Cranio-oro-facial features and masticatory function in patients with craniosynostosis

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โครงสร้างใบหน้าและช่องปาก และความสามารถในการบดเคี้ยวของผู้ป่วยที่มีภาวะกะโหลกศีรษะเชื่อมติดผิดปกติ

น.ส.ญาณิศา วงษ์บัณฑิตย์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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ญาณิศา วงษ์บัณฑิตย์ : โครงสร้างใบหน้าและช่องปาก และความสามารถในการบดเคี้ยวของผู้ป่วยที่มีภาวะกะโหลกศีรษะเชื่อมติดผิดปกติ . (Cranio-oro-facial features and masticatory function in patients with craniosynostosis) อ.ที่ปรึกษาหลัก : รศ. ทพญ. ดร.ขัณฑิรา พรทวีทัศน์

วัตถุประสงค์: เพื่อศึกษาลักษณะที่แสดงออกของโครงสร้างใบหน้า ขากรรไกร ช่องปากและฟัน และ ความสามารถในการบดเคี้ยวของผู้ป่วยที่มีภาวะกะโหลกศีรษะเชื่อมติดผิดปกติเปรียบเทียบกับกลุ่มควบคุมซึ่งเป็นผู้ที่มีสุขภาพร่างกายทั่วไปแข็งแรงไม่มีภาวะกะโหลกศีรษะเชื่อมติดผิดปกติ เพื่อเป็นข้อมูลของประชากรไทย เป็นประโยชน์ต่อการศึกษา และให้การรักษาผู้ป่วยกลุ่มนี้ต่อไป

วิธีการ: ทำการศึกษาในผู้ป่วยที่มีภาวะกะโหลกศีรษะเชื่อมติดผิดปกติจำนวน 13 ราย อายุ 6-17 ปี ที่รับการรักษาที่ศูนย์สมเด็จพระเทพรัตนฯ แก้ไขความพิการบนใบหน้าและกะโหลกศีรษะ โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย และกลุ่มควบคุมจำนวน 30 รายที่มีอายุช่วงเดียวกัน โดยรวบรวมข้อมูลประวัติการตรวจสุขภาพและการรักษาของผู้ป่วย ร่วมกับการตรวจสุขภาพช่องปาก การวิเคราะห์ภาพรังสีกะโหลกศีรษะด้านข้าง ภาพรังสีภายในช่องปาก การทดสอบความสามารถในการบดเคี้ยวของผู้ป่วย และ การทำแบบประเมินการรับประทานอาหาร 6 ชนิด (FIA test) ของผู้ป่วย เปรียบเทียบกับกลุ่มควบคุมที่มีสุขภาพร่างกายแข็งแรง และเทียบดัชนีภาพรังสีกะโหลกศีรษะด้านข้างของผู้ป่วยกับค่ามาตรฐานของประชากรไทย

ผลการศึกษา: ผู้ป่วยที่มีภาวะกะโหลกศีรษะเชื่อมติดผิดปกติจำนวน 13 ราย โดยสี่รายมีภาวะเพดานโหว่ (30.8%) ห้ารายมีการสบเปิดทางด้านหน้า (38.5%) เจ็ดรายมีฟันหน้าสบไขว้ (53.8%) แปดรายมีฟันหลังสบไขว้ (61.5%) แปดรายมีฟันบนซ้อนเก (61.5%) หกรายมีฟันล่างซ้อนเก (46.2%) แปดรายมีภาวะฟันหาย (61.5%) หนึ่งรายมีภาวะฟันเกิน (7.7%) หกรายมีภาวะฟันฝัง (46.2%) เก้ารายมีความเสี่ยงสูงในการเกิดฟันผุ (69.2%) และ แปดรายมีการสบฟันผิดปกติประเภทที่ 3 (61.5%) กลุ่มผู้ป่วยมีอนามัยช่องปาก ค่าเฉลี่ยฟันผุ ถอน อุด ผลการวิเคราะห์ภาพรังสีกะโหลกศีรษะด้านข้าง อาทิ SNA, ANB, Wits, FMA, IMPA, L1-NB, U1-NA, Maxillary depth, Convexity of point A, Mandibular arc, Posterior facial height และ U1 to APog เป็นต้น ความสามารถในการบดเคี้ยว และ ผลการทำแบบประเมินการรับประทานอาหาร 6 ชนิด แตกต่างจากกลุ่มควบคุมอย่างมีนัยสำคัญ

สรุปผลการศึกษา: ผู้ป่วยที่มีภาวะกะโหลกศีรษะเชื่อมติดผิดปกติมีลักษณะของโครงสร้างใบหน้า ขากรรไกร ช่องปากและฟันที่ผิดปกติ ส่งผลกระทบต่อการดูแลสุขภาพช่องปาก มีแนวโน้มสุขอนามัยช่องปากไม่ดี มีความเสี่ยงสูงในการเกิดฟันผุ รวมถึงมีความสามารถในการบดเคี้ยวอาหารลดลง ดังนั้นการให้ความรู้และคำแนะนำที่ถูกต้อง การเน้นย้ำถึงวิธีการดูแลทำความสะอาดช่องปากที่เหมาะสมแก่ผู้ป่วยและผู้ดูแล รวมไปถึงการให้การรักษาอย่างเป็นองค์รวมจากทีมแพทย์สาขาต่างๆ จึงมีความสำคัญเป็นอย่างยิ่งในการส่งเสริมสุขภาพช่องปากและสุขภาพกายของผู้ป่วยที่มีภาวะกะโหลกศีรษะเชื่อมติดผิดปกติ

สาขาวิชา	ทันตกรรมผู้สูงอายุและการดูแลผู้ป่วยพิเศษ	ลายมือชื่อนิสิต .....
ปีการศึกษา	2565	ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

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KEYWORD: Craniofacial abnormalities Craniosynostosis Masticatory muscles Lateral cephalometric Teeth Dentition

Yanisa Wongbanthit : Cranio-oro-facial features and masticatory function in patients with craniosynostosis. Advisor: Assoc. Prof. THANTRIRA PORNTAVEETUS, D.D.S., M.Sc., Ph.D.

Objectives: The aim of this study was to evaluate cranio-oro-facial features and masticatory function in Thai subjects with craniosynostosis.

Methods: Thirteen craniosynostosis (CS) patients aged between 6 - 17 years old who had treatment at the Princess Sirindhorn Craniofacial (PSC) Center, King Chulalongkorn memorial hospital and thirty age-matched non-CS subjects were recruited. Inform consents were obtained. Medical records were retrieved. Craniofacial and oral examination, radiographic evaluation, photograph, and masticatory function were recorded and compared with data of control subjects and that of Thai norms.

Results: Among thirteen CS patients, four cases had cleft palate (30.8%), five had anterior openbite (38.5%), seven had anterior crossbite (53.8%), and one had supernumerary tooth (7.7%). 61.5% of CS patients (8/13) exhibited posterior crossbite, congenital missing teeth, Class III malocclusion and maxillary tooth crowding. Mandibular tooth crowding and tooth eruption failure were observed in six patients (46.2%). Nine patients had high caries risk (69.2%). The simplified oral hygiene index, caries prevalence, lateral cephalometric analysis (e.g. SNA, ANB, Wits, FMA, IMPA, L1-NB, U1-NA, Maxillary depth, Convexity of point A, Mandibular arc, Posterior facial height, and U1 to APog), masticatory performance, and food intake ability test showed significant differences between patient and control groups.

Conclusions: The study shows that CS patients have poor oral hygiene, high caries risk, and compromised masticatory function. The anomalies of craniofacial and oral structures might affect oral hygiene care and mastication of CS patients. We suggest that strict oral hygiene care and frequent dental check-up together with the collaboration of multidisciplinary team are necessary for CS patients to maintain optimal oral and medical health.

Field of Study:	Geriatric Dentistry and Special Patients Care	Student's Signature .....
Academic Year:	2022	Advisor's Signature .....

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Yanisa Wongbanthit

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INTRODUCTION

Background and rationale

Craniosynostosis (CS) is described as the abnormal fusion of one or more cranial sutures. It is a condition causing an increased risk of elevated intracranial pressure, hydrocephalus, brain damage, and skull distortion. Craniosynostosis present not only physical abnormalities(1, 2), but also mental disorders. The previous study indicated that single-suture or isolated CS in children can increase the risk of cognitive deficiency or language/learning disabilities(3). Hence, craniosynostosis can have a major impact on the quality of life, both physical and psychosocial, of the patients and their caregivers.

The prevalence of CS is approximately 1 in 2,100-2,500 live births worldwide, and it has been rising from 1997 to 2013(4-7). The anomalies are found in all nationalities across wide geographic areas and every socioeconomic status(8).

In Thailand, CS is considered as one of the most prevalent craniofacial abnormalities according to the data from The Princess Sirindhorn Craniofacial (PSC) Center at King Chulalongkorn Memorial Hospital. The PSC center is the first and largest craniofacial center in Thailand providing comprehensive treatment for numerous patients with craniofacial deformities. In the year 2012 and 2013, there were 41 and 46 CS patients attending the center, respectively(9). The patients had continuously increased and were recorded up to 360 cases visiting the center in 2018.

Regarding oral manifestations, CS patients have been found having high arched palate, retrognathic maxilla, small mouth, low salivary flow rate, and malocclusion. Compromised ability in mastication and changes in salivary parameters are also reported(10, 11). Despite many patients in Thailand are affected with CS, there has been no systematic records of their cranio-oro-facial features and masticatory function.

This study therefore aims to investigate cranio-facial-oral phenotypes and masticatory function of Thai CS patients. The craniofacial and orodental characteristics

of the patients will be recorded in order to create the valuable database of Thai CS patients. Correlation between masticatory function and each category of CS will reveal a novel understanding of the patient's mastication associated with the feature of synostosis. The patients and caregivers will receive direct benefit including recommendation about mastication, foods, and treatment when possible. For medical and dental sectors, health care professional will gain new knowledge about CS patients. The data obtained from this study will also be valuable for academics and researchers to expand their knowledge and further investigate molecular pathomechanism of CS.

Research question

What are the cranio-oro-facial features and masticatory function in Thai subjects with craniosynostosis?

Research objective

To assess cranio-oro-facial features and masticatory function in Thai subjects with craniosynostosis.

Research hypothesis

Cranio-oro-facial features and masticatory function in craniosynostosis subjects are different from subjects without craniosynostosis.

Scope of research

This research was conducted to assess the cranio-oro-facial features and masticatory function in subjects with craniosynostosis in Thailand. The patient are receiving treatment at Princess Sirindhorn Craniofacial (PSC) Center at King Chulalongkorn Memorial Hospital. It is considered as one of the largest craniofacial center in South East Asia(9), receiving referral patients from several hospitals in

Thailand and neighboring countries. They were referred to Faculty of Dentistry, Chulalongkorn University for evaluation of oral features and masticatory function. An age ranging from 6 to 17 years. Healthy (without craniosynostosis) subjects at the same age range from the Well-Baby Clinic, King Chulalongkorn Memorial Hospital were recruited to the study as controls.

Expected outcomes

1. Enhancing knowledge of clinical and radiographic characteristics and masticatory functions of CS patients.
2. Improving treatment effectiveness for CS patients.
3. Providing oral hygiene care and genetic counselling for CS patients and their families.
4. Generate data records of the Thai CS patients.

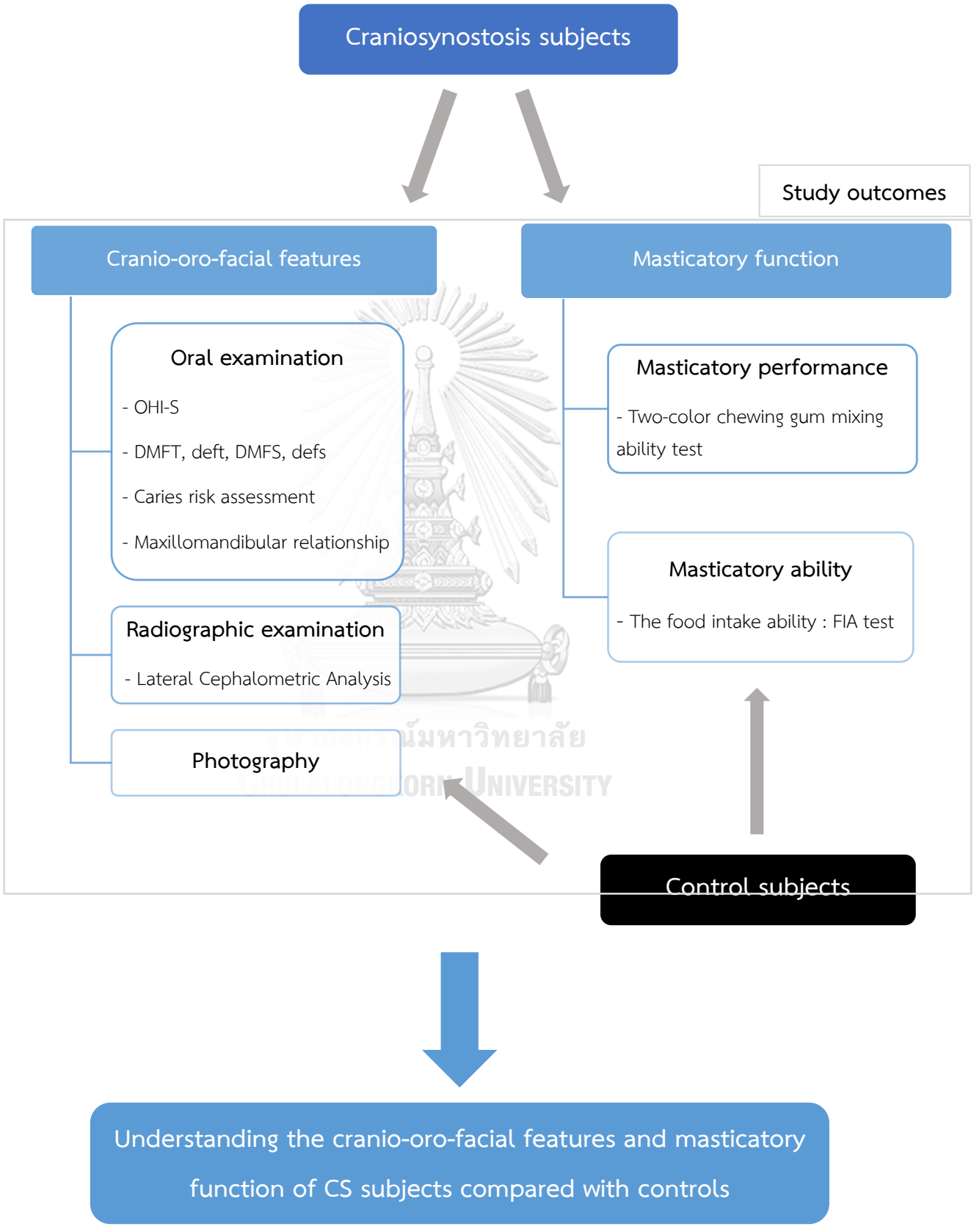
Keywords

Craniofacial abnormalities, Craniosynostosis, Masticatory muscles, Lateral cephalometric, Teeth, Dentition

Type of research

Clinical research

Conceptual framework



CHAPTER II

LITERATURE REVIEW

The cranial development

The human cranial vault is a convoluted structure that consists of several independent cranial bones. It is divided into two main parts which are the neurocranium and the viscerocranium. The neurocranium part is the framework that covers and protects the brain while the viscerocranium part is the part that forms facial skeleton(12). The neurocranium composes of the paired frontal bones, the paired parietal bones and the occipital bone.

Skull vault development begins with the migration of mesenchymal stem cells which can differentiate into various types of cells; i.e. osteoblasts, chondrocytes, adipocytes, and myoblasts(13). The mesenchymal stem cells migrate from embryonic epithelium to the area of the brain and surface ectoderm. The cranial bones develop from different embryonic origins including neural crest (frontal bones) and paraxial mesoderm (parietal bones)(14, 15). Therefore, the abnormalities during the migration, differentiation, or proliferation of mesenchymal cells can result in craniofacial disorders.

Skull sutures

Each of the cranial bones holds together with dense fibrous structure called ‘suture’. The suture is a complex area comprising four principal components: two osteogenic bone fronts, fibrous tissue, dura mater that places underneath suture, and cranial periosteum above suture(16). In early age of life, these sites allow the expansion of calvarial bones and brain growth. Therefore, the cranial sutures act as the center of the skull development(17).

Four major cranial sutures are as follows: 1) the metopic suture (between the frontal bones), 2) the sagittal suture (between the parietal bones), 3) the coronal sutures (between the frontal and parietal bones), and 4) the lambdoid sutures

(between the occipital and parietal bones). Besides, there are spaces between the flat bones that compose of membranous connective tissue, known as 'Fontanelle'. There are six fontanelles in human skull during infancy in which the largest one is the anterior fontanelle(18) and the second largest one is the posterior fontanelle.

Previous studies have demonstrated, various factors that involve in suture fusion: 1) biomechanical signals from the brain during ossification process in response to cranial bone development(19); 2) a dura mater made of dense irregular connective tissue(20); 3) external strain or force which impacts the mineralization and production of bone matrix (21); 4) tensile strain from intracranial pressure (12); 5) masticatory function (22); and 6) genetic factor. Changes in gene expression or 'Gene mutation' has been shown to cause abnormality in suture fusion.

Craniosynostosis (CS)

"Craniosynostosis" was first used by Otto in 1830 to identify the condition that one or more cranial sutures are fused prematurely.

During infancy, the membranous bones of the cranial vault are separated by sutures including metopic suture, sagittal suture, coronal sutures and lambdoid sutures to accommodate brain growth. Thereby the unsealed sutures are necessary during cranial development. If one or more sutures are prematurely fused, the brain usually develops and expands into the direction of lower resistance, resulting in asymmetrical skull(23). Particularly, fusions of multiple sutures can lead to cranio-oro-facial deformation, neurological dysfunction, visual impairment, auditory impairment, respiratory diificulty, and masticatory dysfunction.

Sagittal synostosis is the most prevalence (40-55% of CS cases), followed by coronal synostosis (20-25%), metopic synostosis (5-15%), multiple suture synostosis (5-15%), and lambdoid synostosis (<5%)(24).

The typical features of single-sutured craniosynostosis are as followed(23):

- Scaphocephaly
  - Fused sagittal suture

- Elongated narrow skull shape in anteroposterior direction and shortened in bilateral direction.
- Common in males

- Trigonocephaly
  - Fused metopic suture
  - Prominent ridge in area of forehead, broad at the back of the head, and orbital hypotelorism.
- Brachycephaly
  - Fusion of bilateral coronal sutures or bilateral lambdoid sutures
  - Flattened skull in anteroposterior direction
- Anterior plagiocephaly
  - Fusion of a single coronal suture
  - Flattened forehead on the affected area with a prominent forehead on the other area
  - Common in females
- Posterior plagiocephaly
  - Unilateral lambdoid synostosis
  - Unilateral flattening of the occiput
  - Displacement of ear and mastoid on the affected side

CS can also be classified depending on the mechanism, presentations, and number of abnormal sutures. Nonsyndromic CS, which is the majority of cases, is found that not related to other systemic problems(25). Sagittal suture fusion accounts for 80% of isolated suture cases(11). Syndromic CS has been related to more than 100 syndromes and mutations in several genes.

Both syndromic and non-syndromic CS are associated with cognitive impairment due to limited brain growth and elevated intracranial pressure. Previous studies suggested that children with metopic, unicoronal, and lambdoid suture obliterations tended to have lower intelligence quotient score and math computation abilities compared with the patients with sagittal synostosis (26).

The prevalence of CS in the USA, particularly in Atlanta's metropolitan area, is 4.3 per 10,000 births(4) and in Netherlands was 7.2 per 10,000(5).

The management is based on the severity of the condition, covering from a conventional technique with the remodeling helmet or behavior modification to surgical management such as endoscopic suturectomy and fronto-orbital advancement. Severe cases may need urgent operations to maintain airway, intracranial pressure, eye function, and nutrition intake(23). The operations aim to provide adequate space for cranial development and cosmetically acceptable appearance(7, 27).

Etiology

CS is associated with both environmental and genetic factors. Previous population-based evidences indicated that certain factors such as advanced paternal age(28), maternal age above 35 years old, multiple births, infant birth weight above 4000g, and male gender can increase the risk of developing CS(4). Mutations related to CS have been found in the genes encoding fibroblast growth factor receptor (*FGFR-1, FGFR-2, FGFR-3*), *EFNB1*, and transcription factors *TWIST* and *MSX2*(29).

FGFRs genes are involved in homeostasis and bone development. Imbalanced FGF signaling can cause premature fusion of skull bones(30).

Mutations in *FGFR-2* are associated with Apert, Pfeiffer, Crouzon syndromes, Beare-Stevenson cutis gyrate, Antley-Bixler, Jackson-Weiss, Bent Bone Dysplasia, and Seathre-Chotzen-like syndromes(31, 32).

TWIST, a basic helix-loop-helix transcription factor, implicates in the induction of mesodermal tissues and cytokine expression(33). *TWIST* mutations are found in patients with autosomal dominant Saethre-Chotzen syndrome(34).

MSX is a transcription factor related to tissue interactions during embryogenesis. *MSX2* mutations are linked to Boston-type craniosynostosis(29).

EFNB1 mutations, usually are missense and nonsense, lead to X-linked CS(35, 36).

Cranio-oro-facial manifestations

CS results in skull deformity, facial asymmetry, and dental anomalies(37), especially in syndromic craniosynostosis. Common craniosynostosis syndromes are as follows:

- Crouzon Syndrome

The patients with Crouzon syndrome have early fusion of multiple sutures. The clinical features are diverse depending on the severity of the condition. Those include exophthalmos, hyperterolorism, deviated nasal septum, underdeveloped maxilla, Angle's class III malocclusion, high arched palate, obstructive sleep apnea, crowded teeth, and anterior open bite. Cleft lip, cleft palate, deafness, total blindness, and intellectual disability can be found in some cases(10, 38, 39).

- Apert Syndrome

Premature closure of multiple calvarial sutures is observed in Apert syndrome. Clinical features include ocular proptosis, down-slanting palpebral fissures, depressed nasal bridge, chronic otitis media, excessive sweating, and hydrocephalus. Midface hypoplasia, relative mandibular prognatism, anterior open bite, posterior crossbite, mouth breathing, narrow palate (with or without cleft palate), severe dental crowding, delayed tooth eruption, tooth agenesis, enamel hypoplasia, and airway complication can be found. Syndactyly of hands and feet is a unique characteristic of this syndrome. Synostosis of the elbow and shoulder joints can occur in severe cases(2, 10, 40).

- Pfeiffer Syndrome

This syndrome affects multiple sutures. Prominent proptosis and forehead, hypertelorism, small nose, underdeveloped midface, breathing problems, hearing loss, fused digits, and elbow ankylosis are observed accompanied with several dental complications include microdontia, hypodontia, retained deciduous teeth, class III malocclusion, anterior open bite, and posterior cross bite. The most important diagnostic keys of Pfeifer syndrome are short broad thumb and big toes deviating away from other digits. Developmental delay and neurological problems can exist(1, 41, 42).

- Saethre-Chotzen Syndrome

Common features are bicoronal synostosis, facial asymmetry (individuals with unicoronal synostosis), low frontal hairline, eyelid ptosis, ocular hypertelorism, deviated nasal septum, external ear deformities, soft tissue syndactyly, and mental retardation. Less prevalent characteristics are maxilla hypoplasia, cleft palate, vertebral fusions, and congenital heart diseases(38, 43).

- Muenke Syndrome

Muenke Syndrome exhibits premature coronal suture closure. Mild midfacial hypoplasia, recurrent otitis media, hearing loss, hypertelorism, downslanting palpebral fissures, beaking of the nose, bone anomalies of hands and feet (thimble-like middle phalanges and coned epiphyses), and cognitive developmental delay have been reported(43, 44).

Masticatory function

CS patients have high susceptibility to various types of oral diseases. They are prone to caries and gingivitis(45). It is well known that CS is related to dentofacial deformities including one jaw or two jaws malformations. A previous study suggested that patients with open-bite or malocclusion tended to have prominent type I muscle fibers in masseter muscle, suggesting that CS patients might have prolonged and gentle mastication rather than rapid masticatory movement(46).

- Single-sutured craniosynostosis

An increased risk of difficulties in cognitive, language, and motor abilities was reported in single-sutured CS patients during childhood(3, 47). The single-sutured craniosynostosis might have subclinical effects on the patients' masticatory function. In addition, most of these patients are likely to have inadequate oral cleaning and poor oral hygiene, leading to dental caries, early loss of teeth, and masticatory difficulty(48).

- Multiple-sutured craniosynostosis

Patients with multiple-sutured CS have increased risk of developing orodental anomalies and compromised chewing, swallowing, speaking and breathing(10).

Postoperative muscle dysfunction, craniofacial pain, and masticatory discomfort were also found in some patients(49).

The main objective of mastication is grinding foods into smaller particles that can be mixed with saliva to form the bolus, which is safe to swallow(50). The masticatory function composes of various important parts that work collaboratively to each other including masticatory performance, occlusal bite force, and masticatory(51).

The masticatory performance (MP) is one indicator of oro-facial functional capabilities(52). MP is described as "a measure of the comminution of food attainable under standardized testing conditions"(53). There are several techniques to assess the MP such as the comminution test using sieve, glucose concentration from chewing gummy jelly, digital scanning, spectrophotometer measurement, and degree of mixing ability. The comminution method is considered as a gold standard for assessing MP. The pitfall of this method is that it requires fragmentation of hard food such as silicone impression materials or peanuts, which are uncomfortable for the participants with compromised mastication(54). Furthermore, the unpleasant taste of chewing materials, risk for particles aspiration, and time-consuming may discourage children from having natural chewing function(52, 55). An alternative test is the two-color chewing gum mixing ability test with software analysis, that show high validity and reliability especially in compromised dentition and children(55, 56). A study has showed that the comminution test and the color-mixing ability test are significantly correlated (57). Therefore, the two-color chewing gum mixing ability test is a reliable measurement for studying masticatory performance in children.

Masticatory ability, which is a subjective evaluation, can be measured by using the food intake ability self-assessment questionnaire (FIA test). The questionnaire aims to estimate the masticatory ability while chewing. The foods are categorized into 6 groups based on their toughness as stated by previous studies(58, 59). A positive viewpoint in mastication of harder food is likely to represent good biting ability and development of masticatory function(59, 60).

Masticatory system has been shown to play significant roles in maintaining good quality of life for humans(61). However, there are limited studies showing the masticatory function of patients with CS. Due to the difficulties in daily oral health care, possibilities of poor mastication, reduced salivary flow rates, and abnormal dentition in CS patients (10), it is essential to have a better understanding of these problems and find the best solutions to deliver proper care of patients with CS.

CHAPTER III

RESEARCH METHODOLOGY

Target population

Thai craniosynostosis subjects were recruited from Princess Sirindhorn Craniofacial (PSC) Center at King Chulalongkorn Memorial Hospital to participate in this study carried out at Geriatric and Special Patients Care Clinic, Faculty of Dentistry, Chulalongkorn University. The recruited age range was from 6 to 17 years. A minimum age of 6 years was set based on the patients' ability to cooperate with examinations and tests(55). Patients with any syndromes, systemic diseases, or craniofacial anomalies apart from CS were excluded from the study. In this study, the patients were clinically evaluated by one observer. Informed written consents were gathered from each participant's legal guardians. The patient information, clinical characteristics, radiographs, photographs, and masticatory function tests were recorded.

Inclusion criteria	Exclusion criteria
Subjects with Thai nationality between 6 to 17 years old	Subjects diagnosed with craniofacial syndromes or abnormalities other than CS
Craniosynostosis diagnosis: Non-syndromic CS and syndromic CS (by PSC)	Patients who refused to participate in the project
Received treatment at the Princess Sirindhorn Craniofacial (PSC) Center.	Patients who were not able to perform two-color chewing gum mixing ability test and masticatory ability test.

Control population

Healthy subjects at the same age range from the Well-Baby Clinic, King Chulalongkorn Memorial Hospital were recruited as controls.

Sample size

Prior studies on masticatory function indicate that at least 10 subjects (n=10) were required to test the strength of the study hypothesis (power = 80%, α = 0.05)(49, 62).

The estimated sample size was calculated based on previous study(55). For hypothesis testing, two independent means, mean values in group 1 and 2 were 0.512 and 0.382; Standard deviations (SD) in group 1 and 2 were 0.109 and 0.099; alpha and beta values were 1, 0.05 and 0.2. The estimated sample size was 11 per group. An extra sample size of 10% was considered to compensate the specimen loss for any reason, thus the total sample size was 12 per group.

History taking and clinical data

This study was approved by the Institutional Review Board, Faculty of Medicine, Chulalongkorn University, Thailand (COA no. 1348/2021). Informed consents were obtained from the participants and their legal guardians. Medical records and laboratory data from Chulalongkorn Memorial Hospital were evaluated.

Oral examination

The WHO manual "Oral Health Surveys – Basic Methods" has recommended the standardized reporting system for oral health status evaluation including: caries prevalence, simplified oral hygiene index(63).

- Simplified Oral Hygiene Index(64)

- OHI-S : Simplified Debris Index(DI-S) + Simplified Calculus Index(CI-S)

Debris and calculus were examined by running along the surface area of preselected tooth with No.5 explorer.

The debris classification :

Classification	Information
0	No debris or stain present
1	Soft debris covering not more than one third of the tooth surface, or presence of extrinsic stains without other debris regardless of surface area covered
2	Soft debris covering more than one third, but not more than two thirds, of the exposed tooth surface
3	Soft debris covering more than two thirds of the exposed tooth surface

The calculus classification :

Classification	Information
0	No calculus present
1	Supragingival calculus covering not more than third of the exposed tooth surface
2	Supragingival calculus covering more than one third but not more than two thirds of the exposed tooth surface or the presence of individual flecks of subgingival calculus around the cervical portion of the tooth or both
3	Supragingival calculus covering more than two third of the exposed tooth surface or a continuous heavy band of subgingival calculus around the cervical portion of the tooth or both

- Caries Prevalence

The debris was removed from the teeth before examination using the WHO (1997) criteria and the indices as follow(65):

- DMFT : The Decayed, Missing, Filled Index (Number of permanent tooth)
- deft : The Decayed, Extracted, Filled Index (Number of primary tooth)
- DMFS : The Decayed, Missing, Filled Index (Number of permanent tooth surface)

- defs : The Decayed, Extracted, Filled Index (Number of primary tooth surface)

Besides the WHO recommendation, the following oral examinations, suggested by previous studies(11, 45, 66), were performed and collected.

- Caries risk assessment(11)
- Caries-risk Assessment Form for ≥ 6 Years Old(67)

Table 2. Caries-risk Assessment Form for ≥6 Years Old
(For Dental Providers)

Factors	High risk	Moderate risk	Low risk
Risk factors, social/biological			
Patient has life-time of poverty, low health literacy	Yes		
Patient has frequent exposure (>3 times/day) between-meal sugar-containing snacks or beverages per day	Yes		
Child is a recent immigrant		Yes	
Patient has special health care needs		Yes	
Protective factors			
Patient receives optimally-fluoridated drinking water			Yes
Patient brushes teeth daily with fluoridated toothpaste			Yes
Patient receives topical fluoride from health professional			Yes
Patient has dental home/regular dental care			Yes
Clinical findings			
Patient has ≥1 interproximal caries lesions	Yes		
Patient has active non-cavitated (white spot) caries lesions or enamel defects	Yes		
Patient has low salivary flow	Yes		
Patient has defective restorations		Yes	
Patient wears an intraoral appliance		Yes	

Circling those conditions that apply to a specific patient helps the practitioner and patient/parent understand the factors that contribute to or protect from caries. Risk assessment categorization of low, moderate, or high is based on preponderance of factors for the individual. However, clinical judgment may justify the use of one factor (e.g., interproximal lesions, low salivary flow) in determining overall risk.

Overall assessment of the dental caries risk: High ❒ Moderate ❒ Low ❒

- Maxillomandibular relationship(11)

Angle's Classification that was developed by Edward H. Angle in 1890.

Angle class I occlusion

- Molar relationship : The mesiobuccal cusp of the maxillary first permanent molar occludes with the mesiobuccal groove of the mandibular first permanent molar.
- Canine relationship : The mesial incline of the maxillary canine occludes with the distal incline of the mandibular canine. The distal incline of the maxillary canine occludes with the mesial incline of the mandibular first premolar.

Angle class II occlusion

- Molar relationship : The mesiobuccal groove of the mandibular first molar is distally positioned when in occlusion with the mesiobuccal cusp of the maxillary first molar. Usually the mesiobuccal cusp of maxillary first molar rests in between the first mandibular molar and second premolar.
- Canine relationship : The mesial incline of the maxillary canine occludes anteriorly with the distal incline of the mandibular canine.
- Class II Division 1: The molar relationships are like that of Class II and the maxillary anterior teeth are proclined. A large overjet is present.
- Class II Division 2: The molar relationships are Class II where the maxillary central incisors are retroclined. The maxillary lateral incisor teeth may be proclaimed or normally inclined. A deep overbite exists.

Angle class III occlusion

- Molar relationship : The mesiobuccal cusp of the maxillary first permanent molar occludes distally (posteriorly) to the mesiobuccal groove of the mandibular first molar.
- Canine relationship : Mandibular incisors are in complete crossbite.

Radiographic examination

- Panoramic radiograph or the section could be developed from CBCT if available(68)
- Lateral Cephalometric radiograph or the section could be developed from CBCT if available(68)
- Periapical radiograph

The imaging expense was adhered to each participant's health insurance system. In case that the radiographic examination was not covered by the insurance, the researcher had taken responsibility.

Lateral cephalometric analysis was interpreted by experienced orthodontist and reevaluated at least two weeks afterward. In this study, American Board of

Orthodontics and Ricketts' analysis were referred(69). Cephalometric reference points, reference planes, and angular measurements were described below. Thai norms were presented in previous studies(70, 71).

Description of lateral cephalometric evaluation

Reference points	Description
Nasion (N)	The most anterior point of the frontonasal suture
Glabella (Ga)	The most anterior point of the frontal bone
Porion (Po)	The most superior point of the external auditory canal
Sella (S)	The center of the hypophyseal fossa (pituitary fossa)
Orbitale (Or)	The most anteroinferior point of the orbital margin
ANS	The tip of the anterior nasal spine
PNS	The tip of the posterior nasal spine
Point A	The deepest point of the anterior portion of the maxillary alveolar ridge concavity
Point B	The deepest point of the anterior portion of the mandibular alveolar ridge concavity
Gnathion (Gn)	The most anteroinferior point of the bony chin in the mid sagittal plane
Pogonion (Pog)	The most anterior point of mandibular symphysis in the mid sagittal plane
Menton (Me)	The most inferior point of mandibular symphysis in the mid sagittal plane
Gonion (Go)	The most posteroinferior point on the angle of the mandible
Condylar (Co)	The most posterosuperior point on the head of the condyle

Description of lateral cephalometric evaluation (continued)

Reference points	Description
Articulare (Ar)	The point of the intersection between the posterior margin of the ascending mandibular ramus and the outer margin of the posterior cranial base
Basion (Ba)	The most anterior point of the foramen magnum
Pterygomaxillary fissure (Ptm)	The most posterosuperior point of the pterygomaxillary fissure
Center of cranium point (CC)	The point of intersection between Ba-N plane and Ptm-Gn plane

Reference planes and angulations	Description
Facial plane (NPog)	The plane from N to Pog
SN plane	The plane from S to N
FH plane	The horizontal plane through Po and Or
Occlusal plane	The plane bisecting the occlusion of the first molars and central incisors
Palatal plane	The plane from ANS to PNS
Mandibular plane	The lower border of the mandible tangent to the gonial angle and Me
Ramus plane	The tangent of the most posterior border of the mandibular ramus through the Ar
E-line	The plane from soft tissue of the nasal apex to the most prominent point of soft tissue of chin
Upper incisor (U1)	The long axis of the maxillary incisor
Lower incisor (L1)	The long axis of the mandibular incisor

Description of lateral cephalometric evaluation (continued)

Reference planes and angulations	Description
Wits appraisal (AO-BO)	The distance from the perpendicular plane from point A and B to the occlusal plane
Convexity of point A	The distance from point A to NPog plane
U1-NA (mm)	The distance between the tip of the maxillary incisor and a line from Nasion to point A
U1-NA	The angle formed by the long axis of maxillary incisor to the NA plane
U1-L1	The angle formed by the long axis of maxillary incisor and long axis of mandibular incisor
U1-APog (mm)	The distance from the incisal edge of the maxillary incisor to APog plane
U6-PTV (mm)	The distance from the pterygoid vertical to the distal of the maxillary molar
L1-NB (mm)	The distance between the tip of the mandibular incisor and a line from Nasion to point B
L1-NB	The angle formed by the long axis of mandibular incisor to the NB plane
L1-APog (mm)	The distance from the incisal edge of the mandibular incisor to APog plane
L1-APog	The angle formed by the long axis of mandibular incisor to the APog plane
Lower lip to E-line	The distance from lower lip to E-line
Lower face height	The distance from ANS to Me
Posterior facial height	The distance from S to Gn
Ant cranial base length	The distance from Na to CC
SNA	The angle formed by S, N, A point indicating the sagittal maxillary position

Description of lateral cephalometric evaluation (continued)

Reference planes and angulations	Description
SNB	The angle formed by S, N, B point indicating the sagittal mandibular position
ANB	The skeletal relationship between the maxilla and mandible
NPog-FH	The angle formed by FH plane to NPog plane
SN-GoGn	The angle formed by the SN plane and the GoGn plane
FMA (FH-MP)	The angle formed by FH plane and the mandibular plane
IMPA (L1-MP)	The angle formed by the long axis of mandibular incisor to the mandibular plane
Maxillary depth	The angle formed by FH plane and NA plane
Facial depth	The angle formed by FH plane and NPog plane
Cranial deflection	The angle between FH plane and Ba-N plane
Mandibular arc	The angle formed by the condylar axis and corpus axis
Mandibular plane angle	The angle formed by SN plane and GoMe plane
Facial axis	The angle formed by NBa plane to PtmGn plane

Photography

The photographs provide the information about cranio-facial appearances, Angle's classification, and oral manifestations of the subjects by comparing with CT images (before and after surgical process).

- Extraoral photograph : Front view, Lateral view, Oblique view, Top view
- Intraoral photograph : Front view, Upper view, Lower view, Lateral view

All the photograph data was confidential. In case of published paper, the subject's revealed face was covered with black strap in pupillary line area for personal security. Consents for data publication were obtained from each subject.

Masticatory function

- Masticatory performance: the two-color chewing gum mixing ability test

The two-color chewing gum (Hubba-Bubba Tape Gums, WM. Wrigley Jr. Company, Chicago) was used. Each gum had 30 mm in length and composed of two layers stuck together. Azure color (sour berry flavor) and pink color (fancy fruit flavor) were used according to the original protocol(50, 72). Each participant was asked to chew a fresh gum for 20 cycles(57). After chewing, the gum was stored in labelled plastic bag and squeezed into 1 mm wafers. Both sides were scanned with flatbed scanner and analyzed with ViewGum© software. This software measured a standard deviation of the hue or the variance of the histogram of the hue which had proved to be valid and optimal for masticatory assessment. The less variation in color of hue meant the higher mixing ability(52, 55).

- Masticatory ability: The Food Intake Ability (FIA test)

The questionnaire aimed to estimate the masticatory ability while chewing foods, that were categorized into 6 groups from soft to hard in texture. These foods were soft tofu, watermelon, ham, apple, cookies, and peanut according to previous studies(58, 59). The researcher explained about the foods and then the five-point Likert scale was used for measuring masticatory ability as follows: 1 point – could not chew at all, 2 points – difficult to chew, 3 points – could not explain either way, 4 points – could chew some, 5 points – could chew well. The data was recorded in ordinal number (1, 2, 3, 4, and 5).

Statistical analysis

All statistical computations were performed by IBM SPSS for windows version 22.0 (IBM, Armonk, NY). All the nominal data was analyzed by Chi-square test or Fisher's exact test. All the ordinal data was determined by Mann-Whitney U test. The normality of interval or ratio data was verified by Shapiro-Wilk test (n<50). Differences in variables were determined by independent *t*-test if the data had normal distribution. Mann-Whitney U test was used if data was not normally distributed. In cephalometric analysis, differences between patient group and Thai normative values were analyzed by one-sample t-test. The level of significance was set at *P*-value < 0.05**.**

Subgroup analyses of caries prevalence (deft, DMFT, defs, DMFS) and caries risk assessment was also performed to explore the differences between patients with Angle's classification I and III, and between syndromic and non-syndromic CS patients, The differences in caries prevalence between groups were analyzed using independent t-test or Mann Whitney U test, as appropriate, and those in caries risk assessment between groups were evaluated using Chi-square test.

CHAPTER IV
RESULTS

Thirteen Thai CS patients aged between 6-17 years and thirty age-matched healthy children were recruited.

Part 1: Characteristics of the patients

Among the participants, there were eight female and five male patients. The average age at initial visit was 10.47 years old (± 2.88). The clinical diagnoses included syndromic craniosynostosis (Apert syndrome and Crouzon Syndrome) and non-syndromic craniosynostosis (Multiple sutures craniosynostosis and Right coronal craniosynostosis). Table 1 demonstrated the characteristics of the patients.

Table 1: *Basic characteristics of the patients*

Patients	Clinical diagnosis	Gender	Age at initial visit (years)
P-1	Apert Syndrome	Female	7
P-2	Apert Syndrome	Male	10
P-3	Apert Syndrome	Female	15
P-4	Multiple sutures craniosynostosis	Female	14
P-5	Right coronal craniosynostosis	Female	9
P-6	Right coronal craniosynostosis	Female	7
P-7	Crouzon Syndrome	Male	9
P-8	Crouzon Syndrome	Female	9
P-9	Apert Syndrome	Male	12
P-10	Multiple sutures craniosynostosis	Female	6

Table 1: *Basic characteristics of the patients (continued)*

Patients	Clinical diagnosis	Gender	Age at initial visit (years)
P-11	Crouzon Syndrome	Male	13
P-12	Multiple sutures craniosynostosis	Male	6
P-13	Multiple sutures craniosynostosis	Female	7

P-1,2,3,7,8,9,11 : syndromic craniosynostosis patients.

P-4,5,6,10,12,13 : non-syndromic craniosynostosis patients.

Clinical characteristics and oral manifestations of the patients

- **Apert Syndrome**

P-1

Patient-1 was a 7-year-old girl (Figure 1). Medical records showed that the patient had syndactyly on hands and feet (Figure 1), premature closure of skull sutures, and uncommon shape of the head. At 2 years old, the patient had hearing loss due to Otitis Media (OM). At 7 years old, physical examinations showed maxilla hypoplasia, hypertelorism, exorbitism, and incomplete cleft palate. She received fronto-orbital advancement (FOA) surgery at 1 year old, tonsillectomy with myringotomy at 2 years old, separation of hand webspace at 9 months and 3 years old, and palatoplasty at 7 years old. The patient had severe obstructive sleep apnea (OSA) that needed continuous positive airway pressure (CPAP).

The patient was in mixed dentition with severe Class III malocclusion (Figure 3). Heavy plaque and food debris deposition, multiple dental caries, and poor oral hygiene were shown (Figure 2). The OHI-S score was 2.67 (categorized as fair oral status). The deft score was 13 and defs was 29, indicating high caries prevalence in primary teeth. The teeth 55, 54, 62, 64 and 75 were diagnosed as asymptomatic irreversible pulpitis required extraction or pulpal treatment. She had no caries prevalence in permanent teeth. Overall caries risk assessment indicated high caries risk.

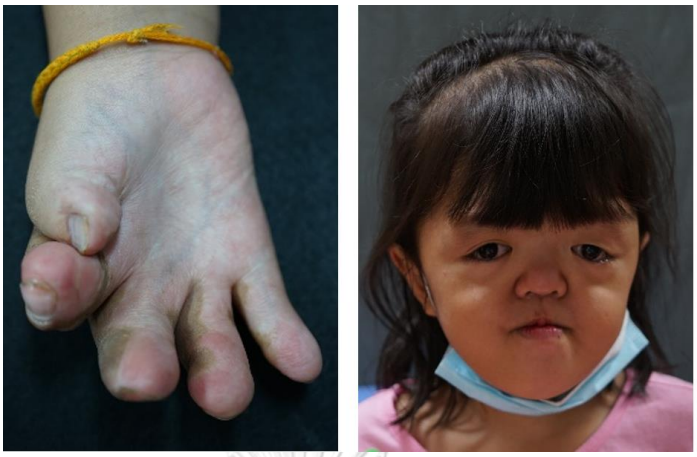


Figure 1: right hand and extraoral frontal view of the P-1

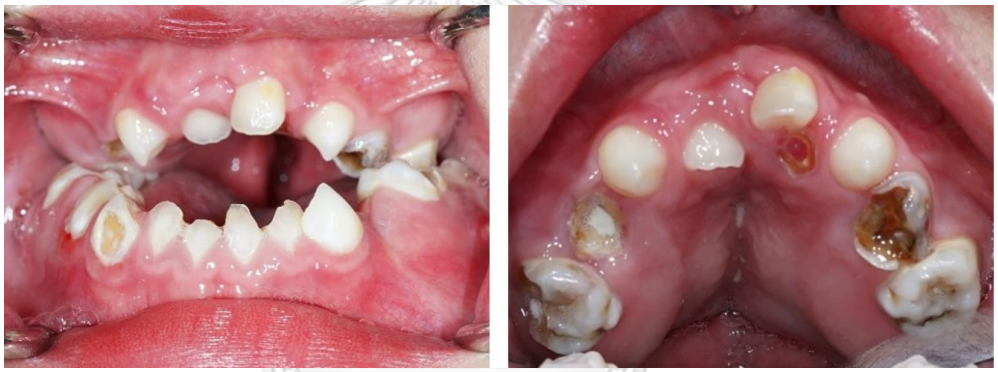


Figure 2: intraoral frontal view and upper view of the P-1

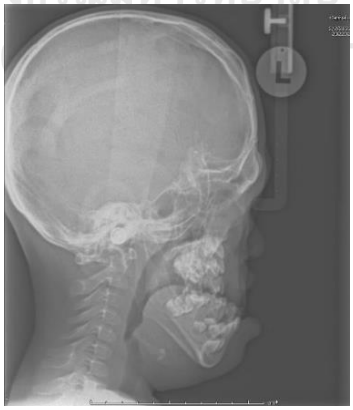


Figure 3: lateral cephalogram of P-1

P-2

Patient-2, 10-year-old boy, had midface retrusion, complex syndactyly of both hands-feet, lagophthalmos on both eyes, and obstructive sleep apnea. The patient underwent several surgeries: fronto-orbital advancement at 2 years old and hand web space separations with full thickness skin grafts (FTSG) at 2, 3 and 9 years old. His Intelligence Quotient score was 32 (Extremely low level), indicating global developmental delay (GDD).

The patient had mixed dentition with multiple deep dental caries (Figure 4, 5) which presented in 9 and 27 as deft and defs scores together with 3 and 4 for DMFT and DMFS scores. The caries risk assessment was high. His OHI-S score was 2.5, indicating fair oral status. He had Class III maxillomandibular relationship, and generalized heavy plaque and moderate calculus deposition. The patient had no complaint of masticatory problem..

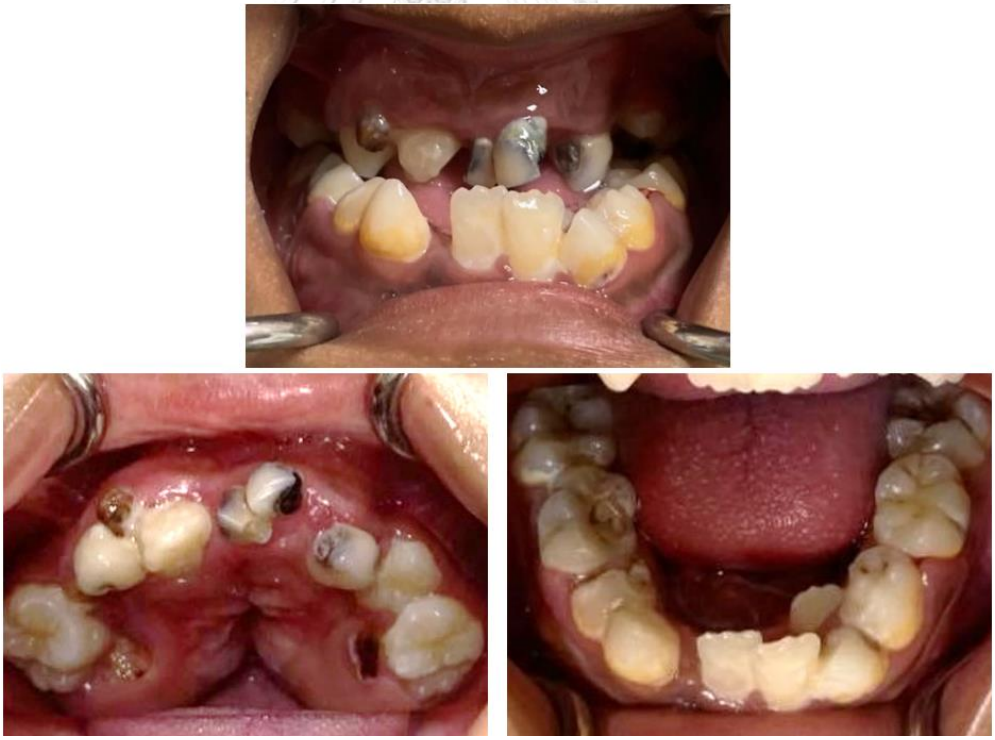


Figure 4: intraoral frontal view, upper view , and lower view of the P-2

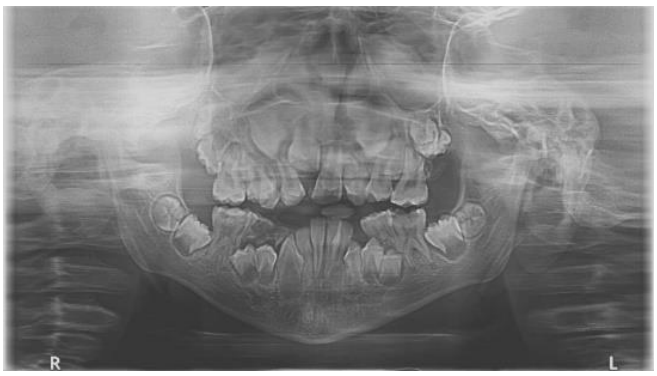


Figure 5: panoramic film of the P-2

P-3

Patient-3 was a Thai 15-year-old girl who was diagnosed as Apert syndrome with intellectual disabilities. The patient received fronto-orbital advancement surgery at 1 and 10 years old , resulting in good forehead contour, no hydrocephalus, and no sign of increased intracranial pressure. She had obstructive sleep apnea with severe hypoventilation, hypercapnia, mid-facial hypoplasia, and syndactyly between fingers of both hands and feet (Figure 6).

Patient-3 was in permanent dentition having severe Angle Class III malocclusion (Figure 7). Anterior openbite with negative overjet about 12-15 mm were recorded. The patient presented with maxillary deficiency and severe dental crowding. The teeth 15, 12, 22, 25 showed complete palatoversion angulation (Figure 8). She had heavy plaque and calculus deposition, which covered entire lower incisor teeth. The OHI-S score was 3.34, indicating poor oral hygiene. Many carious lesions were noted. DMFT score was 7 and DMFS score was 7. Prolong retention of lower left primary canine tooth was observed. She also had cleft soft palate and uvula.

Figure 6: right hand and feet of the P-3

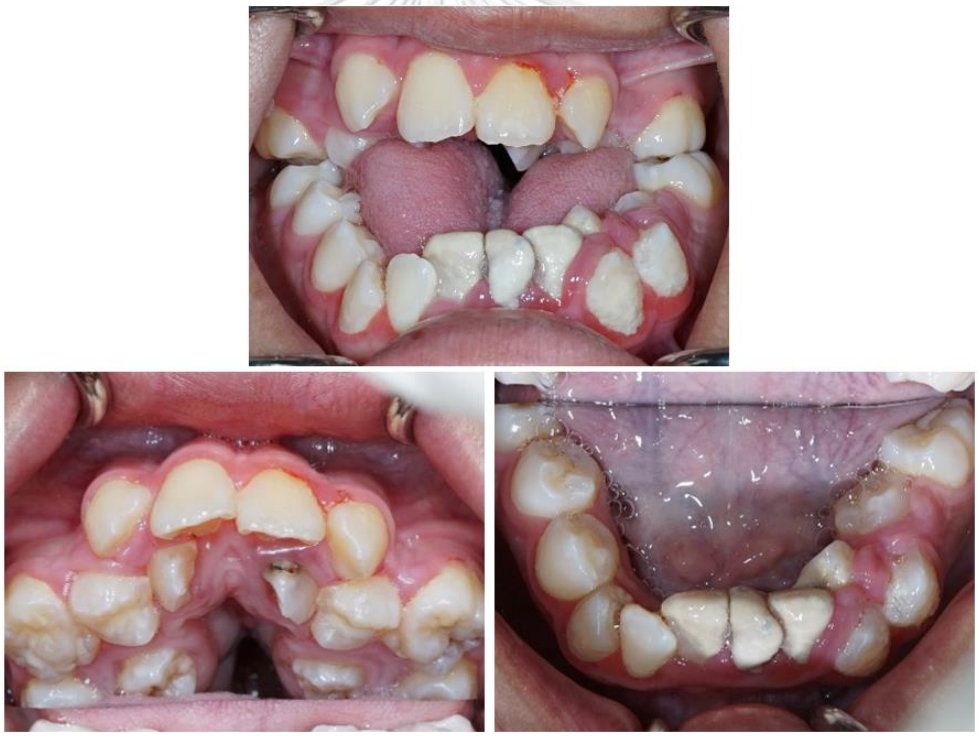


Figure 7: intraoral frontal view, upper view , and lower view of the P-3

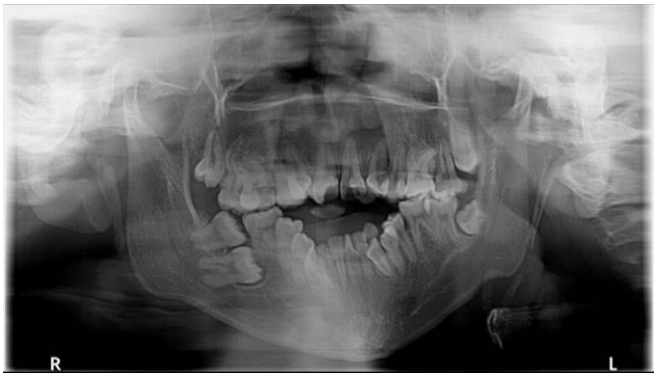


Figure 8: panoramic film of the P-3

P-9

Patient-9 was a 12-year-old boy (Figure 9). He had bilateral otitis media with effusion (OME), adenotonsillar hypertrophy, and acquired subglottic stenosis at 7 years old. Physical examination revealed bilateral coronal synostosis, downslanting palpebral fissures, hypertelorism, exorbitism, cleft palate, mid-facial hypoplasia, bilateral syndactyly of hands and feet, hearing loss, and mild obstructive sleep apnea. The patient underwent several operations including fronto-orbital advancement surgery, left and right ear myringotomy with Pressure Equalizer (PE) tube, and separation of left-right hand webspace. His IQ score was 81, indicating low average intelligence, required psychological therapy.

Patient-9, in the mixed dentition, had Class III malocclusion (Figure 11), severe maxillary teeth crowding, moderate plaque with minimal calculus deposits, gingival inflammation, and fair oral hygienics (Figure 10). The permanent lower left first molar developed pulp necrosis and caused toothache. The DMFT and DMFS scores were 9 and 15 respectively, indicating high caries prevalence in the permanent teeth. The deft and defs score were 1 and 2, respectively (The lower right first molar was the only one primary tooth left). The patient had a history of multiple teeth extraction due to dental caries. Patient had OHI-S score of 1.33. The caries risk assessment was high.

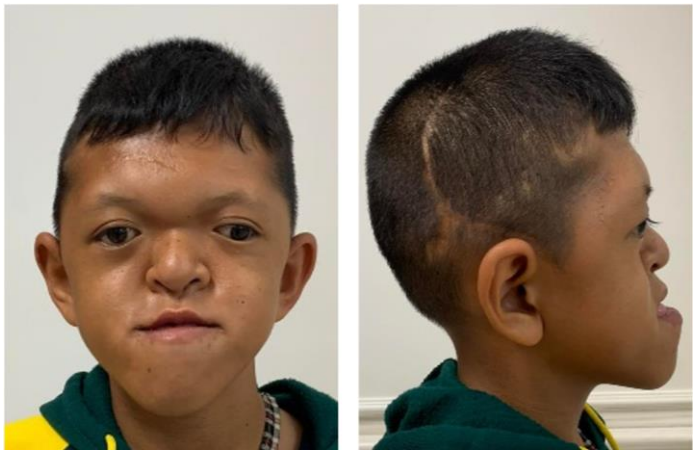


Figure 9: extraoral frontal view and lateral view of the P-9

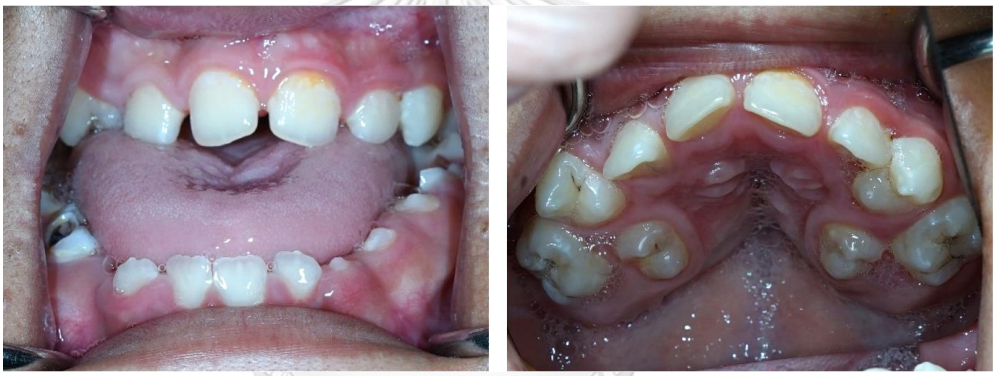


Figure 10: intraoral frontal view and upper view of the P-9

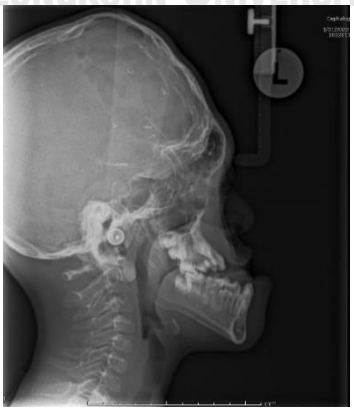


Figure 11: lateral cephalogram of P-9

- **Multiple sutures craniosynostosis**

P-4

The patient was 14 years old. She was identified as delayed milestone with low IQ score and somatic symptom disorder. The patient received fronto-orbital advancement, posterior cranial vault reconstruction, and left superior oblique (LSO) myectomy surgeries. Treatment record showed the history of enuresis and snoring at nights (Figure 12).

Patient-4 was in permanent dentition (Figure 13). Caries prevalence indices (deft, defs, DMFT, DMFS) were zero. Caries-risk analysis showed low risk. OHI-S score was 0.67, indicating good oral care. She had regular dental check-up every 6 months at private dental clinic. Class I occlusion without any abnormalities was observed (Figure 14).

Figure 12: extraoral frontal view and lateral view of the P-4

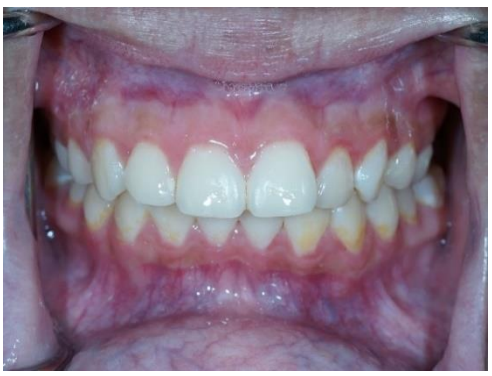


Figure 13: intraoral frontal view of the P-4

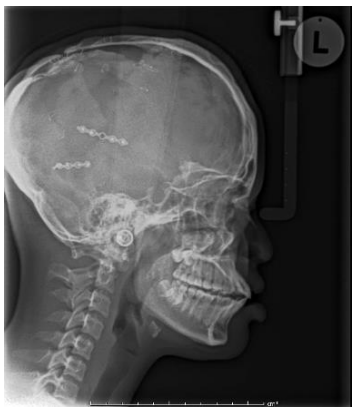


Figure 14: lateral cephalogram of P-4

P-10

Patient-10, 6-year-old girl, had amblyopia with left congenital muscular torticollis and plagiocephaly. She completed fronto-orbital advancement surgery at 1 year old showing good outcome. She received anterior-middle cranial vault remodeling surgery at age of 5 years. Medical documents showed that the patient developed right coronal synostosis, followed by synostoses of left coronal and sagittal sutures. Normal developmental milestones were noted.

The patient had mixed dentition with dental cavities about 19 surfaces on the primary teeth (Figure 15,16). Her OHI-S score was 1. Oral examination showed generalized mild dental plaque with no tartar built-up. The deft and defs scores were 10 and 19, respectively. The DMFT and DMFS scores were both 2. Overall assessment indicated high caries risk.

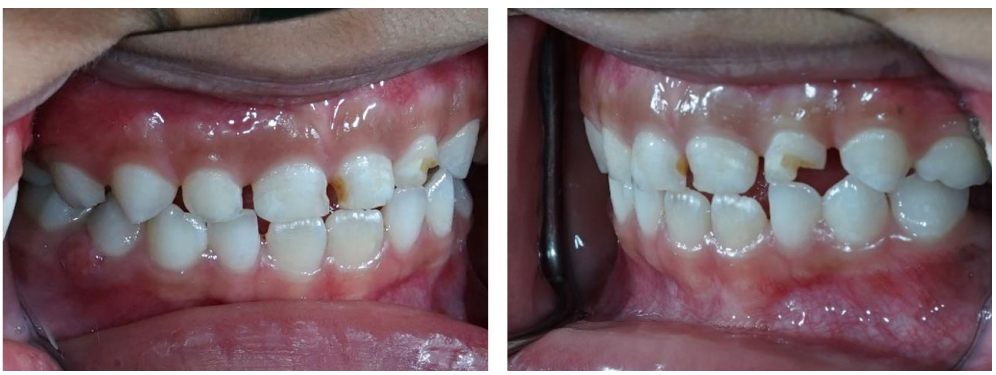


Figure 15: intraoral lateral views of the P-10

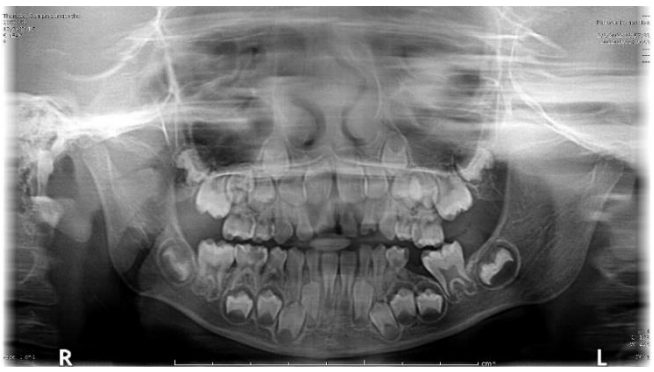


Figure 16: panoramic film of the P-10

P-12

This patient was 6 years old boy who was initially diagnosed with bilateral coronal craniosynostosis. The synostosis then affected other sutures comprising sagittal, bilateral lambdoid, and bilateral squamosal sutures. He had good forehead contour, no headache, no lagopthalmos, no exorbitism, and mild retrusion of midface area after obtaining fronto-orbital advancement surgery and posterior cranial vault reconstruction. He used to have bilateral otitis media with effusion but already resolved with myringotomy surgery. Medical records showed that the patient had severe OSA with loud snoring and polydactyly on right hand (Figure 17).

Patient-12 was in mixed dentition (Figure 18). Multiple deep dental caries was manifested indicating high caries risk. His parents informed that the patient had soft drink, potato chips, cookies, and bubble milk tea almost every day. This patient required diet counselling and dental treatment. He presented fair oral hygiene status with OHI-S score of 2. Class III of Angle's classification with anterior and posterior crossbite due to constricted maxillary arch was observed(Figure 19). He had high labial frenum attachment with dental spacing (1 mm) between two upper incisors.

Figure 17: both hands and extraoral lateral view of the P-12

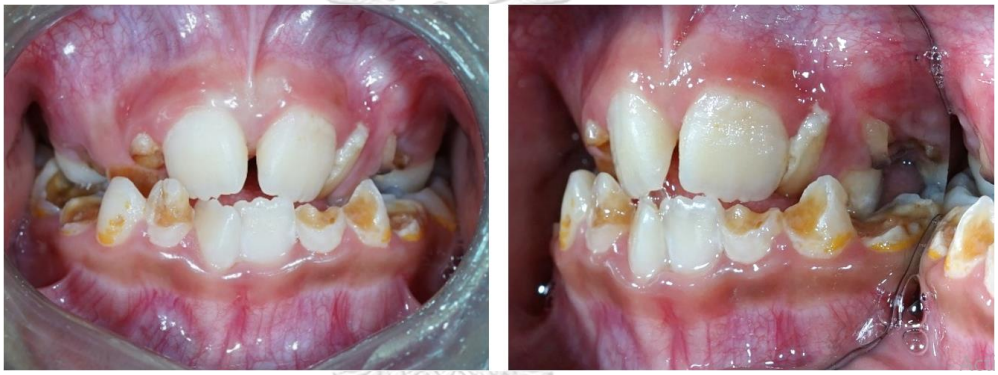


Figure 18: intraoral frontal view and lateral view of the P-12

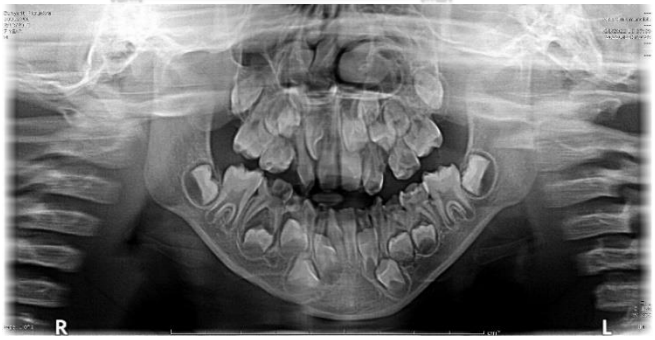


Figure 19: panoramic film of the P-12

P-13

Patient-13, 8-year-old girl, was diagnosed as nonsyndromic multiple craniosynostosis. The patient had posterior cranial vault remodeling surgery at 4 years old and fronto-orbital advancement surgery at 5 years old which resulted in mild temporal hallowing, good forehead contour, no facial asymmetry, and no bony defect.

Medical records indicated that the patient did not have snoring, sleep dysfunction, headache, and any growing issue. The overall development was in a good condition.

Mixed dentition with molar Class I relationship was observed. The patient showed several dental cavities in both primary and permanent teeth. DMFT-DMFS-deft-defs scores were 4-5-5-7. Caries risk assessment indicated high risk. OHI-S score was 2 (fair oral hygiene). Her primary lower lateral incisors were fused to lower canines on both left and right sides (Figure 20). Deep bite was recorded (Figure 21).

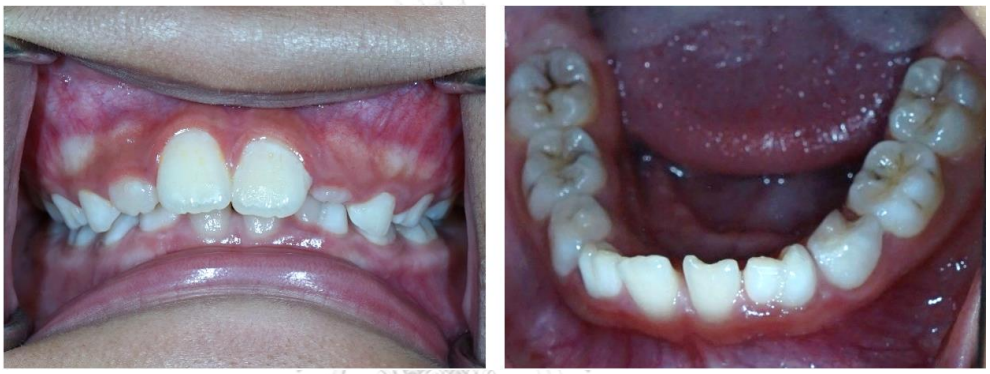


Figure 20: intraoral frontal view and lower view of the P-13

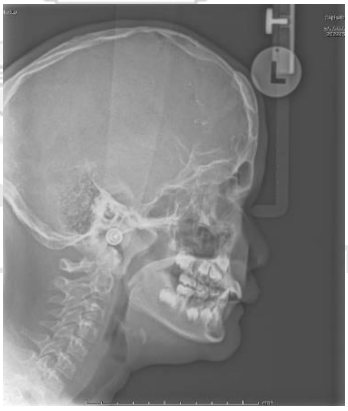


Figure 21: lateral cephalogram of P-13

- **Right coronal craniosynostosis**

P-5

Patient-5 was a 9-year-old girl. Her first visit at Chulalongkorn memorial hospital was at 5 years old. She received the fronto-orbital advancement surgery at one year old with good outcome, normal head shape, and no weakness. She was diagnosed

with low average intelligence and learning disorder. She had hyperopic astigmatism, acanthosis nigrican on neck, low frontal hairline, and right plagiocephaly (Figure 22). No history of obstructive sleep apnea was recorded.

The patient was in permanent dentition. She had good oral hygiene (OHI-S score of 1.33), generalized mild dental biofilm, and no calculus accumulation. She had carious lesion on occlusal surface of the permanent lower left first molar without any symptoms. Her lower left and right lateral incisors were clinically absent. The upper left central incisor was malaligned (Figure 23). The DMFT and DMFS score were 3 and 3, respectively. Moderate caries risk was observed.

Figure 22: extraoral frontal view and lateral view of the P-5

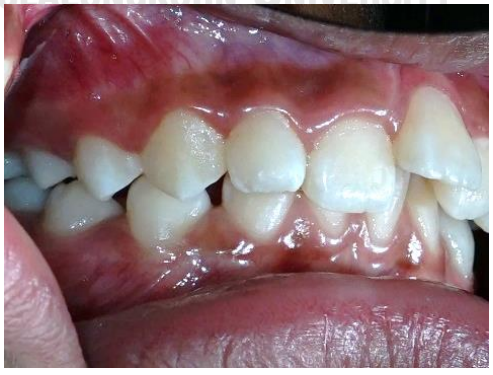


Figure 23: intraoral lateral view of the P-5

P-6

Patient-6 was a 7-year-old girl who was diagnosed with non-syndromic right coronal craniosynostosis and obstructive sleep apnea. The patient showed good forehead shape with slight depression at right coronal and temporal areas. She had undergone anterior cranial vault remodeling surgery and planned to have fronto-orbital advancement surgery. Her IQ score was at borderline intelligence level.

The patient was in mixed dentition and never had any dental treatment She had mild dental plaque deposition and mild gingivitis. No dental tartar was founded (Figure 24). The primary lower right canine had first degree mobility without any symptoms. Her OHI-S score was 1.5, indicating fair oral hygiene. Her dentition was Class I relationship. She did not have any tooth decay, filling, and extraction (Figure 25).

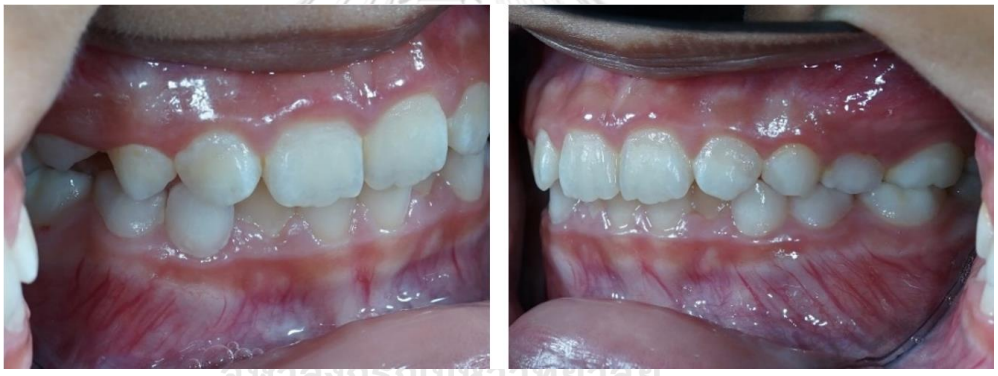


Figure 24: intraoral lateral views of the P-6

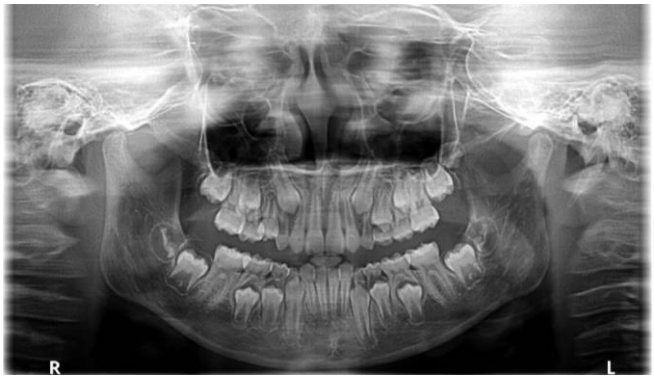


Figure 25: panoramic film of the P-6

- **Crouzon Syndrome**

P-7

This patient was a 9-year-old boy who had Crouzon syndrome. An initial diagnosis was made at 11 months old due to uncommon forehead shape. He received cranial reconstruction with programmable ventriculoperitoneal shunt surgery at 1 year old, and tonsillectomy and adenoidectomy at 7 years old. He presented premature fusion of sagittal and bilateral lambdoid sutures. He also showed midface hypoplasia, cupped ears, and loud snoring which needed polysomnography. His intelligence quotient score was at low average intelligence level.

Patient-7 was in mixed dentition. He had Class III malocclusion, anterior crossbite, and unilateral left posterior crossbite (Figure 26). He had severe dental crowding (Figure 27). The OHI-S score was 2.84, representing fair oral health. Mild calculus and heavy plaque deposition was recorded. The caries prevalence parameters were deft of 5, defs of 9, DMFT of 1, and DMFS of 9, indicating high caries risk.

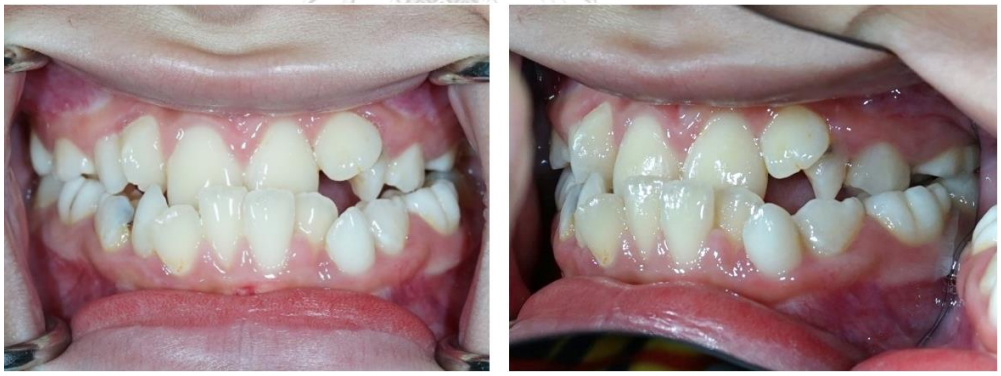


Figure 26: intraoral frontal view and lateral view of the P-7

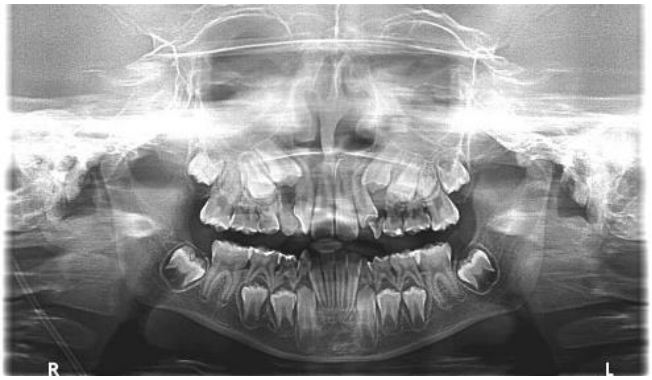


Figure 27: panoramic film of the P-7

P-8

Patient-8 was 9 years old. She exhibited exposure keratopathy (EK) due to prolonged exposure of the ocular surface even while sleeping, and hydrocephalus. She was on tracheostomy tube because of severe upper airway obstruction. The patient had fronto-orbital advancement surgery with MID system, programmable ventriculoperitoneal shunt insertion surgery, and posterior cranial vault reconstruction with posterior fossa decompression. Her appearance showed lethargic eyes with exorbitism and tongue protrusion. Her intellectual disability was moderate.

She was in permanent dentition with poor oral hygiene (Figure 28). Four teeth including teeth 16, 22, 26, and 46 were decayed teeth. She received dental operations under general anesthesia at 7 years old for removal of deciduous teeth and permanent lower left first molar due to carious lesions. She presented thick dental calculus on lower anterior teeth and generalized heavy plaque deposition. Her mother did not allow the patient to use fluoride toothpaste to avoid swallowing large amount of toothpaste and aspiration.

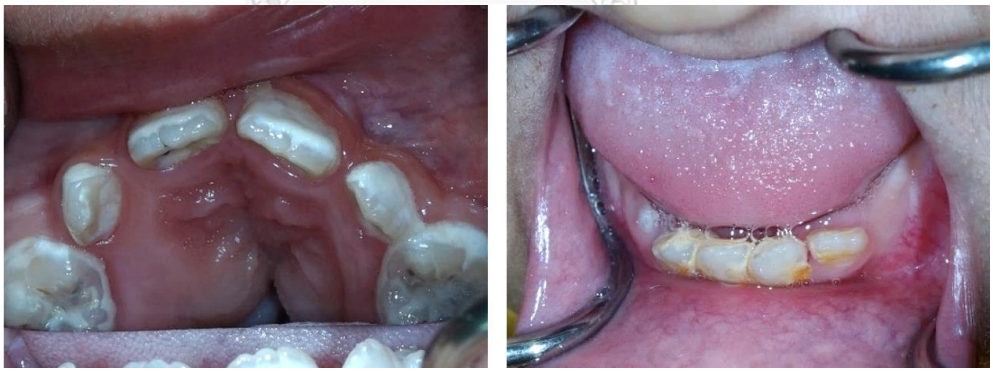


Figure 28: intraoral upper view and lower view of the P-8

P-11

This patient was a 13-year-old boy who was diagnosed with Crouzon syndrome with all sutures synostoses. He had a history of obstructive sleep apnea and increased intracranial pressure. At age of 11 months, he underwent fronto-orbital advancement

surgery and tonsillectomy. He hadlagopthalmos, exorbitism, epiblepharon, plagiocephaly, and mid-facial hypoplasia. He had morbid obesity (Figure 29).

The patient was in permanent dentition. Oral examination showed Angle Class III malocclusion, overbite about 2 mm, negative overjet about 2 mm, narrowing of maxillary arch, and dental crowding (Figure 30). He had heavy dental biofilm with some tartar, indicating fair oral health. OHI-S score was 2.66, DMFT score was 17, and DMFS score was 37. He manifested talon cusp on tooth 12 and tooth 22. He also expressed extra premolar at the area of upper left canine (tooth 23) (Figure 31).

Figure 29: extraoral frontal view and lateral view of the P-11

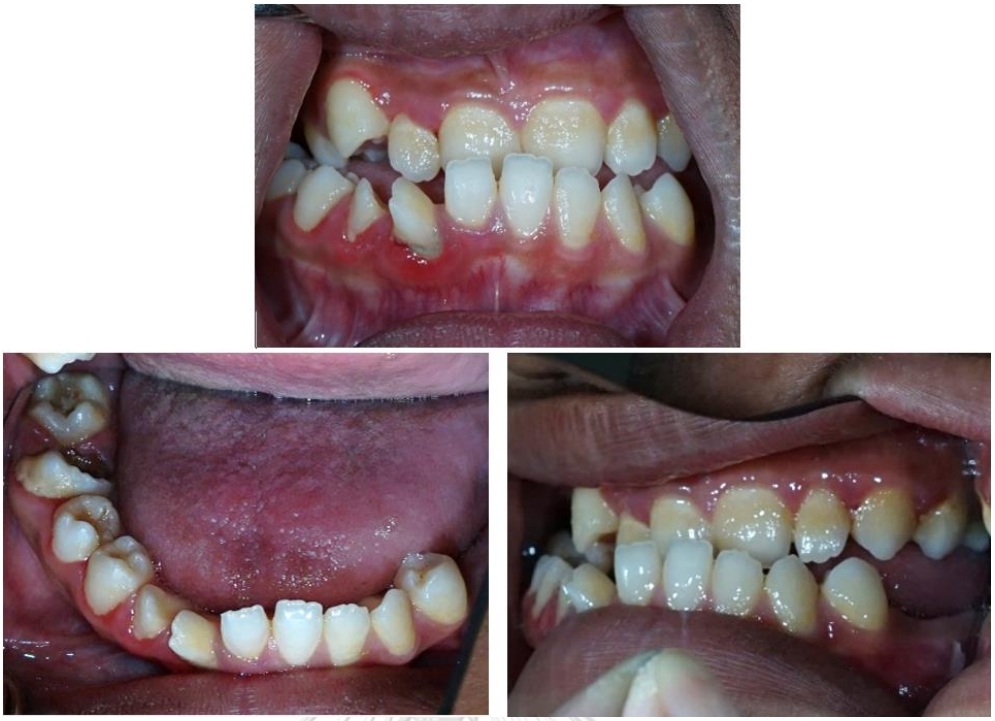


Figure 30: intraoral frontal view, lower view , and lateral view of the P-11

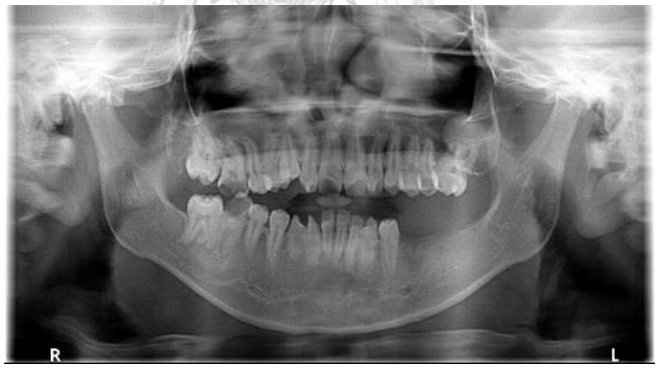


Figure 31: panoramic film of the P-11

Table 2 summarized the patients characteristics and showed that patients and healthy participants had several significant differences, comprising cleft palate (*p*-value=0.006), anterior openbite (*p*-value=0.001), anterior crossbite (*p*-value<0.001), posterior crossbite (*p*-value<0.001), maxillary dental crowding (*p*-value<0.001), mandibular dental crowding (*p*-value<0.001), congenital missing teeth (*p*-value<0.001), failure of tooth eruption (*p*-value<0.001), oral hygiene status (*p*-value=0.003), deft (*p*-value=0.019), DMFT (*p*-value<0.001), defs (*p*-value=0.017), DMFS (*p*-value<0.001),

caries risk assessment (*p*-value<0.001), and maxillomandibular relationship (*p*-value<0.001). However, age, gender and supernumerary teeth were not statistically significant differences between case and control groups.

Table 2: *Patient characteristics according to case and control groups*

Characteristics	Total (N = 43)	Case (N = 13)	Control (N = 30)	*p*-value
Age (year), mean ± SD[b]	10.47 ± 2.88	10.15 ± 2.88	10.60 ± 2.92	0.667
Gender, N (%)[c]				0.766
Male	18 (41.9%)	5 (38.5%)	13 (43.3%)	
Female	25 (58.1%)	8 (61.5%)	17 (56.7%)	
Cleft palate, N (%)[d]	4 (9.3%)	4 (30.8%)	0 (0%)	0.006*
Anterior openbite, N (%)[d]	5 (11.6%)	5 (38.5%)	0 (0%)	0.001*
Anterior crossbite, N (%)[d]	7 (16.3%)	7 (53.8%)	0 (0%)	<0.001*
Posterior crossbite, N (%)[d]	8 (18.6%)	8 (61.5%)	0 (0%)	<0.001*
Dental crowding, N (%)				
Maxillary dental arch[d]	8 (18.6%)	8 (61.5%)	0 (0%)	<0.001*
Mandibular dental arch[d]	6 (14%)	6 (46.2%)	0 (0%)	<0.001*
Congenital missing teeth, N (%) [a,d]	8 (18.6%)	8 (61.5%)	0 (0%)	<0.001*
Supernumerary teeth, N (%) [a,d]	1 (2.3%)	1 (7.7%)	0 (0%)	0.302
Failure of tooth eruption, N (%)[a,d]	6 (14%)	6 (46.2%)	0 (0%)	<0.001*
Oral hygiene status				
OHI-S, mean ± SD[e]	1.55 ± 0.81	2.09 ± 0.88	1.31 ± 0.67	0.003*

Table 2: *Patient characteristics according to case and control groups (continued)*

Characteristics	Total (N = 43)	Case (N = 13)	Control (N = 30)	*p*-value
Caries prevalence				
deft, mean ± SD[b]	2.40 ± 4.10	5.31 ± 5.71	1.13 ± 2.33	0.019*
DMFT, mean ± SD[b]	1.33 ± 3.13	3.85 ± 4.85	0.23 ± 0.63	<0.001*
defs, mean ± SD[b]	5.65 ± 11.48	14.23 ± 17.55	1.93 ± 4.03	0.017*
DMFS, mean ± SD[b]	2.02 ± 6.10	6.15 ± 10.14	0.23 ± 0.63	<0.001*
Caries risk assessment, N (%)[c]				<0.001*
High risk	12 (27.9%)	9 (69.2%)	3 (10%)	
Moderate risk	9 (20.9%)	3 (23.1%)	6 (20%)	
Low risk	22 (51.2%)	1 (7.7%)	21 (70%)	
Maxillomandibular dentition relationship, N (%)[c]				<0.001*
Angle's Class I	32 (74.4%)	5 (38.5%)	27 (90%)	
Angle's Class II	2 (4.7%)	0 (0%)	2 (6.7%)	
Angle's Class III	9 (20.9%)	8 (61.5%)	1 (3.3%)	

*Statistically significant difference ($p<0.05$)

[a]The data collection were derived from panoramic radiographs.

[b]Differences between case and control groups, analyzed by Mann-Whitney U test.

[c]Differences between case and control groups, analyzed by Chi-square test.

[d]Differences between case and control groups, analyzed by Fisher's exact test.

[e]Differences between case and control groups, analyzed by independent *t*-test

Table 3 showed subgroup analyses of CS patients with different Angle's classifications and types of CS. There were no significant differences in both caries prevalence and caries risk assessment between patients with Class III and those with Class I occlusion, and between patients with syndromic CS and those with nonsyndromic CS.

Table 3: *Subgroup analyses of caries prevalence and caries risk assessment according to angle classification and syndromic status of CS patients*

Characteristics	Total case (N = 13)	Angle's class I (N = 5)	Angle's class III (N = 8)	*p*-value
Caries prevalence				
deft, mean ± SD[b]	5.31 ± 5.71	3.00 ± 4.47	6.75 ± 6.18	0.284
DMFT, mean ± SD[a]	3.85 ± 4.85	1.80 ± 1.79	5.13 ± 5.79	0.245
defs, mean ± SD[b]	14.23 ± 17.55	5.20 ± 8.29	19.88 ± 19.85	0.171
DMFS, mean ± SD[b]	6.15 ± 10.14	2.00 ± 2.12	8.75 ± 12.40	0.284
Caries risk assessment, N (%)[c]				0.164
High risk	9 (69.2%)	2 (40%)	7 (87.5%)	
Moderate risk	3 (23.1%)	2 (40%)	1 (12.5%)	
Low risk	1 (7.7%)	1 (20%)	0 (0%)	
Characteristics	Total case (N = 13)	Non-syndromic CS (N = 6)	Syndromic CS (N = 7)	*p*-value
Caries prevalence				
deft, mean ± SD[a]	5.31 ± 5.71	5.17 ± 6.65	5.43 ± 5.32	0.938
DMFT, mean ± SD[a]	3.85 ± 4.85	1.50 ± 1.76	5.86 ± 5.84	0.108
defs, mean ± SD[b]	14.23 ± 17.55	11.33 ± 16.75	16.71 ±19.15	0.534
DMFS, mean ± SD[b]	6.15 ± 10.14	1.67 ± 2.07	10.00 ± 12.83	0.073
Caries risk assessment, N (%)[c]				0.321
High risk	9 (69.2%)	3 (50%)	6 (85.7%)	
Moderate risk	3 (23.1%)	2 (33.3%)	1 (14.3%)	
Low risk	1 (7.7%)	1 (16.7%)	0 (0%)	

*Statistically significant difference ($p<0.05$)

[a]Differences between case and control groups, analyzed by independent t-test

[b]Differences between case and control groups, analyzed by Mann-Whitney U test

[c]Differences between case and control groups, analyzed by Chi-square test

***Table 4** : Intraoral presentations of the patients*

Presentations	Patient-1	Patient-2	Patient-3	Patient-4	Patient-5	Patient-6	Patient-7	Patient-8	Patient-9	Patient-10	Patient-11	Patient-12	Patient-13
Cleft palate	Yes	Yes	Yes	No	No	No	No	No	Yes	No	No	No	No
Anterior openbite	Yes	Yes	Yes	No	No	No	No	Yes	Yes	No	No	No	No
Anterior crossbite	Yes	Yes	Yes	No	No	No	No	Yes	Yes	No	Yes	Yes	No
Posterior crossbite	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	No	Yes	Yes	No
Dental crowding													
- Maxillary dental arch	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	No	Yes	Yes	No
- Mandibular dental arch	No	Yes	Yes	No	No	Yes	Yes	No	No	No	Yes	Yes	No
Congenital missing teeth [a]	No	Yes (15,25)	No	No	Yes (32,42)	No	Yes (13,23)	Yes (13,23)	Yes (13,23)	No	Yes (27)	Yes (14)	Yes (32,42)
Supernumerary teeth [a]	No	No	No	No	No	No	No	Yes	No	No	No	No	No
Failure of tooth eruption[a]	Yes	Yes	Yes	No	No	No	No	Yes	Yes	No	No	Yes	No
Oral hygiene status													
- OHI-S	2.67	2.5	3.34	0.67	1.33	1.5	2.84	3.34	1.33	1	2.66	2	2
Caries prevalence													
- deft	13	9	0	0	0	0	5	10	1	10	0	16	5
- DMFT	0	3	7	0	3	0	1	4	9	2	17	0	4
- defs	29	27	0	0	0	0	9	50	2	19	0	42	7
- DMFS	0	4	7	0	3	0	2	5	15	2	37	0	5
Caries risk assessment	High	High	High	Low	Moderate	Low	High	High	High	High	High	High	High
Maxillomandibular dentition relationship - Angle's classification	Class III	Class III	Class III	Class I	Class I	Class I	Class III	Class III	Class III	Class I	Class III	Class III	Class I

[a]From panoramic radiograph

Part 2: Lateral Cephalometric Analysis

From ABO cephalometric analysis, the measurements that patients significantly differed from Thai normative values were SNA [(°), *p*-value=0.002], ANB [(°), *p*-value=0.004], Wits [(mm), *p*-value=0.009], FMA [(°), *p*-value=0.012], IMPA [(°), *p*-value<0.001], L1-NB [(°), *p*-value=0.003], and U1-NA [(mm), *p*-value=0.039]. The data wasshowed in Table 5.

Table 6 demonstrated the data of Rickett's analysis, maxillary depth [(°), *p*-value=0.009] together with convexity of point A [(mm), *p*-value<0.001], mandibular arc [(°), *p*-value<0.001], posterior facial height [(°), *p*-value=0.002], and U1 to APog [(mm), *p*-value=0.021] in the patients were statistically differed from Thai norms.

Table 5: *Comparison of ABO Cephalometric Analysis between case group and Thai normative values*

Measurements	Case (N = 13)		Thai normative value[a]		*p*-value[b]
	Mean	SD	Mean	SD	
SNA (°)	72.29	9.46	83	4	0.002*
SNB (°)	79.19	3.92	79	3	0.863
NPog-FH (°)	86.71	3.32	85	2	0.087
ANB (°)	-6.90	11.01	4	2	0.004*
Wits (mm)	-11.67	10.00	-3	2	0.009*
SN-GoGn (°)	36.50	8.55	34	6	0.313
FMA (°)	31.71	8.16	25	4	0.012*
IMPA (°)	86.40	8.62	99	4	<0.001*
L1-APog (mm)	6.79	5.30	5	2	0.247
L1-NB (°)	25.31	6.42	32	6	0.003*
L1-NB (mm)	4.71	2.71	6	2	0.112

Table 5 *: Comparison of ABO Cephalometric Analysis between case group and Thai normative values (continued)*

Measurements	Case (N = 13)		Thai normative value[a]		*p*-value[b]
	Mean	SD	Mean	SD	
U1-NA (°)	36.54	17.89	28	4	0.111
U1-NA (mm)	9.48	5.40	6	2	0.039*
U1-L1 (°)	124.71	12.86	118	8	0.084
E-line (mm)	3.10	3.28	3.50	2	0.665

*Statistically significant difference ($p<0.05$)

[a]The Thai normative values were derived from Sorathesn, 1988 (70)

[b]Differences between case group and Thai normative values, analyzed by one-sample *t*-test.

Table 6: *Comparison of Rickett's Cephalometric Analysis between case group and Thai normative values*

Measurements	Case (N = 13)		Thai normative value[a]		*p*-value[b]
	Mean	SD	Mean	SD	
Maxillary depth (°)	80.04	11.93	90.3	3.3	0.009*
Convexity of point A (mm)	-4.35	6.80	4.5	2.3	<0.001*
Cranial deflection (°)	28.52	2.85	28.7	1.6	0.823
Mandibular plane angle (°)	31.69	8.12	29.5	4.9	0.350
Mandibular arc (°)	44.96	7.24	31.1	4.1	<0.001*
Lower face height (°)	52.15	15.39	47.9	3.2	0.339
Facial axis (°)	84.69	4.58	84.7	3.0	0.995
Posterior facial height (°)	48.44	5.91	55	3.3	0.002*
U1 to APog (mm)	5.06	3.31	7.5	2.2	0.021*
L1 to APog (°)	29.06	8.96	27.3	4.8	0.493
Lower lip to E-line (mm)	3.12	3.30	3.6	1.8	0.606

*Statistically significant difference ($p<0.05$)

[a]The Thai normative values were derived from Sorathesn, 1988(70).

[b]Differences between patient group and Thai normative values, analyzed by one-sample t-test.

Part 3: Masticatory performances and masticatory ability of the patients

The chewed gum from thirteen patients were scanned by Brother MFC-J2330DW Multifunction Inkjet Printer and Scanner within the same day of chewing (Figure 32). The ViewGum© software was used to evaluate the gum (Figure 33). The variance of hue (VOH) of each participant was measured for three times. The mean (± SD) of VOH of the two-color chewing gum mixing ability test score represented masticatory performance.

The mean (± SD) score of the patients was 0.12 ± 0.06 and the mean (± SD) score of the control group was 0.06 ± 0.04. Hence, there were significant differences between patient and control groups in masticatory performance (*p*-value<0.001).

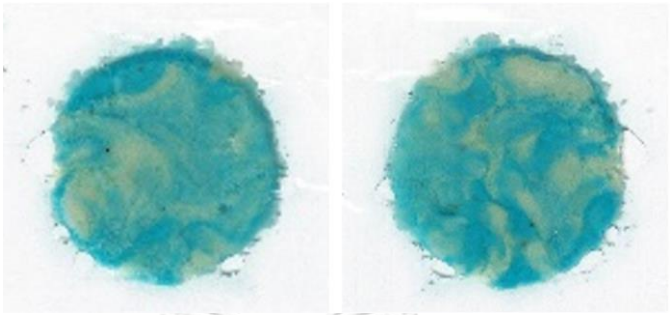


Figure 32: Examples of the scanned chewing gum

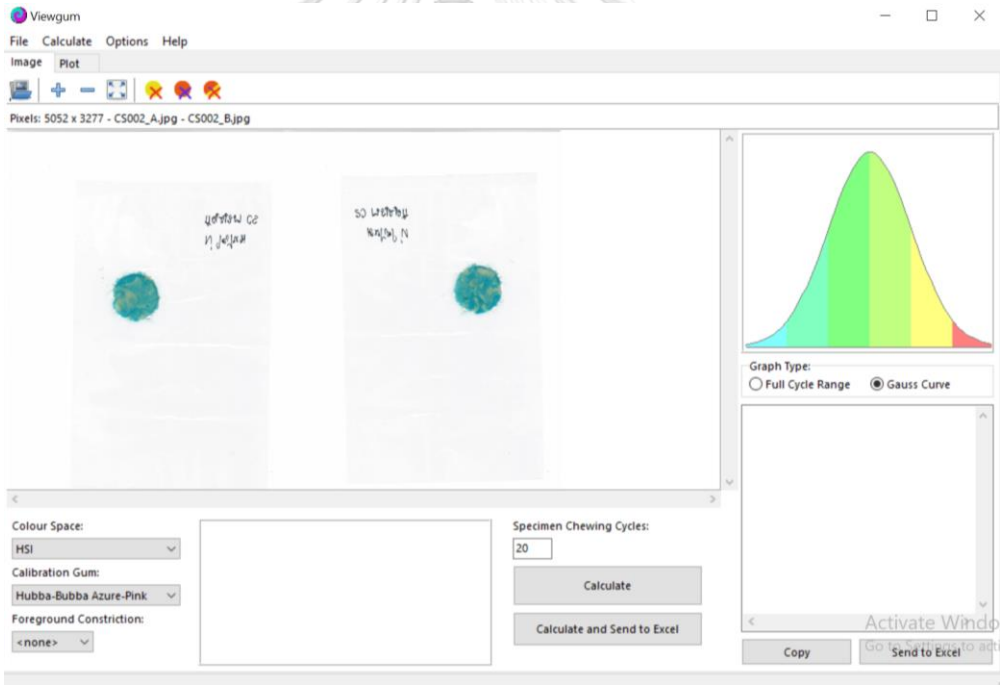


Figure 33: Illustration of ViewGum© software

The food intake ability self-assessment questionnaire (FIA test) was used to assess the masticatory ability of the patients and the control groups. The results of both the patients and the control showed in median with interquartile range (IQR). In case group, FIA test score was 5 (5-5) for soft tofu, 5 (5-5) for watermelon, 5 (4-5) for

ham, 4 (3-5) for apple, 4 (2-5) for cookie, and 4 (2.5-5) for peanut. In control group, FIA test score was 5 (5-5) for soft tofu, 5 (5-5) for watermelon, 5 (5-5) for ham, 5 (5-5) for apple, 5 (5-5) for cookie, and 5 (5-5) for peanut. As demonstrated in table X, the food that had significant difference in masticatory ability between case and control groups were ham (*p*-value=0.026), apple (*p*-value=0.002), cookie (*p*-value<0.001), and peanut (*p*-value=0.001) (Table 7).

Table 7: *Masticatory performance and masticatory ability of the patients according to case and control groups*

Masticatory performance and masticatory ability	Case (N = 13)	Control (N = 30)	*p*-value[a]
Masticatory performance			
The two-color chewing gum mixing ability test score (Variance of the hue), mean ± SD	0.12 ± 0.06	0.06 ± 0.04	<0.001*
The Food Intake Ability (FIA test)			
Soft Tofu, median (IQR)	5 (5-5)	5 (5-5)	1.000
Watermelon, median (IQR)	5 (5-5)	5 (5-5)	0.824
Ham, median (IQR)	5 (4-5)	5 (5-5)	0.026*
Apple, median (IQR)	4 (3-5)	5 (5-5)	0.002*
Cookie, median (IQR)	4 (2-5)	5 (5-5)	<0.001*
Peanut, median (IQR)	4 (2.5-5)	5 (5-5)	0.001*

*Statistically significant difference ($p<0.05$).

[a]Differences between case and control groups, analyzed by Mann-Whitney U test.

CHAPTER V
DISCUSSION

This study reported cranio-oro-facial characteristics and masticatory functions of thirteen Thai craniosynostosis (CS) patients compared with 30 healthy individuals at the ages of 6-17 years. The cephalometric features of CS patients were also compared with Thai norms. The clinical diagnosis of the patients in this study comprised Apert syndrome, Multiple sutures craniosynostosis, Right coronal craniosynostosis, and Crouzon syndrome.

The Thai CS patients showed certain features including cleft palate, anterior openbite, anterior-posterior crossbite, maxillary-mandibular dental crowding, congenital missing teeth, failure of tooth eruption, poor oral hygiene status, high dental caries prevalence, high caries risk, and abnormal maxillomandibular relationship, different from Thai healthy children. Only the supernumerary teeth feature was not significantly different between CS patients and controls. It is possible that the supernumerary teeth are observed mainly in syndromic CS patients(73) or patients with specific gene mutations(74).

According to the 8th Thai national oral health survey (2017), most CS patients had higher caries prevalence than general Thai children at the same age. This finding is correlate with many previous studies(75-77). Here, we observed several factors that make the CS patient prone to food debris deposition including cleft palate, anterior openbite, anterior crossbite, posterior crossbite, and dental crowding, resulting in difficulty in oral hygiene care. The CS patients also had other dentofacial abnormalities such as midface hypoplasia, maxillary constriction, and facial imbalance that increase risk of developing dental cavities and gingival inflammation. Regarding periodontal aspect, the OHI-S scores of CS patients were significantly higher than those in healthy children and also higher than scores reported in the Thai national oral health survey (2017). These can be postulated that the CS patients are prone to have poor oral hygiene which consistent with previous studies(10, 78). Obstacles in oral cleaning

mentioned by patients and care givers include abnormal facial anatomy, small mouth, tooth crowding, and risk of aspiration. Based on the above finding, oral hygiene instructions and vigilant dental check-ups should be provided to all CS patients and their guardians.

Apert syndrome (AS)

In this study, there are 4 patients with AS: P-1, P-2, P-3, and P-9. The AS patients shared common features including syndactyly, maxillary hypoplasia, exorbitism, hypertelorism, OSA, and low IQ score. Both P-1 and P-9 had hearing loss and otitis media that needed myringotomy surgery. All patients underwent FOA surgery when they were infant to correct the shape of cranial vault. From intraoral examinations, cleft palate, anterior openbite, anterior-posterior crossbite, dental crowding, failure of tooth eruption, high caries risk and Class III malocclusion were observed in all patients, suggesting that the AS patients have multiple orodental anomalies that might obstruct oral hygiene care. AS patients manifested gingival inflammation with dental plaque accumulation and multiple decayed teeth, corresponding with previous reports. Multidisciplinary care is strongly recommended(40, 73, 79).

Multiple sutures craniosynostosis

P-4, P-10, P-12, and P-13 are nonsyndromic multiple sutures craniosynostosis (MCS) patients who received FOA and cranial remodeling surgeries. These patients showed diverse features. P-10, P-12, and P-13 had multiple dental caries while P-4 had none. Only P-12 presented Class III malocclusion with anterior-posterior crossbite and mild facial retrusion while others had Class I Angle's classification with normal facial profile. Most of MCS patients (P-10, P-12, and P-13) had normal development, consistent with previous study(80), except P-4 who showed delayed milestone and enuresis.

Right coronal craniosynostosis

The patients with right coronal suture craniosynostosis were P-5 and P-6. They presented Class I occlusion without palatal cleft, supernumerary tooth, anterior openbite, anterior crossbite, and posterior crossbite. P-5 had right plagiocephaly which

commonly occurred in unilateral coronal synostosis patients and affected cognitive function(81). A previous study reported that normally isolated CS patients had more decayed teeth(82), consistent with P-5, but not P-6 who was caries-free.

Crouzon syndrome

Patients with crouzon syndrome were P-7, P-8, and P-11. The common features of these patients were class III malocclusion, posterior crossbite, poor oral hygiene, high risk of carious lesions, and having missing teeth that similar to previous reports(83, 84). P-8 had more severe condition than P-7 and P-11 including hydrocephalus, on tracheostomy tube, moderate intellectual disability, anterior openbite-crossbite, supernumerary teeth, and failure of tooth eruption. P-11 was the only patient that had obesity while others having malnutrition problems.

From ABO Cephalometric Analysis, SNA and maxillary depth showed the position of the maxilla in anteroposterior plane while SNB and NPog-FH revealed the position of the mandible in anteroposterior plane. The relationship between maxilla and mandible indicated by maxilla-mandible sagittal relationship (ANB and Wits) showed that most patients had skeletal and dental Class III. SNA, ANB and Wits of the patients were lower than Thai norms. Therefore, in antero-posterior aspect, the maxilla was underdeveloped while the mandible showed normal development. The earlier study(85) also reported that Apert and Crouzon patients had normal mandibular growth. We observed that the FMA of the patients that was greater than Thai norms might be because of difficulty in setting of the natural head position of the patients (parallel to Frankfort horizontal plane). As a result, the patients tend to have more skeletal openbite than normal. Due to skeletal Class III of the patients, the lower anterior teeth are likely to retroclined in order to compensate the occlusion. Meanwhile, the upper anterior teeth tend to procline more than Thai norms which may cause by the posterior position of the Nasion and point A.

According to Ricketts' Cephalometric Analysis, we discovered that the position of point A of the patients was located posteriorly than usual. The underdeveloped

maxilla can produce inferior value of convexity of point A than Thai norms. In vertical dimension, the angle between condylar process and body of mandible (Mandibular arc) together with the angle between Xi-ANB and Xi-PM (Posterior facial height) were different from Thai normal values. It can explain that the mandible of the patients grows in the direction more forward than downward. Thus, the patients are prone to have more retroclined upper anterior teeth when compared with maxillomandibular position while the teeth are more proclined when compared with cranial base.

The masticatory performances can be evaluated with several methods including the comminution test which is considered as a gold standard(86), color-changeable chewing gum(87), and two-color chewing gum mixing ability test. We selected the two-color chewing gum mixing ability test because of the high reliability, validity, and feasibility of the test, shown in previous studies(50, 55, 72). There are some other advantages of the test. For example. many children were familiar with bubble gum than paraffin wax or silicone so the results tend to be more accurate than comminution test in children and special patients, and the Hubba-Bubba Tape Gums are effortlessly obtainable than color-changeable chewing gum which is available only in some countries. However, this test has some disadvantages. The Hubba-Bubba Tape Gum is not a sugar-free gum hence water rinsing is recommended after chewing to prevent dental demineralization, and the test may be impracticable in severe syndromic patients who have dysphagia conditions and high risk of aspiration.

The masticatory ability is a subjective assessment using the food intake ability (FIA) test. The FIA scores of ham, apple, cookie, and peanut were significantly lower in CS patients. Apple, cookie, and peanut were considered as hard foods while ham as soft food. These imply that the CS patients have more attempt to chew hard food, corresponding with the previous study reporting patients with malocclusion(88). However, participants in this study were children and adolescences so the subjective evaluation process may need to be more vigilant to avoid misunderstandings between mastication ability and food preference.

The limitations of this study include: 1) the patients was limited to those who received treatments at the King Chulalongkorn Memorial Hospital. The craniofacial characteristics and oral manifestations of these patients might differ from the patients who had treatments elsewhere or with other nationalities; 2) the number of sample size in this study was limited due to rarity of CS; 3) difficulty and time consuming in obtaining data from the patients ; 4) masticatory performance and masticatory ability might reflex only some aspects of the masticatory functions of the patients. A complete assessment of masticatory process should be performed in future studies.

Further genetic investigations, multi-centered studies, and a larger number of sample size are required in the future studies to fulfil all the gaps of knowledge about CS patients.

CHAPTER VI

CONCLUSION

CS patients exhibit unique cranio-oro-facial features, lateral cephalometric data, and masticatory functions. Cleft palate, anterior openbite, anterior crossbite, posterior crossbite, maxillary dental crowding, mandibular dental crowding, congenital missing teeth, failure of tooth eruption, oral hygiene status, deft, DMFT, defs, DMFS, caries risk, maxillomandibular relationship, masticatory performance and masticatory ability in the CS patients were significantly different from normal.

The ABO Analysis viz SNA, ANB, wits, FMA, IMPA, L1-NB, and U1-NA together with the data of Rickett's analysis including maxillary depth, convexity of point A, mandibular arc, posterior facial height and U1 to APog in the CS patients showed significantly differences from Thai norms.

The CS patients are prone to have higher susceptibilities to orodenal diseases and masticatory difficulties than healthy people. A multidisciplinary team is required to provide comprehensive treatment for the patients and the dentist should deliver vigilant oral hygiene care to the patients and caregivers. Regular dental check-ups are necessary for the CS patients to prevent orodental diseases and promote optimal oral and medical health.

APPENDIX

Table 8: *Lateral cephalometric measurements (mean) ABO Analysis of the CS patients*

Measurements	Thai norm	Range	Patient-1	Patient-2	Patient-3	Patient-4	Patient-5	Patient-6	Patient-7	Patient-8	Patient-9	Patient-10	Patient-11	Patient-12	Patient-13
ABO* format															
- SNA	83 ± 4	79 – 87	63.25	71.75	81.5	79.5	82.5	84	65.5	61	57.75	84.5	63.5	73.75	71.25
- SNB	79 ± 3	76 – 82	80.75	80.25	82.5	81.75	77	81	78.5	85.25	84	77	75.5	73	73
- NPog-FH	85 ± 2	83 – 87	82.25	90.25	86	85	88.75	91.25	82.25	89	84	90	82	87.5	89
- ANB	4 ± 2	2 – 6	-17.5	-8.5	-1	-2.25	5.5	3	-13	-24.25	-26.25	7.5	-12	0.75	-1.75
- Wits (mm)	-3 ± 2	(-5) – (-1)	-24.5	-12.25	-5.75	-6.5	-0.25	-7.25	-12.75	-27.5	-30.25	-1	-14.75	-4	-5
- SN-GoGn	34 ± 6	28 – 40	49	40	26	28	25	31.5	30.5	38	42.75	40.5	44.5	49.25	29.5
- FMA	25 ± 4	21 – 29	45.5	32.5	27.5	30.5	19	24.25	24.75	37.5	43.25	30	38.5	36.5	22.5
- IMPA	99 ± 4	95 – 103	74.75	75.75	90.25	100.5	96.5	93.75	91.5	89.25	74.5	90.5	85	78.5	82.5
- L1-APog (mm)	5 ± 2	3 – 7	11	7.5	2.75	10.25	0.25	4	8.25	13	13.5	2	14	3	-1.25
- L1-NB	32 ± 6	26 – 38	25	20	22.5	36	22.25	30	21	35.25	23	30	27	24.5	12.5
- L1-NB (mm)	6 ± 2	4 – 8	4	4.5	4	9.75	3	6	2.5	8	5.5	5	7	3	-1
- U1-NA															
- U1-NA (mm)	28 ± 4	24 – 32	43	31	20.5	43	40.5	21.5	49.5	69.5	53.5	0	40	19.5	43.5
- U1-L1	6 ± 2	2 – 8	7	6.5	3	15	6	3.25	12.5	17	19	8.5	13	3	9.5
- E-line (mm)															
	118 ± 8	110 – 126	129	138.5	137.5	103.25	111.5	128	121.25	99	130.25	135	125.25	137.25	125.5
	3.5 ± 2	1.5 – 5.5	6.5	1.5	2.75	7	0.75	3	2.25	5.25	6.75	1.75	6.75	0	-4

*American Board of Orthodontics

Table 9: *Lateral cephalometric measurements (mean) Rickett's Analysis of the CS patients*

Measurements	Thai norm	Range	Patient-1	Patient-2	Patient-3	Patient-4	Patient-5	Patient-6	Patient-7	Patient-8	Patient-9	Patient-10	Patient-11	Patient-12	Patient-13
Ricketts's Analysis															
- Ant cranial base	54.7 ± 2.7(9 y)	52.0 - 57.4	44 (9 y)				48 (9 y)	39.5 (7 y)	46 (9 y)	44 (9 y)		41.5 (6 y)		39 (6 y)	51 (7 y)
length (SN-FH)	55.2 ± 2.7 (10 y)	52.5 - 57.9		40.75 (10 y)											
	56.2 ± 2.7 (12 y)	53.5 – 58.9									45.5 (12 y)				
	56.7 ± 2.7 (13 y)	54.0 - 59.4											50 (13 y)		
	57.2 ± 2.7 (14 y)	54.5 - 59.9				54.75 (14 y)									
	57.7 ± 2.7 (15 y)	55.0 - 60.4			38.5 (15 y)										
- Maxillary depth	90.3 ± 3.3	87.0 - 93.6	67.5	81	84	82.5	92.75	94	71.5	65	60	97	71.25	89	85
- Facial depth	85.0 ± 3.2 (9 y)	81.8 - 88.2	82.25 (9 y)				88.75 (9 y)	91.25 (7 y)	46 (9 y)	89 (9 y)		90 (6 y)		87.5 (6 y)	89 (7 y)
	85.3 ± 3.2 (10 y)	82.1 - 88.5		90.25 (10 y)											
	86.0 ± 3.2 (12 y)	82.8 - 89.2									84 (12 y)				
	86.3 ± 3.2 (13 y)	83.1 - 89.5											82 (13 y)		
	86.7 ± 3.2 (14 y)	83.5 - 89.9				85 (14 y)									
	87.0 ± 3.2 (15 y)	83.8 - 90.2			86 (15 y)										
- Convexity of point A	4.5 ± 2.3	2.2 - 6.8	-8.5	-6	-0.5	-2	3	2	-7	-15	-16.5	6	-9	0.5	-3.5
- Cranial deflection	28.7 ± 1.6	27.1 - 30.3	25.75	32	29	23.75	28.5	31.5	30	31.5	23.5	30	26.25	30	29
- Mandibular plane	29.5 ± 4.9	24.6 - 34.4	45	32.5	27.5	30.5	19	24.25	24.75	37.5	43.5	30	38.5	36.5	22.5
angle															
- Mandibular arc	31.1 ± 4.1	27.0 - 35.2	43.5	48	44.75	51.5	58	46	55.5	44	33	38	39	37	46.25
- Lower face height	47.9 ± 3.2	44.7 - 51.1	74.5	59	45	38	27.75	45	46	74	78.25	47	51	53.5	39
- Facial axis	84.7 ± 3.0	81.7 - 87.7	77.75	80	85	89.5	91.75	83.5	83.5	83	85.5	85	83	80	93.5
- Posterior facial height	55.0 ± 3.3	51.7 - 58.3	51.5	49	43.5	61.25	51.5	51	45	41.5	49.75	40	51	41.75	53
- U6 to PTV (mm)	10.9 ± 2 (9 y)	8.9 - 12.9	-0.5 (9 y)				11 (9 y)	9.25 (7 y)	3.5 (9 y)	13 (9 y)		15.25 (6 y)		1 (6 y)	9.75 (7 y)
	11.8 ± 2 (10 y)	9.8 - 13.8		8 (10 y)											
	13.6 ± 2 (12 y)	11.6 - 15.6									5.5 (12 y)				
	14.5 ± 2 (13 y)	12.5 - 16.5											2.75 (13 y)		
	15.4 ± 2 (14 y)	13.4 - 17.4				85 (14 y)									
	16.3 ± 2 (15 y)	14.3 - 18.3			5.75 (15 y)										

Table 9: *Lateral cephalometric measurements (mean) Rickett's Analysis of the CS patients (continued)*

Measurements	Thai norm	Range	Patient-1	Patient-2	Patient-3	Patient-4	Patient-5	Patient-6	Patient-7	Patient-8	Patient-9	Patient-10	Patient-11	Patient-12	Patient-13
Ricketts's Analysis															
- U1 to APog (mm)	7.5 ± 2.2	5.3 - 9.7	0.25	1	3	13	8	5	5	7	3	5.25	5.25	3	7
- L1 to APog (mm)	3.8 ± 1.9 (9 y)	1.9 - 5.7	11.25 (9 y)				0.25 (9 y)	4 (7 y)	8 (9 y)	12.75 (9 y)		2 (6 y)		3 (6 y)	-1.25 (7 y)
	4.0 ± 1.9 (10 y)	2.1 - 5.9		7.5 (10 y)											
	4.4 ± 1.9 (12 y)	2.5 - 6.3									13.5 (12 y)				
	4.6 ± 1.9 (13 y)	2.7 - 6.5											14 (13 y)		
	4.8 ± 1.9 (14 y)	2.9 - 6.7				10.25 (14 y)									
	5.0 ± 1.9 (15 y)	3.1 - 6.9			2.75 (15 y)										
- L1 to APog	27.3 ± 4.8	22.5 - 32.1	29	25.75	24	38.5	19.5	27.25	28.5	49.75	37	20.5	35.75	23	19.25
- Lower lip to E-line (mm)	3.6 ± 1.8	1.8 - 5.4	6.5	1.5	2.75	7	0.75	3	2.25	5.25	7	1.75	6.75	0	-4

Table 10: *Masticatory performance of the CS patients*

Patients	The two-color chewing gum mixing ability test score (Variance of the hue)
Patient-1	0.14
Patient-2	0.19
Patient-3	0.15
Patient-4	0.07
Patient-5	0.12
Patient-6	0.07
Patient-7	0.14
Patient-8	0.21
Patient-9	0.17
Patient-10	0.07
Patient-11	0.13
Patient-12	0.06
Patient-13	0.03
Total (The mean ± SD)	0.12 ± 0.06

Table 11: *Masticatory ability of the CS patients*

Patients	The Food Intake Ability (FIA test)					
	Soft Tofu	**Watermelon**	**Ham**	**Apple**	**Cookie**	**Peanut**
Patient-1	5	5	4	3	3	3
Patient-2	5	5	5	4	4	4
Patient-3	5	5	4	5	5	5
Patient-4	5	5	5	5	5	4
Patient-5	5	5	5	5	5	5
Patient-6	5	5	5	5	5	4
Patient-7	5	4	4	3	4	2
Patient-8	5	5	3	3	2	1
Patient-9	5	5	5	4	1	5
Patient-10	5	5	5	1	1	1
Patient-11	5	5	4	4	4	4
Patient-12	5	5	5	5	4	3
Patient-13	5	5	4	3	2	5
Total Median (IQR)	5 (5-5)	5 (5-5)	5 (4-5)	4 (3-5)	4 (2-5)	4 (2.5-5)

REFERENCES

1. Greig AV, Wagner J, Warren SM, Grayson B, McCarthy JG. Pfeiffer syndrome: analysis of a clinical series and development of a classification system. J Craniofac Surg. 2013;24(1):204-15.

2. Carinci F, Pezzetti F, Locci P, Becchetti E, Carls F, Avantaggiato A, et al. Apert and Crouzon syndromes: clinical findings, genes and extracellular matrix. J Craniofac Surg. 2005;16(3):361-8.

3. Speltz ML, Kapp-Simon KA, Cunningham M, Marsh J, Dawson G. Single-suture craniosynostosis: a review of neurobehavioral research and theory. J Pediatr Psychol. 2004;29(8):651-68.

4. Boulet SL, Rasmussen SA, Honein MA. A population-based study of craniosynostosis in metropolitan Atlanta, 1989-2003. Am J Med Genet A. 2008;146a(8):984-91.

5. Cornelissen M, Ottelander B, Rizopoulos D, van der hulst R, Molen A, Horst C, et al. Increase of prevalence of craniosynostosis. Journal of Cranio-Maxillofacial Surgery. 2016;44.

6. Lajeunie E, Le Merrer M, Bonaiti-Pellie C, Marchac D, Renier D. Genetic study of nonsyndromic coronal craniosynostosis. Am J Med Genet. 1995;55(4):500-4.

7. Betances EM, Mendez MD, J MD. Craniosynostosis. StatPearls. Treasure Island (FL)2019.

8. Singer S, Bower C, Southall P, Goldblatt J. Craniosynostosis in Western Australia, 1980-1994: a population-based study. Am J Med Genet. 1999;83(5):382-7.

9. Dangsomboon A, Jirapaet V. Experiences of Caregivers Having Children with Craniosynostosis Using Distractor Devices. Journal of Health Research. 1970;31(2):119-26.

10. Vilan Xavier AC, Pinto Silva LC, Oliveira P, Villamarim Soares R, de Almeida Cruz R. A review and dental management of persons with craniosynostosis anomalies. Spec Care Dentist. 2008;28(3):96-100.

11. Vargervik K, Rubin MS, Grayson BH, Figueroa AA, Kreiborg S, Shirley JC, et al. Parameters of care for craniosynostosis: dental and orthodontic perspectives. Am J Orthod Dentofacial Orthop. 2012;141(4 Suppl):S68-73.

12. Katsianou MA, Adamopoulos C, Vastardis H, Basdra EK. Signaling mechanisms implicated in cranial sutures pathophysiology: Craniosynostosis. BBA Clin. 2016;6:165-76.

13. Mishina Y, Snider TN. Neural crest cell signaling pathways critical to cranial bone development and pathology. Exp Cell Res. 2014;325(2):138-47.

14. Couly GF, Coltey PM, Le Douarin NM. The triple origin of skull in higher vertebrates: a study in quail-chick chimeras. Development. 1993;117(2):409-29.

15. Yoshida T, Vivatbutsiri P, Morriss-Kay G, Saga Y, Iseki S. Cell lineage in mammalian craniofacial mesenchyme. Mech Dev. 2008;125(9-10):797-808.

16. Opperman LA. Cranial sutures as intramembranous bone growth sites. Dev Dyn. 2000;219(4):472-85.

17. Wilkie AO. Craniosynostosis: genes and mechanisms. Hum Mol Genet. 1997;6(10):1647-56.

18. D'Antoni AV, Donaldson OI, Schmidt C, Macchi V, De Caro R, Oskouian RJ, et al. A comprehensive review of the anterior fontanelle: embryology, anatomy, and clinical considerations. Childs Nerv Syst. 2017;33(6):909-14.

19. Shibazaki-Yorozuya R, Wang Q, Dechow PC, Maki K, Opperman LA. Changes in biomechanical strain and morphology of rat calvarial sutures and bone after Tgf-beta3 inhibition of posterior interfrontal suture fusion. Anat Rec (Hoboken). 2012;295(6):928-38.

20. Opperman LA, Passarelli RW, Morgan EP, Reintjes M, Ogle RC. Cranial sutures require tissue interactions with dura mater to resist osseous obliteration in vitro. J Bone Miner Res. 1995;10(12):1978-87.

21. Oppenheimer AJ, Rhee ST, Goldstein SA, Buchman SR. Force-induced craniosynostosis in the murine sagittal suture. Plastic and reconstructive surgery. 2009;124(6):1840-8.

22. Ulgen M, Baran S, Kaya H, Karadede I. The influence of the masticatory hypofunction on the craniofacial growth and development in rats. Am J Orthod Dentofacial Orthop. 1997;111(2):189-98.

23. Kajdic N, Spazzapan P, Velnar T. Craniosynostosis - Recognition, clinical characteristics, and treatment. Bosn J Basic Med Sci. 2018;18(2):110-6.

24. Reardon W. Craniosynostosis. Diagnosis, evaluation and management. J Med Genet. 2000;37(9):727.

25. Hermann CD, Hyzy SL, Olivares-Navarrete R, Walker M, Williams JK, Boyan BD, et al. Craniosynostosis and Resynostosis: Models, Imaging, and Dental Implications. J Dent Res. 2016;95(8):846-52.

26. Speltz ML, Collett BR, Wallace ER, Starr JR, Cradock MM, Buono L, et al. Intellectual and academic functioning of school-age children with single-suture craniosynostosis. Pediatrics. 2015;135(3):e615-23.

27. Sharma RK. Craniosynostosis. Indian J Plast Surg. 2013;46(1):18-27.

28. Barik M, Bajpai M, Das RR, Panda SS. Study of environmental and genetic factors in children with craniosynostosis: A case-control study. J Pediatr Neurosci. 2013;8(2):89-92.

29. Lenton KA, Nacamuli RP, Wan DC, Helms JA, Longaker MT. Cranial suture biology. Curr Top Dev Biol. 2005;66:287-328.

30. Moosa S, Wollnik B. Altered FGF signalling in congenital craniofacial and skeletal disorders. Semin Cell Dev Biol. 2016;53:115-25.

31. Johnson D, Wilkie AOM. Craniosynostosis. Eur J Hum Genet. 2011;19(4):369-76.

32. Azoury SC, Reddy S, Shukla V, Deng C-X. Fibroblast Growth Factor Receptor 2 (FGFR2) Mutation Related Syndromic Craniosynostosis. Int J Biol Sci. 2017;13(12):1479-88.

33. Kress W, Schropp C, Lieb G, Petersen B, Busse-Ratzka M, Kunz J, et al. Saethre-Chotzen syndrome caused by TWIST 1 gene mutations: functional differentiation from Muenke coronal synostosis syndrome. Eur J Hum Genet. 2006;14(1):39-48.

34. Chun K, Teebi AS, Jung JH, Kennedy S, Laframboise R, Meschino WS, et al. Genetic analysis of patients with the Saethre-Chotzen phenotype. Am J Med Genet. 2002;110(2):136-43.

35. Twigg SR, Matsumoto K, Kidd AM, Goriely A, Taylor IB, Fisher RB, et al. The origin of EFNB1 mutations in craniofrontonasal syndrome: frequent somatic mosaicism and explanation of the paucity of carrier males. Am J Hum Genet. 2006;78(6):999-1010.

36. Passos-Bueno MR, Sertie AL, Jehee FS, Fanganiello R, Yeh E. Genetics of craniosynostosis: genes, syndromes, mutations and genotype-phenotype correlations. Front Oral Biol. 2008;12:107-43.

37. Slater BJ, Lenton KA, Kwan MD, Gupta DM, Wan DC, Longaker MT. Cranial sutures: a brief review. Plast Reconstr Surg. 2008;121(4):170e-8e.

38. Derderian C, Seaward J. Syndromic craniosynostosis. Semin Plast Surg. 2012;26(2):64-75.

39. Kyprianou C, Chatzigianni A. Crouzon Syndrome: a Comprehensive Review. Balkan Journal of Dental Medicine. 2018;22.

40. López-Estudillo AS, Rosales-Bérber MA, Ruiz-Rodríguez S, Pozos-Guillén A, Noyola-Frías MÁ, Garrocho-Rangel A. Dental approach for Apert syndrome in children: a systematic review. Medicina oral, patologia oral y cirugia bucal. 2017;22(6):e660-e8.

41. Chokdeemboon C, Mahatumarat C, Rojvachiranonda N, Tongkobpetch S, Suphapeetiporn K, Shotelersuk V. FGFR1 and FGFR2 mutations in Pfeiffer syndrome. J Craniofac Surg. 2013;24(1):150-2.

42. Vogels A, Fryns JP. Pfeiffer syndrome. Orphanet J Rare Dis. 2006;1:19.

43. Cunningham M, Seto M, Ratisoontorn C, Heike C, Hing A. Syndromic craniosynostosis: from history to hydrogen bonds. Orthodontics & Craniofacial Research. 2007;10(2):67-81.

44. Doherty ES, Lacbawan F, Hadley DW, Brewer C, Zalewski C, Kim HJ, et al. Muenke syndrome (FGFR3-related craniosynostosis): expansion of the phenotype and review of the literature. Am J Med Genet A. 2007;143a(24):3204-15.

45. Mustafa D, Lucas VS, Junod P, Evans R, Mason C, Roberts GJ. The dental health and caries-related microflora in children with craniosynostosis. Cleft Palate Craniofac J. 2001;38(6):629-35.

46. Rowlerson A, Raoul G, Daniel Y, Close J, Maurage CA, Ferri J, et al. Fiber-type differences in masseter muscle associated with different facial morphologies. Am J Orthod Dentofacial Orthop. 2005;127(1):37-46.

47. Knight SJ, Anderson VA, Spencer-Smith MM, Da Costa AC. Neurodevelopmental outcomes in infants and children with single-suture craniosynostosis: a systematic review. Dev Neuropsychol. 2014;39(3):159-86.

48. Garrocho-Rangel A, Manriquez-Olmos L, Flores-Velazquez J, Rosales-Berber MA, Martinez-Rider R, Pozos-Guillen A. Non-syndromic craniosynostosis in children: Scoping review. Med Oral Patol Oral Cir Bucal. 2018;23(4):e421-e8.

49. Martini M, Wiedemeyer V, Heim N, Messing-Junger M, Linsen S. Bite force and electromyography evaluation after cranioplasty in patients with craniosynostosis. Oral Surg Oral Med Oral Pathol Oral Radiol. 2017;124(6):e267-e75.

50. Schimmel M, Christou P, Miyazaki H, Halazonetis D, Herrmann FR, Muller F. A novel colourimetric technique to assess chewing function using two-coloured specimens: Validation and application. J Dent. 2015;43(8):955-64.

51. Takeshima T, Fujita Y, Maki K. Factors associated with masticatory performance and swallowing threshold according to dental formula development. Arch Oral Biol. 2019;99:51-7.

52. Vaccaro G, Pelaez JI, Gil JA. Choosing the best image processing method for masticatory performance assessment when using two-coloured specimens. J Oral Rehabil. 2016;43(7):496-504.

53. The Glossary of Prosthodontic Terms: Ninth Edition. J Prosthet Dent. 2017;117(5s):e1-e105.

54. van der Bilt A, Mojet J, Tekamp FA, Abbink JH. Comparing masticatory performance and mixing ability. J Oral Rehabil. 2010;37(2):79-84.

55. Kaya MS, Guclu B, Schimmel M, Akyuz S. Two-colour chewing gum mixing ability test for evaluating masticatory performance in children with mixed dentition: validity and reliability study. J Oral Rehabil. 2017;44(11):827-34.

56. Elgestad Stjernfeldt P, Sjögren P, Wårdh I, Boström A-M. Systematic review of measurement properties of methods for objectively assessing masticatory performance. Clin Exp Dent Res. 2019;5(1):76-104.

57. Silva LC, Nogueira TE, Rios LF, Schimmel M, Leles CR. Reliability of a two-colour chewing gum test to assess masticatory performance in complete denture wearers. J Oral Rehabil. 2018;45(4):301-7.

58. Changsiripun C, Pativetpinyo D. Masticatory function after bite-raising with light-cured orthodontic band cement in healthy adults. Angle Orthod. 2019.

59. Yamanaka R, Akther R, Furuta M, Koyama R, Tomofuji T, Ekuni D, et al. Relation of dietary preference to bite force and occlusal contact area in Japanese children. J Oral Rehabil. 2009;36(8):584-91.

60. Le Reverend BJ, Edelson LR, Loret C. Anatomical, functional, physiological and behavioural aspects of the development of mastication in early childhood. Br J Nutr. 2014;111(3):403-14.

61. Nokubi T. Efforts of Occlusion and Mastication toward Improving Quality of Life. Journal of Japanese Society for Mastication Science and Health Promotion. 2007;17(1):3-15.

62. Curtis DA, Plesh O, Miller AJ, Curtis TA, Sharma A, Schweitzer R, et al. A comparison of masticatory function in patients with or without reconstruction of the mandible. Head Neck. 1997;19(4):287-96.

63. Petersen PE, Baez RJ, World Health O. Oral health surveys: basic methods. 5th ed ed. Geneva: World Health Organization; 2013 2013.

64. Greene JC, Vermillion JR. THE SIMPLIFIED ORAL HYGIENE INDEX. J Am Dent Assoc. 1964;68:7-13.

65. Petersen PE. The World Oral Health Report 2003: continuous improvement of oral health in the 21st century--the approach of the WHO Global Oral Health Programme. Community Dent Oral Epidemiol. 2003;31 Suppl 1:3-23.

66. Choi TM, Kragt L, Goos JAC, Mathijssen IMJ, Wolvius EB, Ongkosuwito EM. Deviating dental arch morphology in mild coronal craniosynostosis syndromes. Clin Oral Investig. 2019;23(7):2995-3003.

67. Caries-risk Assessment and Management for Infants, Children, and Adolescents. Pediatr Dent. 2017;39(6):197-204.

68. Coşkun İ, Kaya B. Cone Beam Computed Tomography in Orthodontics. Turk J Orthod. 2018;31(2):55-61.

69. Ricketts RM. Planning Treatment on the Basis of the Facial Pattern and an Estimate of Its Growth. The Angle Orthodontist. 1957;27(1):14-37.

70. Sorathesn K. [Craniofacial norm for Thai in combined orthodontic surgical procedure]. J Dent Assoc Thai. 1988;38(5):190-201.

71. Suwanwitid P, Jaruprakorn T, Changsiripun C. The importance of controlling vertical movement of posterior teeth for a Class II malocclusion in a non-growing patient: a case report. Orthodontic Waves. 2021;80(3):185-92.

72. Schimmel M, Christou P, Herrmann F, Müller F. A two-colour chewing gum test for masticatory efficiency: development of different assessment methods. J Oral Rehabil. 2007;34(9):671-8.

73. Kobayashi Y, Ogura K, Hikita R, Tsuji M, Moriyama K. Craniofacial, oral, and cervical morphological characteristics in Japanese patients with Apert syndrome or Crouzon syndrome. Eur J Orthod. 2021;43(1):36-44.

74. Nieminen P, Morgan NV, Fenwick AL, Parmanen S, Veistinen L, Mikkola ML, et al. Inactivation of IL11 signaling causes craniosynostosis, delayed tooth eruption, and supernumerary teeth. Am J Hum Genet. 2011;89(1):67-81.

75. Shin K, Moreno-Uribe LM, Allareddy V, Burton RG, Menezes AH, Fisher MD, et al. Multidisciplinary care for a patient with syndromic craniosynostosis: A case report with 20 years of special care. Spec Care Dentist. 2020;40(1):127-33.

76. Azoulay-Avinoam S, Bruun R, MacLaine J, Allareddy V, Resnick CM, Padwa BL. An Overview of Craniosynostosis Craniofacial Syndromes for Combined Orthodontic and Surgical Management. Oral Maxillofac Surg Clin North Am. 2020;32(2):233-47.

77. Letra A, de Almeida AL, Kaizer R, Esper LA, Sgarbosa S, Granjeiro JM. Intraoral features of Apert's syndrome. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103(5):e38-41.

78. Múfalo PS, Kaizer Rde O, Dalben Gda S, de Almeida AL. Comparison of periodontal parameters in individuals with syndromic craniosynostosis. J Appl Oral Sci. 2009;17(1):13-20.

79. Droubi L, Laflouf M, Tolibah YA, Comisi JC. Apert Syndrome: Dental management considerations and objectives. J Oral Biol Craniofac Res. 2022;12(3):370-5.

80. Jimenez DF, Barone CM. Multiple-suture nonsyndromic craniosynostosis: early and effective management using endoscopic techniques. J Neurosurg Pediatr. 2010;5(3):223-31.

81. Proctor MR, Meara JG. A review of the management of single-suture craniosynostosis, past, present, and future. J Neurosurg Pediatr. 2019;24(6):622-31.

82. Awadh W, Pegelow M, Heliövaara A, Rice DP. Dental age, agenesis, and morphological anomalies in individuals with Van der Woude syndrome and isolated cleft palate. Eur J Orthod. 2021;43(4):387-93.

83. Stavropoulos D, Tarnow P, Mohlin B, Kahnberg KE, Hagberg C. Comparing patients with Apert and Crouzon syndromes--clinical features and cranio-maxillofacial surgical reconstruction. Swed Dent J. 2012;36(1):25-34.

84. Torun GS, Akbulut A. Crouzon syndrome with multiple supernumerary teeth. Niger J Clin Pract. 2017;20(2):261-3.

85. Reitsma JH, Balk-Leurs IH, Ongkosuwito EM, Wattel E, Prahl-Andersen B. Dental maturation in children with the syndrome of crouzon and apert. Cleft Palate Craniofac J. 2014;51(6):639-44.

86. Sato S, Fueki K, Sato H, Sueda S, Shiozaki T, Kato M, et al. Validity and reliability of a newly developed method for evaluating masticatory function using discriminant analysis. J Oral Rehabil. 2003;30(2):146-51.

87. Barrera LM, Buschang PH, Throckmorton GS, Roldán SI. Mixed longitudinal evaluation of masticatory performance in children 6 to 17 years of age. Am J Orthod Dentofacial Orthop. 2011;139(5):e427-34.

88. Choi TH, Kim BI, Chung CJ, Kim HJ, Baik HS, Park YC, et al. Assessment of masticatory function in patients with non-sagittal occlusal discrepancies. J Oral Rehabil. 2015;42(1):2-9.

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