, presenting a distinctive blend of cognitive impairments, growth delays, developmental anomalies, and specific oral health challenges [1]. The condition now known FHS was first identified in 1973 by researchers at Boston Floating Hospital and Harbor General Hospital [2]. It presented a diagnostic challenge due to its distinctive symptoms, including growth delays, unique facial features, and skeletal irregularities. This complex combination of traits made the condition difficult to diagnose [3]. The condition, caused by mutations in the SRCAP gene on chromosome 16p11.2, was identified as the genetic basis in the early 2000s, marking a significant breakthrough in understanding this syndrome. The SRCAP gene, located on chromosome 16p11.2, encodes a SNF2-related chromatin remodeling ATPase crucial for chromatin remodeling, gene expression, DNA damage response, and cell division [4]. The SRCAP protein, abundant in human cell nuclei, contains several functional domains, including the SNF2-like ATPase structural domain, the CREBBP-binding domain, and AT-hook structural domains. Mutations leading to truncated SRCAP proteins that lose the AT-hook domains result in impaired activation of the CREBBP gene, contributing to stunted development and the varied clinical manifestations of FHS [5]. This variability encompasses not only facial features and growth disturbances but also gastrointestinal, cardiac, and genitourinary disorders [6]. Key areas of focus include oto-ocular issues (Figure 1) such as hyperopia, strabismus, nystagmus, and

conductive hearing loss; ear, pumice powder (Neelkanth healthcare Pvt. ltd.), sand paper (120 and 400 grit), Incubator (NSW India), artificial saliva (Wet Mouth-ICPA Health Products Ltd), specimen containers, nose, and throat problems like cleft lip, pseudolabial, palatopharyngeal atresia, and posterior nostril atresia; and dental abnormalities including caries, widely spaced teeth, and small teeth.




**Courtesy:** Asseidat I, Kaufman LM. Ocular abnormalities in Floating-Harbor syndrome. J Am Assoc. Pediatr. Ophthalmol Strabismus. 2009; 13(2):218-20

**Fig 1:** Ocular abnormalities in FHS

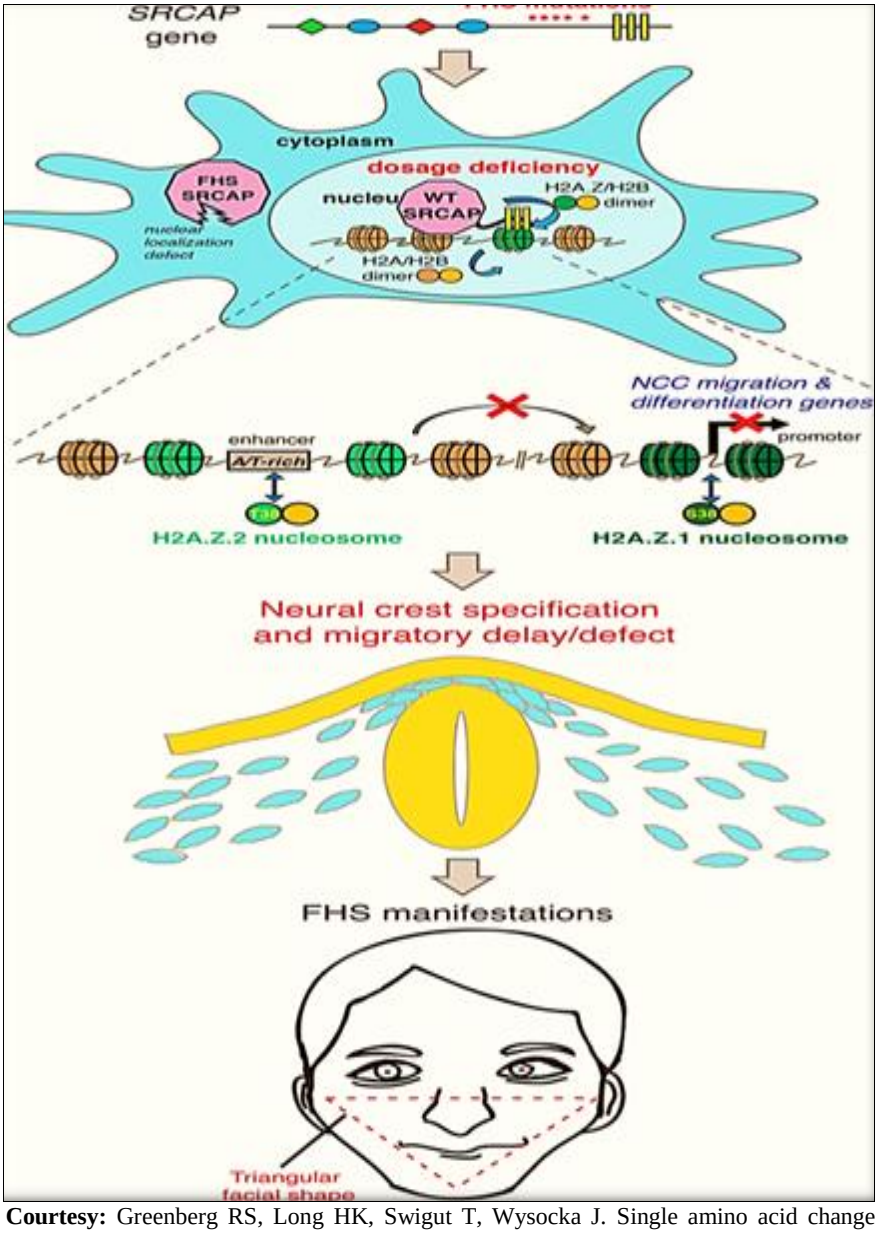
Vigilant monitoring is also necessary for congenital heart defects [6]. Additionally, gastrointestinal disorders such as gastroesophageal reflux, celiac disease, and constipation must be managed, alongside genitourinary abnormalities like renal stones, hydronephrosis, renal cysts, hypouricemia, cryptorchidism, small penis, and small testes [7]. Addressing these diverse conditions effectively underscores the importance of a multidisciplinary approach to meet the complex and varied needs of individuals with FHS. It is marked by distinctive facial features including a triangular face, deep-set eyes, low hanging coulemella and a prominent nose (Figure 2-4) [8].

**Courtesy:** Nikkel S, Dauber A, Boycott K, *et al*. The phenotype of Floating-Harbor syndrome. Medicine. 2013; 92(8):63

**Fig 2:** Facial dysmorphic features in paediatric patients with FHS

**Courtesy:** https://medlineplus.gov/

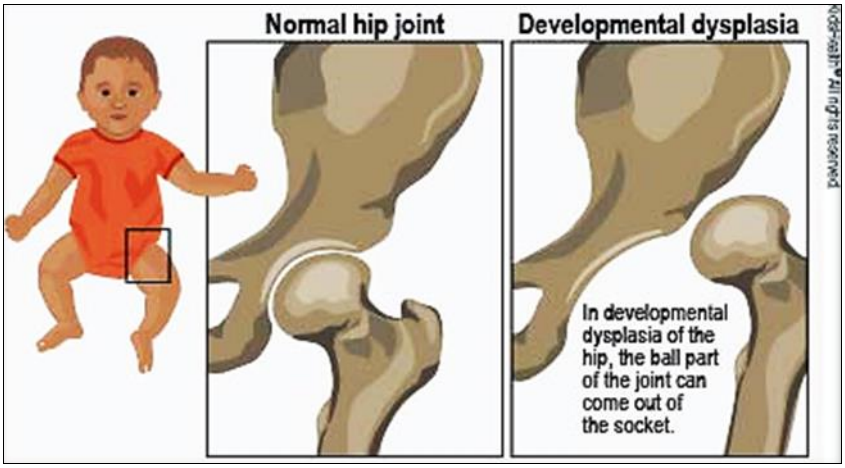
**Fig 3:** Low hanging coulemella




**Courtesy:** Greenberg RS, Long HK, Swigut T, Wysocka J. Single amino acid change underlies distinct roles of H2A.Z subtypes in human syndrome. Cell. 2019;178(6):1421-1436.e24

**Fig 4:** Proposed model for FHS

Affected individuals often experience delayed bone development and reduced height, which become more pronounced with age. Key characteristics include a short stature, unique facial traits, delayed bone maturation, and speech development. Skeletal abnormalities such as wide thumbs, short fingers, and tapered epiphyses are common, with some cases presenting pseudarthrosis-like clavicle deformities and hip dysplasia (Figure 5) [9].



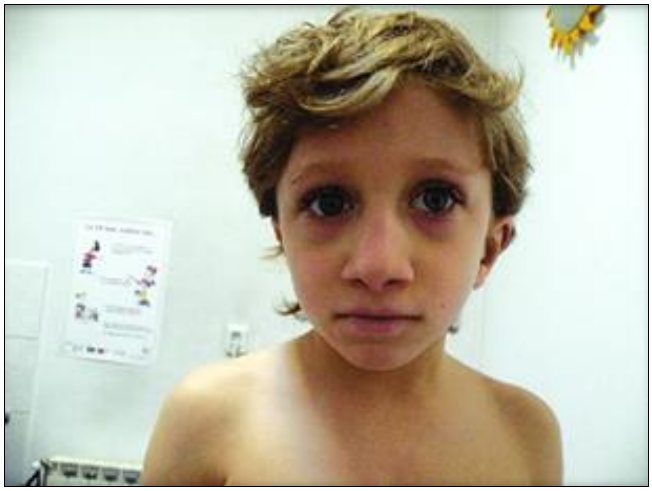

**Courtesy:** https://kidshealth.org/en/parents/ddh.html

**Fig 5:** Hip dysplasia in FHS

Additionally, individuals may have a high-pitched voice, nasal resonance, and delayed expressive language development. Intellectual disabilities and behavioral issues like Attention Deficit Hyperactivity Disorder (ADHD) and anxiety further complicate the clinical picture [10]. Developmentally, while language acquisition may be delayed, comprehension of language and nonverbal communication is often advanced. Intellectual development is typically affected, with many individuals showing mild to moderate cognitive impairments [11]. The SRCAP gene, which encodes a crucial chromatin-remodeling ATPase, is responsible for this condition. Mutations in this gene, which occur spontaneously during early development or reproductive cell formation, are not usually inherited [12]. This genetic anomaly, which is typically not passed down through generations, arises spontaneously either early in embryonic development or during the formation of reproductive cells. Despite considerable advances in understanding the genetics of FHS, the rarity of the condition has posed challenges for researchers and healthcare providers in fully grasping its effects and future treatment possibilities [13]. Many individuals with FHS and their families continue to lead fulfilling lives despite these challenges. With advancements in genetics and personalized medicine, there is renewed hope that a deeper understanding of FHS will lead to more effective interventions, offering patients with this condition a brighter outlook [14]. Despite progress in genetics, the rarity of FHS continues to present challenges for fully understanding its impact and developing targeted treatments. Ongoing advancements in genetics and personalized medicine offer hope for more effective treatments, improving prospects for those affected by this complex disorder. Understanding FHS is crucial for providing effective care and support to affected individuals. Due to its rarity and diverse manifestations, FHS requires a specialized and comprehensive approach to management. This review consolidates essential insights and strategies to enhance the management of this complex condition [15].

## Discussion

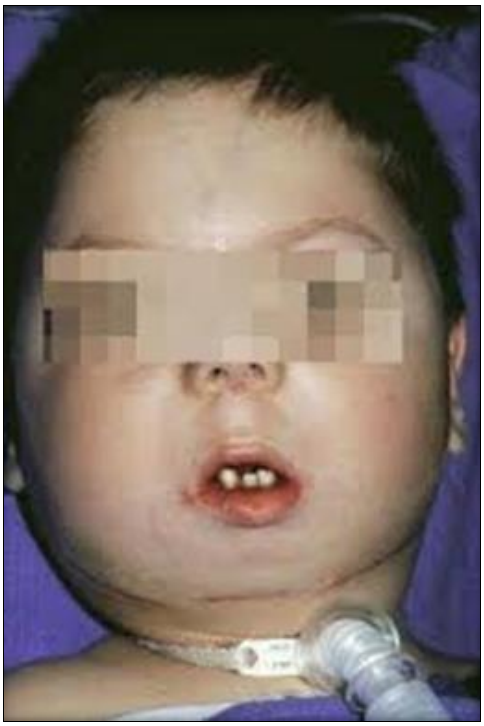
FHS is a rare genetic condition [16]. Although intellectual disability is a known feature of the syndrome, its severity can vary greatly among affected individuals [17]. Typically, patients with this syndrome have impaired speech, and alternative communication methods, such as signing and gestures, are often used [18]. Initially, inhalation sedation was considered to help the patient adjust, but the ‘triangular’ facial morphology (Figure 6) made the use of a nasal hood ineffective [19].



**Courtesy:** Budisteanu M, Bögershausen N, Papuc SM, Moosa S, Babes V. Floating-Harbor Syndrome: Presentation of the first Romanian patient with a SRCAP mutation and review of the literature. Balkan J Med Genet. 2018; 21(1):83-6

**Fig 6:** Peculiar triangular shape morphology in FHS

The nasal hood's poor fit around the patient's nasal contours severely restricted upper lip movement, complicating nasal breathing. For patients with FHS, anesthetic management is particularly challenging due to anatomical features such as a short neck, restricted neck mobility, malocclusion, and microstomia (Figure 7), all of which can complicate airway management and intubation. Effective management of FHS requires meticulous planning and specialized anesthetic techniques to address these complexities [20].



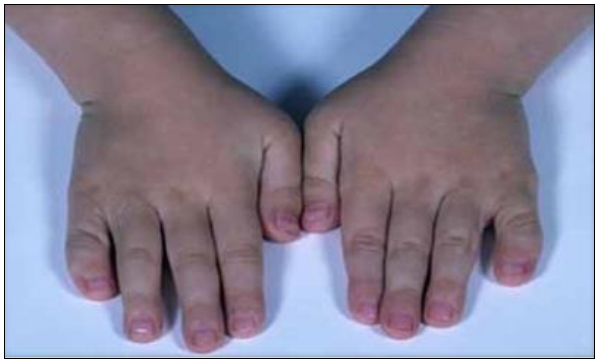
**Courtesy:**https://reference.medscape.com/?_gl=1*mc1jo7*_gcl_au*MTk4ODcyNTQ2MS4xNzI0NDAxMjkw

**Fig 7:** Microstomiain FHS

It is a rare autosomal dominant disorder characterized by growth retardation, short stature, and distinct facial features, which become more pronounced with age [21]. The short stature observed in FHS may arise from issues with the skeletal growth plate, where chondrocyte proliferation and hypertrophy are crucial for bone elongation [22]. In the growth plate, chondrocytes undergo proliferation, hypertrophy, and secretion of cartilage extracellular matrix components. This process leads to the formation of new cartilage tissue, which is then transformed into bone tissue. Over time, this newly formed bone gradually replaces cartilage in the growth plate, facilitating bone elongation and contributing to the increase in height during childhood. Disruptions in key signaling pathways, including Indian hedgehog (IHH), parathyroid-related protein (PTHrP), fibroblast growth factor, and bone morphogenetic protein (BMP), hinder chondrocyte maturation and growth plate development [23]. Additionally, abnormalities in the Notch signaling pathway, which typically governs chondrocyte differentiation, worsen delayed bone growth and skeletal irregularities [24]. Growth hormone therapy (rhGH) has shown promise in improving growth rates and height standard deviation scores (SDS) for some FHS patients [25]. However, responses to rhGH can vary, with some individuals experiencing limited progress, possibly due to accelerated bone age or early puberty [26]. Regular monitoring of IGF-1 levels, blood pressure, renal function, and neurological health is crucial due to potential side effects such as spinal cord embolism or nephrotic syndrome [27]. Despite these risks, rhGH remains a viable option for enhancing height in FHS patients, although its long-term effectiveness and safety require further investigation. Individuals with FHS often present with a triangular facial shape, deep-set eyes, a prominent nose, thin lips, and backward-rotated ears [28]. Additional physical traits include small teeth with increased spacing, broad digits, hypoplastic nails, brachydactyly (Figure 8), and clinodactyly (Figure 9), along with cognitive impairments and a high-pitched voice [29].

**Courtesy:** https://medlineplus.gov/

**Fig 8:** Brachydactyly in paediatric patient with FHS

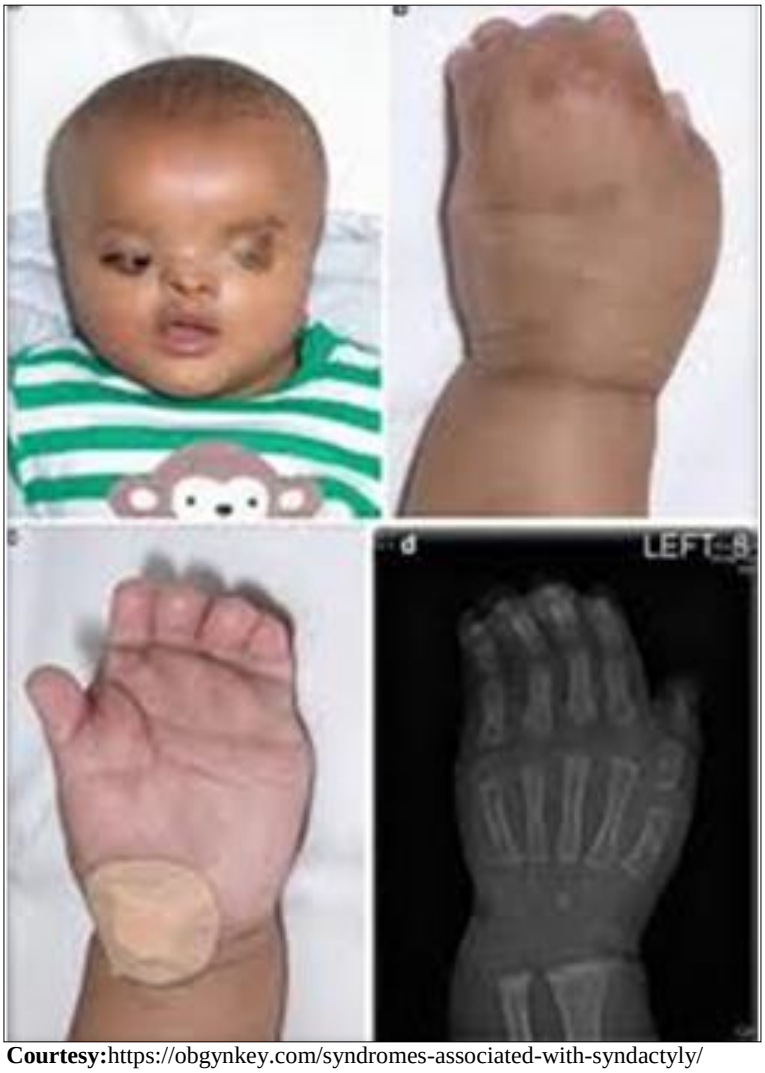


**Courtesy:** https://medlineplus.gov/

**Fig 9:** Bilateral Clinodactly of fifth finger in paediatric patient with FHS

**Roentographic features**

It present with a variety of clinical features, including distinctive radiographic characteristics [30]. Pediatric patients with FHS often exhibit shortened digits, particularly in the distal phalanges, which are the bones at the tips of the fingers (Figure 10) and toes [31]. Additionally, these digits may appear flattened due to abnormal bone growth patterns. Both the metacarpals and metatarsals can also be shortened [32]. Radiographic images might reveal abnormal bone density, and there can be a noticeable delay in skeletal maturation compared to chronological age, with bones appearing underdeveloped on radiographs (Figure 11) [33]. These skeletal abnormalities are often reflective of the developmental delays commonly associated with FHS [34]. In some cases, patients are treated with growth hormone, and follow-up radiographs may show improvements in bone growth as a result. For an accurate diagnosis and assessment, detailed radiographic examination, including radiographs of the hands and feet, is crucial for evaluating the specific skeletal manifestations of FHS [35].




**Courtesy:**https://obgynkey.com/syndromes-associated-with-syndactyly/

**Fig 10:** Clinical and roentographic image depicting syndactly and shortened metacarpals

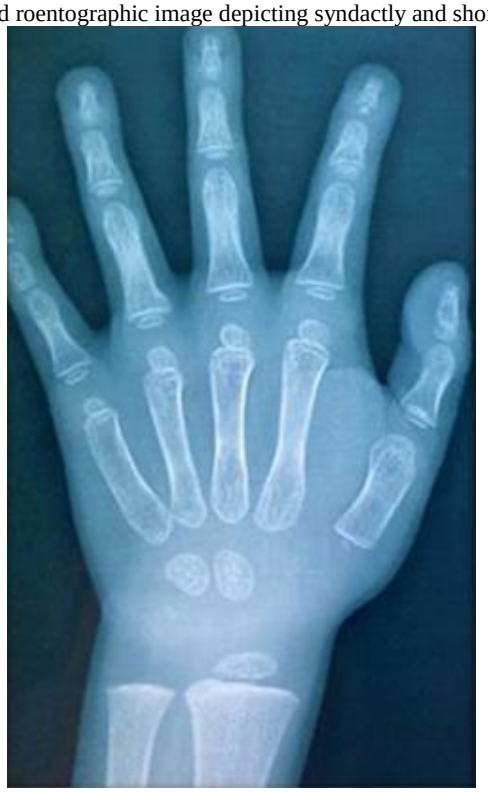
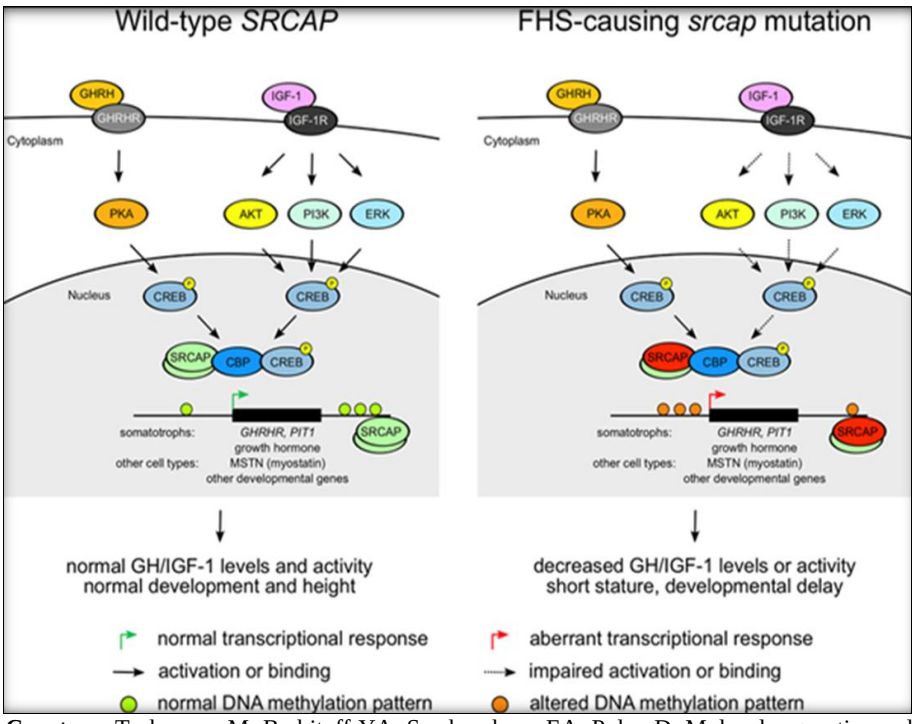


**Fig 11:** Hand wrist radiograph of the child's left hand shows bone age at 4 years, which is 3 years behind the child's actual age. Findings include short, thin finger bones, prominent distal phalanges, an inwardly curved little finger, and irregularly shaped middle phalanges of the little finger in patient with FHS

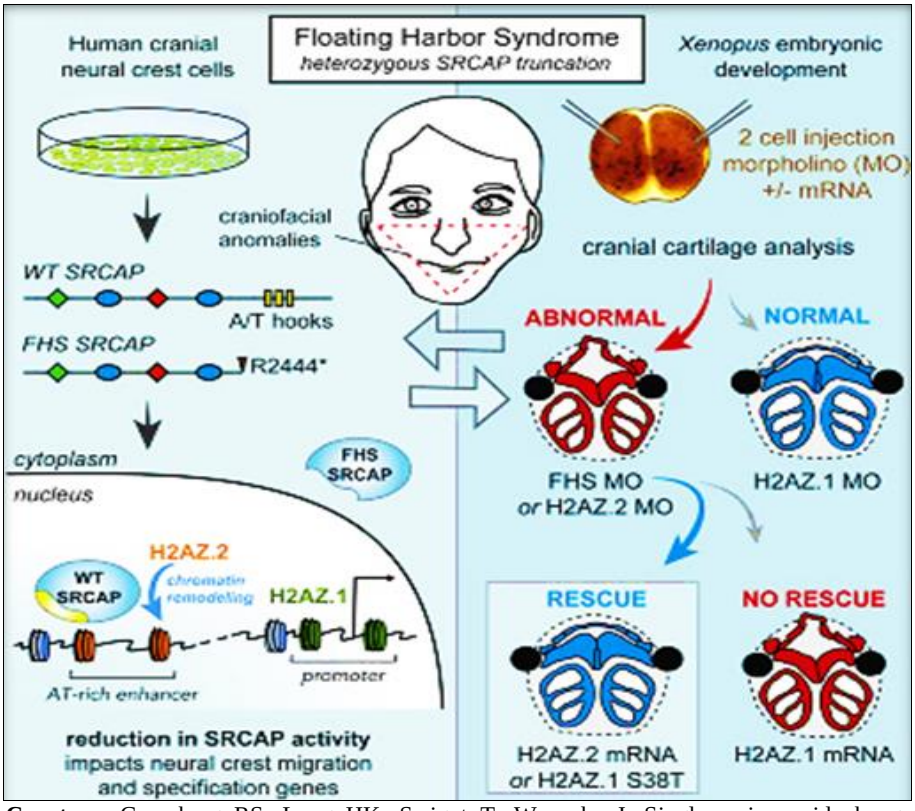
**Courtesy:** Bo H, Jiang L, Zheng J, Sun J. Floating-Harbor syndrome treated with recombinant human growth hormone: a case report and literature review. Front Pediatr. 2021; 9:747353.

The condition is driven by heterozygous mutations in the SRCAP gene, notably truncating mutations in exon 34, which disrupt DNA methylation and create distinct epigenetic signatures (Figure 12, 13). One specific mutation, c.7401delC; p.Ile2468Phefs7, identified as a frameshift mutation in exon 34, was confirmed through Sanger sequencing. Importantly, neither parent carried this mutation, underscoring its de novo origin and its critical role in the disease [36].




**Courtesy:** Turkunova M, Barbitoff YA, Serebryakova EA, Polev D. Molecular genetics and pathogenesis of the Floating Harbor syndrome: case report of long-term growth hormone treatment and a literature review. Front Genet. 2022; 13:846101

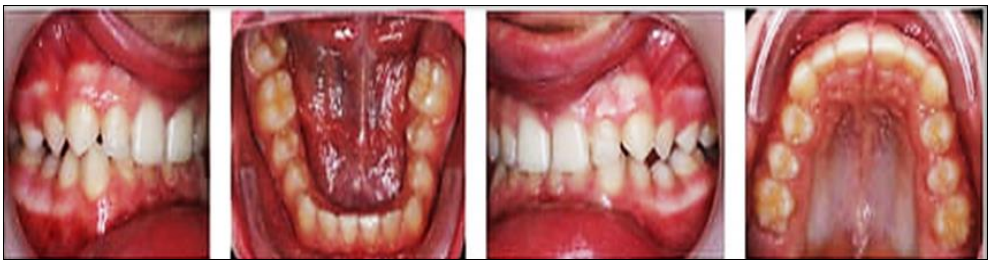
**Fig 12:** Gene mutation in FHS




**Courtesy:** Greenberg RS, Long HK, Swigut T, Wysocka J. Single amino acid change underlies distinct roles of H2A.Z subtypes in human syndrome. Cell. 2019;(6):1421-1436.e24

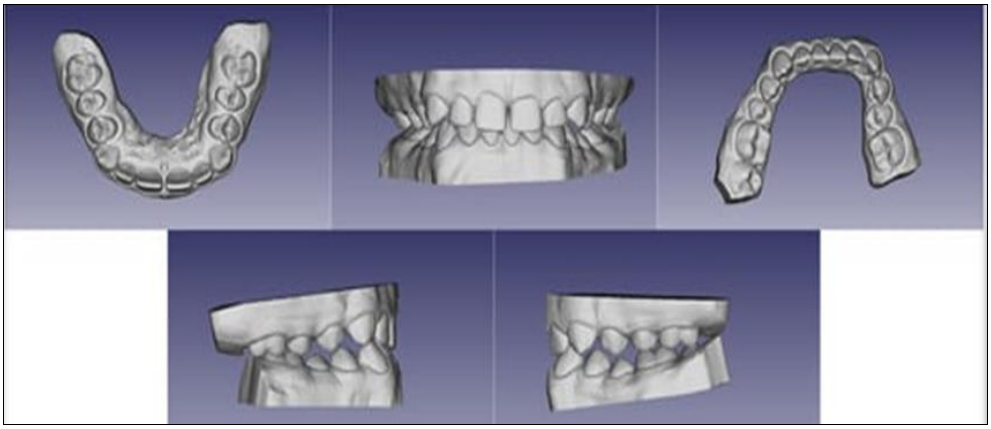
**Fig 13:** Genetic mutation in FHS

**Oral Manifestations:** Dental issues are prevalent in these patients, including delayed tooth eruption, malformed teeth (Figure 14), malocclusion, and gingival hyperplasia (Figure 15) [37].



**Courtesy:** Dobrzynski W, Stawinska-Dudek J, Moryto N, Lipka D, Mikulewicz M. Floating-Harbor Syndrome: A Systematic Literature Review and Case Report. J Clin Med. 2024; 13(12):3435

**Fig 14:** Intraoral pictures depicting malocclusion

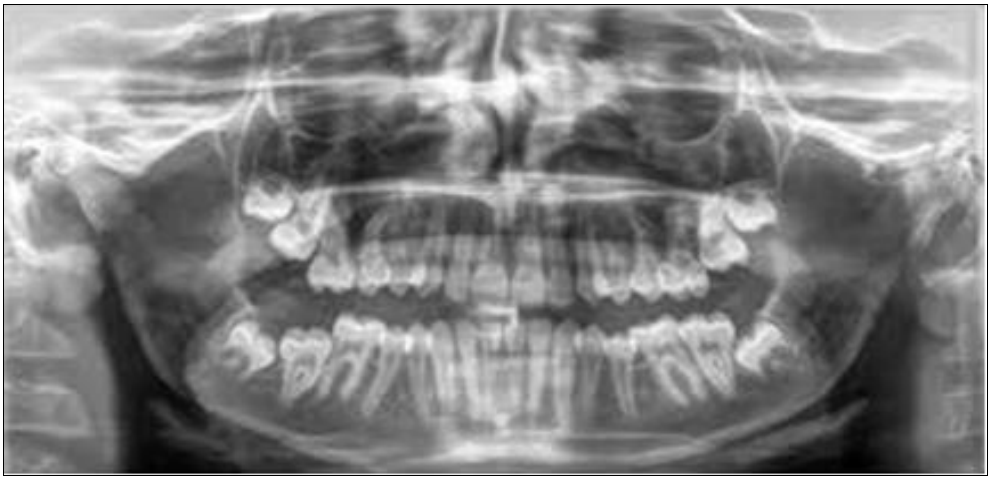


**Courtesy:** Dobrzynski W, Stawinska-Dudek J, Moryto N, Lipka D, Mikulewicz M. Floating-Harbor Syndrome: A Systematic Literature Review and Case Report. J Clin Med. 2024; 13(12):3435

**Fig 15:** Intraoral scan of patient with FHS

The presence of retained extra teeth, spacing problems, ankyloglossia, plaque-induced gingivitis, and carious lesions highlights the necessity for early orthodontic evaluation and timely management of unerupted teeth to prevent malocclusion [38]. Additionally, individuals with FHS often exhibit various oral mucosal changes and developmental anomalies in the oral cavity, emphasizing the importance of a comprehensive evaluation by both medical and dental professionals [39].

**Management:** Managing FHS demands a comprehensive, multidisciplinary approach due to the complex and varied needs of affected individuals [40]. A thorough initial assessment is crucial, including a detailed clinical evaluation of physical features, growth parameters, and developmental milestones, as well as genetic testing to confirm mutations in the SRCAP gene. Imaging studies, such as panoramic radiographs (Figure 16), are essential for evaluating dental development and identifying issues such as unerupted or supernumerary teeth; with oral radiologists playing a critical role in this diagnostic process [41].



**Courtesy:** Dobrzynski W, Stawinska-Dudek J, Moryto N, Lipka D, Mikulewicz M. Floating-Harbor Syndrome: A Systematic Literature Review and Case Report. J Clin Med. 2024; 13(12):3435

**Fig 16:** Panaromic radiograph analysis in FHS

Effective management of FHS requires a thorough screening for associated conditions to ensure tailored clinical care. Pediatric dentists are pivotal in the ongoing dental and orthodontic care, which includes regular check-ups to monitor for anomalies like delayed tooth eruption, malformed teeth, and malocclusion [42]. Early orthodontic assessments and interventions are vital to manage impacted or unerupted teeth and correct malocclusion. Emphasis on oral hygiene helps prevent issues like plaque-induced gingivitis and carious lesions, and prosthodontic treatments may be necessary to address missing or malformed teeth [43]. Growth and endocrine management involve regular monitoring of height and weight, with evaluations to determine the suitability of growth hormone therapy (rhGH) for addressing short stature [44]. Regular checks of IGF-1 levels and periodic bone age assessments are crucial to tailor treatment and monitor response [45]. Speech and language therapy should be initiated early to address delayed speech development and enhance communication skills, with ongoing evaluations to adapt therapy as needed [46]. Anesthesia and surgical considerations require meticulous planning due to potential airway management challenges posed by anatomical features like a short neck and restricted neck mobility [47]. Specialized anesthesia techniques are necessary to address these challenges and ensure safe procedures [48]. Behavioral and psychological support is also essential, involving psychological evaluations to identify intellectual disabilities and behavioral issues such as ADHD, anxiety disorders, or obsessive-compulsive disorder [49]. Therapeutic interventions should provide appropriate support to address these emotional and behavioral challenges. Moreover, monitoring and managing associated conditions is critical. Regular eye exams and hearing screenings are needed to address oto-ocular issues, while ear, nose, and throat (ENT) assessments help manage conditions such as cleft lip and nasal atresia [50]. Cardiovascular health should be monitored for congenital heart defects, gastrointestinal issues like gastroesophageal reflux and celiac disease must be managed, and genitourinary abnormalities require ongoing assessment [51]. Long-term care involves annual comprehensive reviews to track overall health, growth, and development, with coordination among a multidisciplinary team including pediatricians, endocrinologists, orthodontists, psychologists, pediatric dentists, and oral radiologists [52]. Providing education and support to patients and their families is crucial for managing the syndrome's challenges effectively. Additionally, developing an emergency plan for potential complications, particularly related to anesthesia and severe medical conditions, is essential for optimal management of FHS. This proactive and coordinated approach ensures the best possible outcomes for individuals with FHS [53].

**Challenges and Perceptions:** Children with FHS face challenges in pediatric dentistry due to developmental delays, growth variations, and communication barriers. Developmental delays in speech and motor skills can affect cooperation during dental visits, potentially leading to the perception of non-compliance, which is actually a result of their developmental stage rather than intentional defiance [54]. Short stature and delayed bone age can complicate traditional growth charts and developmental milestones, making treatment planning more complex and potentially leading to the perception that care is less straightforward [55]. The syndrome may also involve specific dental anomalies or unusual growth patterns, requiring tailored approaches rather than standard treatments, which can be seen as more challenging to manage [56]. Communication difficulties due to speech delays further complicate interactions, leading to potential misunderstandings about the child's engagement or understanding. Addressing these challenges involves using developmentally sensitive behavior management techniques, customizing treatment plans based on the child's unique growth patterns, employing alternative communication methods, educating families about the syndrome's implications, and emphasizing empathy and patience in care [57]. Collaboration with other healthcare professionals is crucial for a holistic approach, ensuring comprehensive and effective treatment while acknowledging and addressing these challenges and perceptions [58].

**Futuristic Considerations**

Advances in genetic sequencing are set to revolutionize the management of FHS by offering deeper insights into the specific mutations responsible for the condition. This progress will enable more precise diagnoses and personalized treatment plans. Techniques such as CRISPR hold promise for addressing the genetic roots of FHS, potentially improving long-term outcomes [59]. Enhanced diagnostic tools powered by Artificial Intelligence and machine learning are expected to refine early detection and predict dental issues, allowing for proactive care. Innovations in regenerative medicine and 3D printing will transform treatment options, offering tailored prosthetics and orthodontic devices. Integrated care models that involve collaboration among pediatric dentists, geneticists, endocrinologists, and other specialists will ensure a comprehensive approach to managing FHS [60]. Telemedicine will enhance access to specialized care, while patient-centric technologies like Virtual Reality (VR) and Augmented Reality (AR) will improve patient education and comfort. Additionally, smart dental devices and health data analytics will provide real-time insights and track long-term outcomes, further refining treatment strategies. CAD/CAM (Computer-Aided Design and Computer-Aided Manufacturing) technology plays a pivotal role [61]. It enables the creation of highly customized orthodontic appliances and prosthetics through precise 3D scans and digital impressions. CAD/CAM also enhances surgical planning with detailed simulations, improving surgical outcomes and minimizing complications [62]. By streamlining the production of dental and orthodontic devices, CAD/CAM technology ensures high accuracy and reduces fabrication time. It supports long-term monitoring and adjustments, creating digital records of craniofacial structures that facilitate timely updates to orthodontic and prosthetic devices [63]. Overall, these advancements and technologies collectively enhance the management of FHS, leading to more effective, personalized, and comprehensive care for affected individuals [64].

**Conclusion**

FHS presents unique challenges in pediatric care, requiring a comprehensive and individualized approach to diagnosis and management. Early intervention, regular monitoring, and coordination among healthcare providers are essential to optimize outcomes and improve the quality of life for affected children. Continued research and clinical experience will enhance understanding of pediatric dentists and other dentists in management of this rare genetic disorder.

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**Conflicts of interest:** There are no conflicts of interest

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