GEOMETRIC MORPHOMETRIC ANALYSIS OF DENTAL CAST AND CEPHALOMETRICS OF MALAYS CLEFT LIP AND PALATE

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GEOMETRIC MORPHOMETRIC ANALYSIS OF DENTAL CAST AND CEPHALOMETRICS OF MALAYS CLEFT LIP AND PALATE

by

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ABSTRAK

Rekahan bibir dan lelangit (RBL) atau sumbing adalah kecacatan muka kongenital yang paling lazim ditemui. Pesakit yang menderita keadaan ini mempunyai masalah makan, jangkitan telinga tengah dan juga masalah psikologi. Rawatan untuk pesakit RBL memerlukan rawatan daripada pelbagai disiplin bermula dari lahir sehingga berumur 20 atau 21 tahun. Tambahan pula, perkembangan pesakit RBL selepas pembedahan untuk membetulkan keadaan juga tidak sama dengan perkembangan tumbesaran pesakit biasa yang lain. Oleh itu, kajian ini bertujuan untuk menjelaskan perbezaan morfologi kanak-kanak Melayu yang tidak mengalami RBL/sumbing dengan kanak-kanak yang sumbing dari segi saiz, bentuk dan perubahan berarah dengan menggunakan morfometri geometri. Sebanyak 93 acuan gigi dan sefalometri lateral dikumpul dalam kajian ini yang dijalankan ke atas kanak-kanak berusia 6-12 tahun dengan purata umur 9.5 ± 1.3 tahun. Subjek kajian dibahagikan kepada 3 kumpulan; tiada rekahan atau tidak sumbing (TR), rekahan bibir dan lelangit sesisi (RBLS) dan rekahan bibir dan lelangit dwisisi (RBLD). Sebanyak 24 tanda berhomologos didigitkan pada acuan gigi atas dan bawah dan sebanyak 11 tanda berhomologos pada sefalometri lateral. Min kumpulan yang dibandingkan dianalisa dengan “analisa elemen terhingga” menggunakan perisian MorphoStudio untuk menunjukkan punca perkembangan heterogenik morfogenesis.

Dalam kajian yang dijalankan, subjek kumpulan yang tidak sumbing menunjukkan perbezaan yang signifikan dengan subjek kumpulan yang sumbing / dengan rekahan bibir dan lelangit. Perbezaan dari segi morfologi yang tinggi dapat dilihat antara lengkung gigi atas dan kompleks maksila dengan lengkung gigi bawah dan mandibel kerana keadaan sumbing mempengaruhi pertumbuhan bahagian ini. Keputusan perbandingan antara RBLS dengan RBLD sama kecuali keputusan jarak antara kanin dalam RBLD lebih terhad berbanding dengan RBLS. Jarak maksila bagi pesakit RBLD juga lebih panjang berbanding dengan pesakit dengan RBLS. Lengkung gigi atas dan komplek maksila juga menunjukkan banyak perubahan dari segi bentuk berbanding lengkung gigi bawah dan mandibel. Sementara itu, perubahan berarah kumpulan-kumpulan yang dibandingkan juga di dapati tidak homogen.

Keputusan kajian ini mungkin menunjukkan ciri pesakit Melayu yang sumbing di HUSM. Ciri-ciri ini amat berguna dalam menyediakan protokol rawatan yang lebih ideal dan seterusnya menyumbang kepada kualiti hidup yang lebih baik untuk pesakit sumbing.

GEOMETRIC MORPHOMETRIC ANALYSIS OF DENTAL CAST AND CEPHALOMETRICS OF MALAYS CLEFT LIP AND PALATE

ABSTRACT

Cleft lip and palate (CLP) is the most common congenital oro-facial deformity. Patients with CLP may have difficulty in feeding, middle ear infection as well as psychological problems. Management of CLP requires interventions from multiple disciplines which start from the first day of life and continue up to the adulthood. Moreover, the development of CLP patients does not follow usual developmental growth after corrective surgeries. In this study, we aim to document the morphological differences of Malay children between non-cleft (NC) and CLP, in term of size, shape and directionality changes applying geometric morphometrics method. This study includes 6-12 years old children, with average age 9.5 ± 1.3 years. They were divided into three groups; non-cleft (NC), unilateral cleft lip and palate (UCLP), bilateral cleft lip and palate (BCLP). Ninety three dental casts and lateral cephalometrics were collected. Twenty four homologous landmarks were digitized on upper and lower dental cast and eleven homologous landmarks on lateral cephalometric. The mean of compared groups were subjected to finite element analysis (FEA) using MorphoStudio™ software to demonstrate the sources of heterogeneity in the CLP in term of size changes, shape changes and directionality of shape changes.

In this study, NC group showed significant differences from CLP group. Upper dental arch and maxillary complex showed high morphological differences than lower dental arch and mandible, as cleft affect growth of this area. In comparison of UCLP and BCLP, they were comparable in result except intercanine width was more constricted in BCLP. Moreover, maxillary length was

longer in BCLP compared to UCLP. For shape changes, upper dental arch and maxillary complex showed significant changes than lower dental arch and mandible, while directionality changes of compared groups were non-homogenous.

The difference in morphology of CLP versus NC in this study could contribute important information to clinician treating the patients.

CHAPTER ONE

INTRODUCTION

1.1 Background

Cleft lip or hare lip is a deformity affecting the lip (Johnson and Moore, 1997). Cleft palate can be defined as 'a furrow in the palatal vault'. It may also be defined as 'breach in continuity of palate'. Cleft lip and palate (CLP) comprises 65% of all anomalies affecting the head and neck (Moore and Persaud, 2003), which is characterized by abnormality of the upper anterior region due to alveolar cleft (Motohashi and Kuroda, 1999). Cleft lip and palate (CLP) may be isolated deformities or may be part of a syndrome (Mars, 2001). At the present time, most studies suggest that 70% of CLP cases are non-syndromic and the remaining 30% of cases associated with structural abnormality outside the region of the cleft (Schutte and Murray, 1999; Cobourne, 2004). Non syndromic is restricted to cleft cases where the affected individuals have no other physical or developmental anomalies and no recognized maternal environmental exposure (Schutte and Murray, 1999). Etiological factors of orofacial cleft are complex, including genetic and environmental factors (Schutte and Murray, 1999).

There are multiple morpho-functional problems associated with CLP patients. These problems include feeding, dental, hearing, speech and psychological problems. CLP patients also show craniofacial growth disturbance (Sasaki *et al.*, 2004).

Therefore, morphological problem is significant to understand the development, treatment planning and prognosis of patients with cleft lip and palate (McAlarney and Chiu, 1997).

1.2 Overview of Normal Embryonic Craniofacial Development

a) Development of the face

The face develops around the stomedeum between the 4th and 8th week of development (Johnson and Moore, 1997). However, face originates from five primordials, single frontonasal prominences, paired maxillary prominences and paired mandibular prominences (Carlson, 1994).

By the end of the 4th week, primordial of the nose and nasal cavities have developed on the inferolateral parts of the frontonasal prominence. During the 5th week maxillary prominences grow medially toward each other and to the nasal prominences (Moore and Persaud, 2003). By the end of the 6th week, each maxillary prominence has begun to merge with the lateral nasal prominence (Arosarena, 2007).

Between the 7th and 10th week, the medial nasal prominences merge with each other and with the maxillary and lateral nasal prominences. As these prominences fuse together, they form an intermaxillary segment (Johnson and Moore, 1997). Intermaxillary segment gives rise to the philtrum of the upper lip, the premaxillary part of maxilla and its associated gingival and the primary palate.

Furthermore, lateral parts of the upper lip and the secondary palate merge laterally with the mandible prominences (Moore and Persaud, 2003).

For the mandible, it is formed in a simple manner. The bilateral mandibular prominences enlarge and their medial components merge in the midline (Jugessur and Murray, 2005) (Fig 1.1)

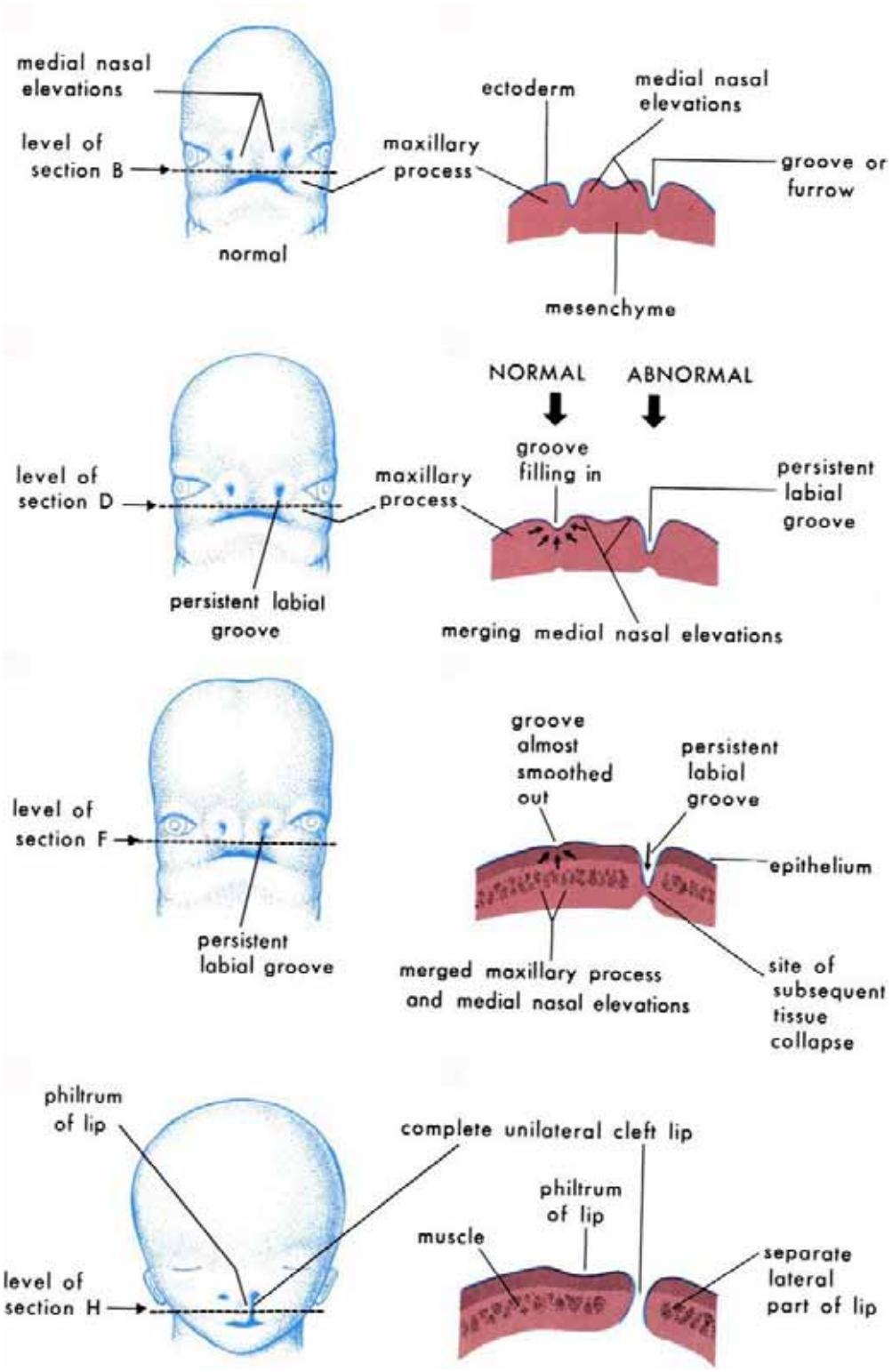

Figure1.1 Face development, adopted from Moore and Persaud (2003)

b) Development of Palate

The palate develops from two primordia, primary and secondary palate. Development of the palate begins at the end of the 5th until the 12th week. The critical period of development is between 6th and 9th week (Moore and Persaud, 2003). Usually, cleft of the primary palate develops between the 4th and 7th embryonic weeks, while cleft of the secondary palate develops between the 8th and 12th embryonic weeks (Heinrich *et al.*, 2006).

At the 6th week, the primary palate begins to develop from the deep part of the intermaxillary segment of the maxilla, which forms the premaxilla (Moore and Persaud, 2003). It extends posteriorly to the incisive foramen, which is located immediately behind the alveolar ridge (Bender, 2000).

Secondary palate forms from two maxillary prominences, which is the primordium of the hard and soft palate that extend posteriorly from the incisive fossa (Arosarena, 2007). At the 6th week, palatal shelves project inferomedially on each side of the tongue (Johnson and Moore, 1997). As the jaws develop, the tongue moves inferiorly. During the 7th and 8th week, palatal shelves ascend to a horizontal position superior to the tongue (Moxham, 2003).

Gradually, the shelves approach each other and fuse in the median plane. These shelves contact with the primary palate anteriorly and the free margins fuse together (Arosarena, 2007).

Fusion of the hard palate is completed by the tenth week while development of the soft palate and uvula are completed in the twelfth week (Bender, 2000). The incisive foramen

comes to lie at the junction of the primary and secondary palate in the midline. Fusion proceeds from front to back and, at the same time, nasal septum is growing downwards to fuse with the palatal shelves in the midline, completing the separation of the two nasal cavities (Mars, 2001) (Fig 1.2).

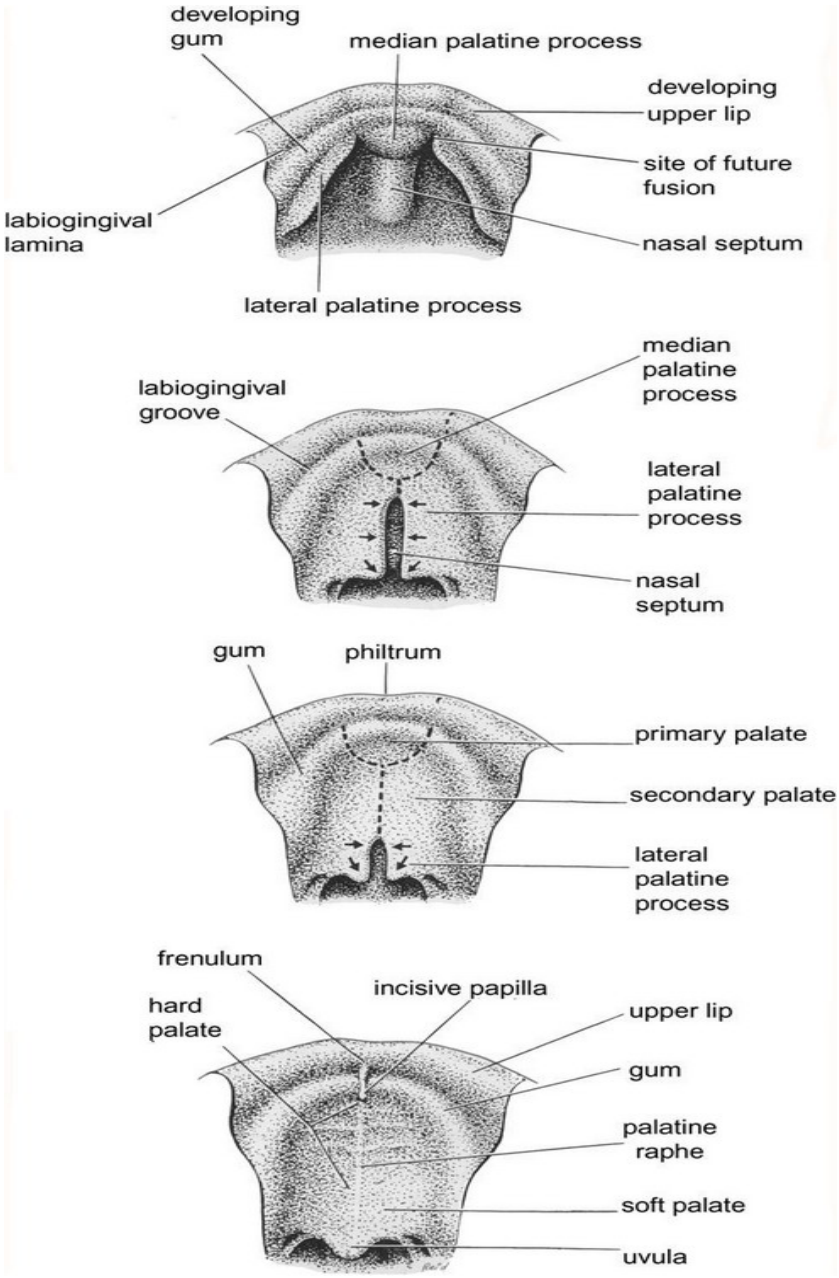

Figure1.2 Development of secondary palate, adopted from Moore and Persaud (2003)

1.3 Classification of Cleft lip and Palate

There is an almost infinite variation in the presentation of clefts of the lip and palate, but it is necessary to classify them into groups in order to describe them, to study their causes, and to compare the results of their management (Lees, 2001). As a result, many classifications have been proposed. Some of these classifications are based on the location of the cleft relative to alveolar process as a significant landmark, while others considered the incisive foramen as a significant landmark (Thornton *et al.*, 1996).

Most commonly used classification at present time introduced by Kernahan and Stark (1958) (Fig 1.3) (Lees, 2001). This is an embryological classification using incisive foramen that divides the primary palate from the secondary palate. This is subdivided into:

Clefts of primary palate only (unilateral, median or bilateral), Clefts of secondary palate only (complete, incomplete or submucosal) and Clefts of primary and secondary palate (unilateral, median or bilateral) (Thornton *et al.*, 1996). This thesis deals with cleft of primary and secondary palate (unilateral and bilateral cleft).

Combined Cleft Lip and Palate (UCLP and BCLP)

Subjects with combined cleft lip and palate have clefts in both the primary and secondary palate. The cleft malformation may be complete or incomplete; unilateral or bilateral.

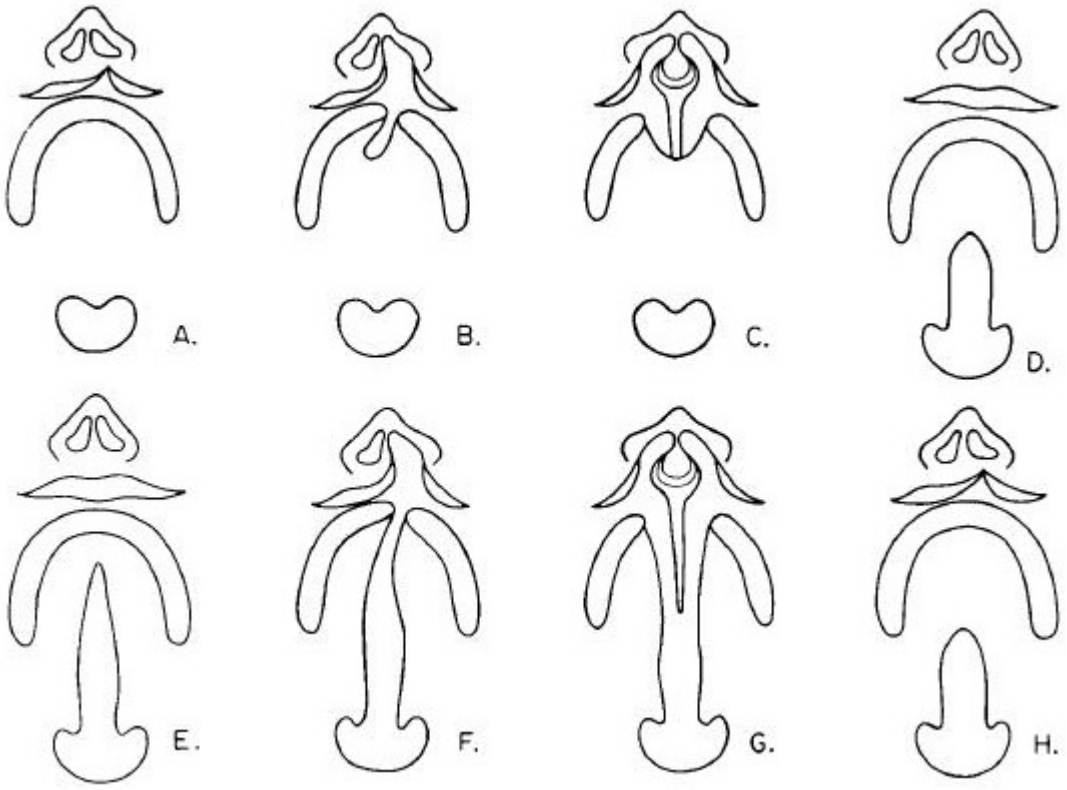

Figure 1.3 The classification of Kernahan. This divides the deformity into three groups: clefts of the primary palate alone, clefts of the secondary palate alone, and clefts of the primary and secondary palates.

1.4 Problems associated with cleft lip and palate

1.4.1 Feeding problem

There is an obvious communication between the oral and nasal cavities in cleft palate. Therefore, the baby cannot suck because it cannot achieve a vacuum. Mothers should be advised that breastfeeding is unlikely to be successful and that bottle-feeding should be done with a soft plastic bottle or enlarged, cross-cut, or wide-based nipples which need less pressure to squeeze the milk into the oral cavity. Babies can swallow the milk by

positioning the baby upright and tilted slightly backward, so this help in swallowing of the milk and reduced nasal regurgitation.

1.4.2 Speech problem

Cleft has the potential to influence articulatory development; poorer articulation proficiency might be expected even after primary palatoplasty (Paliobei *et al.*, 2005).

It appears that atypical patterns of articulation may develop as the child attempts to mask and compensate for the perceptual consequences of an incompetent mechanism prior to palatoplasty (Paliobei *et al.*, 2005).

During speech, the soft palate elevates, forming an airtight seal with the lateral and posterior wall of the pharynx, preventing airflow into the nasopharynx. Elevation of the soft palate is also important during swallowing to stop food and drink passing into the nasopharynx.

The speech problems usually associated with cleft include hyper nasality, excessive nasal air emission, altered resonance or tone, weak pressure consonants or plosive sounds, and disturbed voice quality.

Dental problems also may affect speech. Many consonants are produced by the lower lip or tongue making contact against the upper teeth.

1.4.3 Velopharyngeal incompetence (VPI)

Velopharyngeal incompetence is the incomplete closure of the velopharyngeal sphincter during speech, the most common cause of VPI is a cleft of the secondary palate (Lam *et al.*, 2006). VPI occurs as a result of valve dysfunction. The main manifestation of VPI is airflow into the nasal space when talking which gives the voice an increased resonant quality (hyper nasality) (Sloan, 2000). Also, it forces the child to use the posterior part of their tongue to produce sounds. However, escape of air through the velopharynx into the nasal cavity during speech may cause nasal emission (Conley *et al.*, 1997).

1.4.4 Hearing problem

Another important role of the soft palate muscles (particularly the tensor velipalatini) is to open and close the Eustachian tube to equalize the pressure within the middle ear and aid in drainage of mucous secretion. Impairment of this mechanism in patients with cleft palate leads to glue ear (accumulation of fluid in the middle ear) and impairs function of the tympanic membrane. All that leads to increase the risk of infection in the middle ear and mild hearing loss.

1.4.5 Psychological problem

Researchers have shown that attractive children are seen by others as brighter and have more positive social behavior and receive more positive treatment than their less attractive counterparts (Hunt *et al.*, 2005). Studies of CLP shows that reduced attractiveness and

ability to communicate verbally has an important influence upon an individual's psychological well being (Turner *et al.*, 1998). This is due to high incidence of teasing over facial appearance. In a systematic review by Hunt *et al.,* (2005), they examined the published scientific research on psychological impact of CLP patients. He reported that CLP patients do not appear to experience major psychological problems but specific problems may arise, such as dissatisfaction with facial appearance, depression and anxiety (Hunt *et al.*, 2005).

Also, other studies had studied the effect of psychological problems on school underachievement. They reported some factors which include; behavioral inhibition in the classroom, lower parent and teacher expectations, teachers' underestimating the intelligence of children with facial disfigurements, and dissatisfaction with facial appearance (Millard and Richman, 2001).

1.4.6 Dental anomalies

Dental anomalies are extremely common in children with orofacial clefting. The most commonly affected tooth is the maxillary lateral incisor at the cleft side (Ranta, 1989). This is due to disruption of the dental lamina. Anomalies may include:

- Supernumerary teeth, usually termed "fissural teeth"
- Defects of enamel (hypoplasia and opacities) is common in the teeth adjacent to the cleft site.
- Disorders of morphogenesis (size and shape).
- Congenital absence of teeth.

Also, a higher prevalence of caries, gingivitis, cross bite and crowding has been reported in both the primary and permanent dentitions of children with a cleft compared with those of children without a cleft (Wong and King, 1998).

1.5 Statement of the problem

Cleft lip and/or palate is one of the craniofacial deformities affecting Malay population (Boo and Arshad, 1990). This deformity is affecting patients' craniofacial growth either functionally or cosmetically. Craniofacial growth is characterized by time-dependent changes of size and shape that many methods for diagnosis and analysis can be used in diagnosis. Thus, the ability to describe form difference between two objects or changes in one object over time provide specialists with valuable information (McAlarney and Chiu, 1997). Geometric morphometry can describe and quantify changes in certain area and compare these changes with other group either in size or shape. Therefore, behavior of these structures can be evaluated and expected either favorable or unfavorable. This information will give better understanding of the growth and development of cleft patients as well as in assessing the effects of surgical, orthopedic and orthodontic treatments. Moreover, it will provide researchers with text and graphical result, which facilitates interpretation and statistical analysis.

As far as we are aware, with the advance of imaging and computer technology and the introduction of geometric morphometric, this study is new in Malaysia.

An awareness of this need has led to the research reported in this thesis.

1.6 Objectives

A. General objective:

The purpose of this study was to evaluate the morphological differences between Malay children between NC and CLP in term of size, shape, and directionality changes of dental cast and cephalograph using finite element analysis (FEA).

B. Specific objectives:

(i) To compare size, shape and directionality changes of maxillary dental arches between NC and CLP on dental cast.

(ii) To compare size, shape and directionality changes of mandibular dental arches between NC and CLP on dental cast.

(iii) To compare size, shape and directionality changes of mid-facial complex between NC and CLP on the cephalograph.

(iv) To compare size, shape and directionality changes of mandible between NC and CLP on the cephalograph.

Comparisons were done between unilateral cleft lip and palate (UCLP) vs NC, bilateral cleft lip and palate (BCLP) vs NC and UCLP vs BCLP using both dental cast and cephalograph.

1.7 Hypothesis

It is hypothesized that Malays with CLP are anatomically and morphologically different from NC.

CHAPTER TWO

LITERATURE REVIEW

Section A

2.1 History of cleft lip and palate research

Description of cleft lip and palate has been related to many centuries. Artifact showing cleft lips date back more than 4000 years. One example, exhibited at the Tokyo national museum, is clay statue showing a median cleft lip (Pirsig *et al.*, 2001).

The first proven description of treatment of a cleft lip and palate appeared in ancient China (Bill *et al.*, 2006). In about 400 AD, a Chinese physician succeeded in suturing a cleft lip. Also, Parea a French surgeon in 1562 was the first to try to put an obturator to fill the cavity of cleft in order to facilitate eating and speech (Pirsig *et al.*, 2001).

2.2 Etiology

Cleft lip and palate is a major congenital structural abnormality that is the cause of significant morbidity and has a complex etiology (Cobourne, 2004).

The prevalence of orofacial cleft depends on the geographic origin, racial background and socioeconomic status (Schutte and Murray, 1999). Epidemiological studies and complex segregation analysis have established the importance of genetic and environmental factors in clefting (Suazo *et al.*, 2004).

2.2.1 Genetic factors

Genes play an important role in the development of normal craniofacial structures (Schutte and Murray, 1999). A more recent genetic studies in families with multiple cases of non-syndromic CLP concluded that no single major CLP locus exists and a multifactorial model was the most likely explanation of the genetic component of this disorder (Cobourne, 2004).

Few studies reported an association between non-syndromic CLP and genetic variation at the TGFα (Mitchell, 1997). TGFα has been mapped on chromosome 2q13 (Vieira, 2006). During craniofacial development, TGFα is expressed at the medial edge epithelium of fusing palatal shelves, which promotes synthesis of extracellular matrix and mesenchymal cell migration and leads to palatal fusion (Jugessur and Murray, 2005) .

Vieira (2006), attributed risk of TGFα for cleft is 20% with family history (Vieira, 2006). While, others found an association between restriction fragment length polymorphism (RFLPs) and TGFα (Carinci *et al.*, 2007).

Also other studies reported that TGFB3 gene on chromosome 14q24 was associated with non-syndromic CLP in different population (Wong and Hagg, 2004). This gene has important role during fusion of the secondary palate, directly controlling the differentiation of epithelium to mesenchyme in the midline seam between adjacent palatal shelves (Cobourne, 2004). Also, some studies reported an interaction between TGFB3 and MSX1 which result in increasing cleft susceptibility (Carinci *et al.*, 2007; Lidral *et al.*, 1998).

On the other hand, different studies investigate the localization of cleft lip and palate gene on chromosome 6 (6p). These studies proved association of cleft lip and palate with mutation involving the short arm of 6p (Prescott *et al.*, 2001).

Scapoli *et al.*, (1997) had studied 38 multicomplex CLP families. They found linkage between 6p23 and CLP. Also, he reported no significant difference between male and female associated with CLP. However, successive linkage studies have provided further indications for the involvement in CLP of regions on the 6P. These include 6P 23-24, 6P 24.3 and 6P 23. These findings present a real possibility that a gene on human 6P may play a role in non-syndromic clefting (Cobourne, 2004).

While, Martinelli *et al*., (1998) examined the linkage between BCL3 and orofacial cleft in a sample composed of 40 Italian families using parametric and non-parametric method. They support a role for BCL3 in orofacial clefts (Martinelli *et al.*, 1998).

Wyszynski *et al*., (1997) studied the role of BCL3 in 30 families from USA and 11 families from Mexico. They reported BCL3 role in orofacial clefts (Wyszynski *et al.*, 1997) . Gaspar *et al.*, (2002) study on Brazilian population, using 98 CLP patients and their parents analyzed the association between BCL3 and non-syndromic CLP. He also reported that BCL3 play a role in the etiology of non-syndromic CLP.

Also, Retinoic Acid receptor α (RARA) is one of the candidate genes for pathogenesis of non-syndromic CLP. Kanno *et al.*, (2002) studied the association between RARA gene and non-syndromic CLP in Japanese patients. This study was done on 48 families. They found that the RARA gene variations do not contribute to the development of non-syndromic CLP in the Japanese populations (Kanno *et al.*, 2002).

2.2.2 Environmental factors

Many factors have been implicated in the etiology of CLP. Cigarette smoking during pregnancy show not strong association with CLP, but it is significant (Wong and Hagg, 2004). Several studies have estimated relative risks about 1.34 (95% confidence interval) for CLP (Jugessur and Murray, 2005). When maternal smoking is associated with genetic background, the combined effect was more significant (Wong and Hagg, 2004). Moreover, maternal alcohol consumption (frequently with cigarette smoking) can result in an increase risk of CLP (Cobourne, 2004).

In addition, Folic acid has a role in orofacial clefts. Folic acid is water soluble "B" vitamin. Its chemical name is pterylmonoglutamic acid. It is required for the synthesis of DNA and RNA. Thus it is essential for growth and differentiation, as well as for host defence (Hall and Solehdin, 1998). van Rooij *et al.*, (2004) and Wong and Hagg, (2004) demonstrate that maternal folic acid supplement reduce the risk for CLP.

2.3 Incidence of CLP

Studies report that usually cleft affects 1 in 700 live births (Singh, 2004). This number varies among races and with socioeconomic status. In white American it affects 1 in 1000 births, with high rate in Asian and Native American 1 in 500 births and least in Africans 1 in 2400 to 2500 births (Arosarena, 2007). While, CLP occur more frequently among boys as opposed to girls. However, cleft palate (CP) affect female more than male (Singh, 2004). Also, CLP occur twice as frequently on the left side compared to the right side (Lambrecht *et al.*, 2000). While, unilateral cleft lip and palate (UCLP) is twice as common as bilateral cleft lip and palate (BCLP) (Bender, 2000) .

In a study in the south east of Scotland (1971-1990), cleft affects 1 in 711 live births. Also, primary palate was affected by 25%, secondary palate by 45% and 30% affect both palate. Males affected were 58% compared to 42% female. Clefts of secondary palate were more common in female 65% compared to male 44% (Bellis and Wohlgemuth, 1999).

Also, in an epidemiological study in Korea for CLP incidence through 1993 to 1995. Incidence of CLP was 1 per 554 births. The cleft lip: cleft lip and palate: cleft palate alone ratio was 1.13: 1:1.19. The male: female ratio was 2.1:1 in the cleft lip group, and 2.5:1 in the cleft lip and palate group. The left: right: bilateral ratio was 1.9:1:0.23 in cleft lip group, and the ratio was 2.2:1:1.1 in the cleft lip and palate group (Kim *et al.*, 2002).

Finally, in a study in Malaysia on 52,379 babies delivered in the Maternity Hospital, Kuala Lumpur, over a 2-year period, 64 were born with cleft lip and/or palates. The rate of occurrence of cleft was 1.24 per 1000 live births or 1.20 per 1000 deliveries. The Chinese babies had the highest incidence (1.9 per 1000 deliveries) while the Malays had the lowest (0.98 per 1000 deliveries). The most common type was unilateral cleft of the primary and secondary palates. Among the Indian babies, cleft of the secondary palate was most common. 18.8 percent of all the affected babies had positive family history of cleft. 10.9% of the mothers of affected babies had positive history of drug ingestion especially Chinese herbs during pregnancy. Associated congenital abnormalities occurred in 15.6% of the babies with cleft lip and/or palate (Boo and Arshad, 1990).

2.4 Cleft Management

Management of children with cleft lip and palate should go through a multidisciplinary team who will provide the optimal treatment (Bill, 2006). More predictable therapeutic

outcomes are achieved when such a team provides comprehensive diagnosis, planning, and treatment. The cleft team usually includes orthodontist, maxillofacial surgeon, plastic surgeon, prosthodontist, speech therapist, audiologist (ENT specialist), psychologist, and pediatrician.

2.4.1 Birth time

The main potential problem at this stage is feeding. Early referral to the infant-feeding specialist or nurses associated with cleft teams can facilitate this problem solving. Infants with CLP will require special feeding techniques. These include the usage of spoon feeding bottles, squeeze bottles, modified bottle nipples, and palatal appliances which allow milk to be delivered to the back of throat where it can be swallowed (Endriga *et al*., 1998). Such prosthesis could be effective in increasing the volume of fluid intake, decreasing time of feeding, and promoting adequate growth and gain in infants with cleft lip and palate (Turner *et al*., 1998). Some babies may not have the energy to suck from a teat, and here a cup and spoon method may be helpful.

2.4.2 Lip repair

There is a wide variation in the timing and techniques of primary lip repair depending upon the preference and protocol of the surgeon and cleft team involved. Some protocols perform lip repair at 3 months of age and palate repair at 12 months of age as in case of Millard technique, while others advocate soft palate repair at 3 months of age and lip and hard palate repair at 6 months of age as in the case of Malek protocol (Di Silva Filho *et al*., 2001). However, the best technique aims to dissect out and re-oppose the muscles of the lip and alar base in the correct anatomical position but there is some controversy as

whether tissue movement should be achieved by subperipostal dissection or supraperiosteal dissection and skin lengthening cuts.

An earlier surgical intervention is also important to the normal speech development. Others tend to delay any surgical procedures justifying that with the fact that the tissues would be able to grow and mature thereby giving the surgeon more muscles mass to work on. In addition, growth restriction resulted from scar tissue formation would be less if surgery is performed later.

2.4.3 Palate repair

Hard and soft palate repair is undertaken on average, 9 and 18 months of age with the philosophy that any unwanted effects upon growth caused by repair at this stage (which can be compensated for to a degree by orthodontics and surgery) are preferable to prevent the development of poor articulatory habits, which can be extremely difficult to eradicate after the age of 5 years (Mars, 2001).

2.4.4 Primary dentition (2-6 years)

The first formal speech assessment is usually carried out at 18 months of age depending upon the needs of the child (Sommerlad, 2002). Monitoring of speech should continue through childhood, preferably at joint clinics to pick up any developing problems that may arise with growth. Assessment with an ENT surgeon should also be arranged if this specialty has not been involved at the time of primary repair. Lip revision prior to the start of schooling should be performed only if clearly indicated. Closure of any residual palatal fistula may also be considered to help speech development (Paliobei, 2005).

Orthodontic treatment in this stage is limited to the correction of certain posterior crossbite and anterior crossbite of mild to moderate degree. During this age, it is important to develop good dental care habits, instituting fluoride supplements in non-fluoridated areas (Rivkin *et al*., 2000).

2.4.5 Mixed dentition (6-12 years)

During this stage the restraining effect of surgery upon growth becomes more apparent. With the eruption of permanent incisors, defects in tooth number, formation, and position can be assessed. This stage includes also facial orthopedics (bone graft) to correct the maxillary alveolar bone defects.

A short period of orthodontic treatment is undertaken in the mixed dentition to reposition the dentition adjacent to the cleft to prepare the cleft side, but such procedure must be postponed until the development of the incisor roots to avoid any resorptive effect of the orthodontic treatment.

2.4.6 Permanent dentition

At this time a definitive orthodontic treatment must be performed. The goals are no different from those for noncleft patients, but certain conditions must be kept in mind during the treatment planning. These include maintenance of the integrity of the dentition and supporting structures especially for teeth adjacent to the alveolar cleft, correction of impactions and transpositions and management of congenitally missing teeth.

Once the permanent dentition has been established, the patient should be assessed regarding the need for orthognathic surgery to correct mid-face retrusion. The degree of

maxillary retrognathia, the magnitude and effect of any future growth, and patient wishes should be all taken into consideration. If surgical correction is indicated, this should be delayed until growth is complete. Finally, surgical revision of the nose (rhinoplasty) can be carried out, as movement of the underlying bone will affect the contour of the nose.

Section B

2.5 Overview of Geometric Morphometrics

2.5.1 Definition

Morphometrics is derived from the Greek words 'morph', shape, and 'mentron', measurement, used in contemporary investigations to define size and shape (McIntyre and Mossey, 2003) . Size change refers to a proportional increase or decrease in all dimensions of the form under examination, often accompanied by a change in shape. Changes in shape require a change in the outline of the form under examination, often resulting from localized size changes (McIntyre and Mossey, 2003). Size-changes are expressed as positive or negative allometry (it shows a relative increase or decrease in size related to shape-change), while shape-changes are expressed as isotropic (uniformity in the nature of the shape change) and anisotropic (non-uniformity in the nature of the shape change) (Singh and Clark, 2001).

Geometric morphometery is a statistical shape analysis tool that includes procrustes superimposition, finite element analysis (FEA), thin-plate spline analysis and Fourier analysis. All these analysis produce shape information if the forms under comparison are scaled to an equivalent size (McIntyre and Mossey, 2003).

Bookstein, (1982) was the earlier researcher who evaluated size and shape changes. He introduced tensor analysis for evaluation; later finite element analysis becomes widely recognized. Tensor analysis facilitates the construction of transformation grids that show the extent of deformation (Bookstein, 1982).

However, tensor analysis only determines size- and shape-change at specific landmarks; FEA provides information on deformation within the geometrical configuration and between the defining anatomical landmarks (Singh *et al.*, 1997), which enable FEA application in many studies on dental casts and cephalometrics.

2.5.2 Analysis of Dental Cast

Dental cast is a replica of patient's mouth, which is consided as important tool in diagnosis and treatment planning for dentist and orthodontist. After clinical diagnosis, clinician analyze the dental cast and plan the treatment (Hayashi *et al.*, 2003). Usually, dental cast analysis can be done by several methods. These methods ranging from manual, 2D digitization of casts to 3D analysis of dental cast (Santoro *et al.*, 2003).

Traditionally, conventional calipers have been used to measure dental casts manually (Hayasaki *et al.*, 2005). In a study in Brazil, (Claro *et al.*, 2006) caliper has been used to measure lengths on dental cast, to assess the correlation between transverse expansion and the increase in upper arch perimeter, after maxillary expansion. Also, different methods have been compared with caliper to prove its validity. For instance, Schirmer and Wiltshire, (1997) evaluated the accuracy and reliability of computer-aided space analysis; two investigators independently measured teeth on models with a vernier. Intraexaminer and interexaminer reliability was done. For computer-aided space analysis, each dental cast set

were photocopied using a Photostat machine, also interexaminer and intraexaminer reliability were tested. They found that vernier was more reliable than computer-aided space analysis. Moreover, Motohashi and Kuroda, (1999) introduced the computer aided dentistry (CAD) system for the diagnostic set-up of dental cast in orthodontic diagnosis and treatment planning, and its preliminary clinical application. Furthermore, Paredes *et al.*, (2005) scanned dental cast with scanner and used computer program for space analysis. Hayasaki *et al.*, (2005) introduced a mechanical 3-dimensional digitizer, MicroScrib for dental cast analysis, by digitizing points on the model. Moreover, The bias of the system was evaluated by comparing the distance between 2 points as determined by the new system and as measured with digital calipers. These methods show valuability in cleft studies, as it facilitates diagnosis and treatment planning and subsequently improve prognosis.

Also, Kilpelainen and Laine-Alava, (1996) evaluated palatal height, width and depth in cleft lip and palate subjects using Moiré photography technique. The sample consisted of 95 subjects with cleft palate and 68 controls of Caucasoid origin. The ages ranged from 5 to 24 years, with a mean of 13.1 ± 4.2 years in the cleft group and from 8 to 23 years, with a mean of 12 ± 3.2 years in control group. The cleft group was divided into subgroups; cleft of occult submucous (5), cleft of primary palate (6), cleft of secondary palate including hard palate (42), cleft of the right primary and secondary palate (8), cleft of the left primary and secondary palate (17), cleft of the bilateral primary and secondary palate (17). They found that cleft subjects show remarkable decrease in palatal width and position of maxillary first molars. Also, the severity of cleft affects palate in both anteroposterior and transverse plane.

Moreover, Heidbuchel and Kuijpers-Jagtman, (1997), described maxillary and mandibular dental arches in BCLP compared with normal over the age 3 to 17 years old. They studied longitudinal records of 22 patients. They reported that maxillary arch width and depth of BCLP were significantly smaller than normal. While, mandibular dental arch measurements were similar in both groups.

Braumann *et al.*, (1999) studied 5 patients with UCLP to visualize the growth of the edentulous maxilla of cleft lip and palate in infants. Maxillary dental casts were taken at 1 month, 3, 6 and 12 months. They studied these dental casts using 3-dimensional digitizing instrument where computer superimposition of reconstructed consecutive casts was employed to facilitate a visualization of the extent and direction of morphological changes. They concluded it is possible to quantify the growth rate of defined segments of the maxilla using 3D method.

Braumann *et al.*, (2001) concluded that, two-dimensional measurement procedures are appropriate in principle cast analysis in patients with cleft lip and palate. Casts were taken from ten patients at 1 week, and at 3, 6, and 12 months, respectively. Cast surfaces were digitized two-dimensionally using a scanner. Subsequently, landmarks were identified on screen and the previously defined maxillary dimensions were determined automatically by computer. Additionally, three-dimensional measurement was carried out using reflex microscope. Reflex microscope is an instrument that provides measurements from stationary objects in three dimensions without directly touching the specimen and requires interface with a personal computer (Braumann *et al.*, 2001).