UNIVERSITI PUTRA MALAYSIA

DEVELOPMENT AND VALIDATION OF SEGMENTAL LENGTH EQUATIONS TO ESTIMATE HEIGHT AMONG CEREBRAL PALSY CHILDREN IN SOUTHERN AND CENTRAL REGIONS OF PENINSULAR MALAYSIA

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By

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Chairman : Rosita binti Jamaluddin, PhD
Faculty : Medicine and Health Sciences

Cerebral Palsy (CP) involves a group of chronic movement and posture disorders caused by a non-progressive lesion in an immature brain. 70-80% of CP have spastic clinical features such as increased deep tendon reflexes, tremors, and muscular hypertonia which causes stiffness and walking difficulty. It is the most common cause of physical disability in children, with a worldwide incidence of 2.11 per 1000 live births. Children with cerebral palsy (CP) typically suffer from congenital deformities such as scoliosis and contractures. Therefore, it is a challenge to measure the actual height or stature of CP children in a standing position. Studies have proposed that predictive equations based on segmental length (SL), i.e. knee height (KH), tibia length (TL), and upper arm length (UAL) can be used as an alternative method to measure the actual height. The standing height and recumbent length (RL) has become the gold standard for the actual height measurement. However, the current predictive equation has not been tested among the Malaysian population. Previous studies developed the predictive equations in a certain population, different ages, and did not include all Gross Motor Function System Classification (GMFCS) levels of CP. This study aimed to develop and validate the predictive equations based on KH, TL, and UAL for CP children in outpatient pediatric clinics and community rehabilitation centres (CBR) in the Central and Southern Regions of Malaysia. This cross-sectional study consisted of two phases in which Phase 1 is the evaluation of the existing fourteen equations and the development of new equations. Phase 2 was the validation of the new equations established in Phase 1. The study was conducted from August 2018 to December 2019. The subjects of this study were CP children with GMFCS I – V, aged 2 to 18 years.CP children with acute diarrhea, prolong vomited, and other medical illnesses or disabilities such as down syndrome will be excluded. Subjects were categorized into Phase 1 Equation Development Group (EDG) and Phase 2 Cross Validation Group (CVG). For the EDG, a total of 177 subjects were recruited from six outpatient paediatric clinics. 23.7% were GMFCS level I, 14.1% GMFCS level II, 5.7% GMFCS level III, 5.7% level IV, and 50.8% level V. As for the

CVG, 139 subjects were recruited from 18 community-based rehabilitation centres (CBR). The CVG subjects were 15% GMFCS Level I, 23% level II, 14% level III,14% level IV and 73% level V. All the clinics and CBR were sampled from the central and southern regions of Malaysia. The independent variables (IV) in this study were KH, TL, UAL, and age while the dependent variables (DV) in this model were actual height and recumbent length. The standing height was determined using a stadiometer. If CP children were unable to stand, recumbent length was taken using the standard procedure. A flexible Seca measuring tape was used to measure the recumbent and segmental lengths of all participants. In phase 1, 14 existing equations that have been developed from previous studies from the year 1994 to 2003 were tested. The equations have been selected based on knee height, tibia length, and upper arm length. The population of the previous studies was from CP and healthy children in the United States, Australia, China, and Japan. In Phase 1, based on the Bland Altman test, all fourteen existing equations (Eq1-Eq14) showed a weak agreement with the actual height of the CP subjects. Hence, six new predictive equation models were developed using multiple linear regression. This regression model was developed using the segmental length KH, TL, and UAL which were in Model 1 KH, Model 3TL, and Model 5 UAL. Equations that used age as a covariate factor for each segmental length in Model 2 KHA, Model 4 TLA, and Model 6 UALA were also developed. Others covariates such as age and gender not included in the model as the demography data shows not significant with the height measurements among CP population. The new KH-based equations included Model 1KH: Y_1 = 22.54+2.679 KH and Model 2KHA: Y_2 = 31.5 + 2.11 KH + 1.228A. The new equation model based on TL were Model 3TL: Y_3= 32.18+3.139 TL and Model 4TLA: Y_4 = 39.905 + 2.417 TL+ 1.31 A. Lastly, Model 5UAL: Y_5 = 20.469 +3.83 UAL and Model 6UALA: Y_6 = 33.15 + 2.771 UAL + 1.55A were based on UAL. In Phase 2, all six new models were cross-validated to validate the predictive equations. Model 3TL showed the lowest standard error (SEM), i.e. 1.42 compared to other models. Intra-correlation coefficient (ICC) analysis demonstrated a strong agreement between the actual and estimated heights for all models except for Model 1KH and Model 2KH (0.58). Apart from that, Model 3TL: Y3= 32.18+3.139 TL demonstrated a strong correlation with the actual height (R^2 = 0.834) and showed a small SEM (1.42) and high ICC (0.929). In conclusion, six new equations have been developed in Phase 1. All new models have been validated in Phase 2 to ensure the accuracy and reliability of the model in the CP population. All new equations were valid to use in CP Malaysia population, however, validation results showed that the Model 3TL was the most suitable segmental length prediction equation to be used in estimating the height of CP children aged two to 18 years. Further testing of the new equation for CP subjects in all regions of Malaysia is needed so that its use can be generalised to all the paediatric CP subjects in the Malaysian population.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

PEMBENTUKAN DAN VALIDASI FORMULA PENGUKURAN PANJANG SEGMEN TUBUH UNTUK MENGANGGAR KETINGGIAN KANAK KANAK CEREBRAL PALSI DI ZON PANTAI BARAT SERTA SELATAN SEMENANJUNG MALAYSIA

Oleh

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Cerebral Palsy (CP) adalah melibatkan pergerakan kronik dan juga gangguan postur yang disebabkan oleh lesi tidak progresif dalam otak yang tidak matang. 70-80% CP mempunyai ciri-ciri klinikal spastik seperti refleks tendon yang tinggi, gegaran, dan hipertonia otot yang menyebabkan kekejangan dan kesukaran berjalan. Ia adalah punca kecacatan fizikal yang paling biasa pada kanak-kanak, dengan kejadian di seluruh dunia 2.11 setiap 1000 kelahiran hidup. Kanak-kanak CP biasanya mengalami kecacatan kongenital seperti '*scoliosis*' dan kontraksi. Oleh itu, untuk mengukur ketinggian sebenar kanak-kanak CP dalam keadaan berdiri adalah sukar dan mencabar. Kajian telah mencadangkan formula persamaan ramalan ketinggian berdasarkan panjang segmen (SL), iaitu ketinggian lutut (KH), panjang tibia (TL), dan panjang lengan atas (UAL) boleh digunakan sebagai kaedah alternatif untuk mengukur ketinggian sebenar. Ketinggian berdiri dan panjang *'Recumbent'* (RL) menjadi piawaian utama untuk pengukuran ketinggian sebenar. Walau bagaimanapun, formula persamaan ramalan ketinggian yang sedia ada belum diuji di kalangan kanak kanak CP di Malaysia. Kajian kajian sebelum ini yang membangunkan formula persamaan ketinggian hanya melibatkan populasi dan umur tertentu, dan tidak termasuk semua tahap *'Gross Motor Function Classification System'* (GMFCS). Oleh itu, kajian ini bertujuan untuk membangunkan dan mengesahkan formula persamaan ramalan berdasarkan KH, TL, dan UAL untuk kanak-kanak CP di klinik pediatrik pesakit luar dan Pusat Pemulihan Komuniti (CBR) di Wilayah Tengah dan Selatan Malaysia. Kajian ini adalah 'kajian keratan rentas' yang melibatkan dua fasa di mana Fasa 1 adalah penilaian empat belas formula persamaan yang sedia ada dan juga penghasilan formula persamaan baru bagi menganggar ketinggian. Fasa 2 adalah pengesahan dan validasi formula persamaan baru yang dibina dalam Fasa 1. Kajian ini dijalankan dari Ogos 2018 hingga Disember 2019. Subjek kajian ini adalah kanak-kanak CP dengan SGMFCS I – V, berusia 2 hingga 18 tahun. Kanak-kanak CP yang mengalami cirit-birit akut, muntah berpanjangan, dan penyakit perubatan atau kecacatan lain seperti sindrom down akan dikecualikan. Subjek

telah dikategorikan ke dalam Kumpulan Pembangunan Persamaan Fasa 1 (EDG) dan Kumpulan Rentas Pengesahan Fasa 2 (CVG). Bagi EDG, sebanyak 177 subjek telah diambil dari enam klinik pediatrik pesakit luar. Subjek ini terdiri daripada. 23.7% adalah GMFCS tahap I, 14.1% GMFCS tahap II, 5.7% GMFCS tahap III, 5.7% tahap IV, dan 50.8% tahap V. Bagi CVG pula, seramai 139 subjek telah direkrut dari 18 Pusat Pemulihan dalaman Komuniti (CBR). Subjek bagi CVG melibatkan 15% GMFCS tahap I, 23% tahap II, 14% tahap III,14% tahap IV and 73% tahap V. Kanak kanak dari kedua fasa ini adalah terdiri daripada kawasan tengah dan selatan Malaysia. Pembolehubah bebas (IV) dalam kajian ini adalah KH, TL, UAL, dan umur manakala pembolehubah bergantung (DV) dalam model ini adalah ketinggian berdiri dan RL. Ketinggian berdiri ditentukan menggunakan stadiometer. Sekiranya kanak kanak CP tidak dapat berdiri, panjang segmen badan telah diambil menggunakan prosedur standard. Pita pengukur Seca yang fleksibel digunakan untuk mengukur panjang dan segmen semua peserta. Dalam Fasa 1, 14 formula persamaan sedia ada yang telah dibangunkan dari kajian terdahulu dari tahun 1994 hingga 2003 telah diuji. Persamaan yang telah dipilih adalah berdasarkan ketinggian lutut, panjang tibia, dan panjang lengan atas. Populasi kajian sebelumnya adalah terdiri daripada kanak – kanak CP dan kanak kanak yang normal di Amerika Syarikat, Australia, China, dan Jepun. Dalam Fasa 1, berdasarkan analsis ujian Bland Altman, semua empat belas persamaan sedia ada (Eq1-Eq14) menunjukkan perjanjian yang lemah dengan ketinggian sebenar subjek CP. Oleh itu, Enam model persamaan ramalan baru telah dibangunkan menggunakan regresi linear berganda. Model regresi ini dibangunkan menggunakan panjang segmen KH, TL, dan UAL yang berada dalam Model 1 KH, Model 3TL, dan Model 5 UAL. Formula persamaan yang mengambilkira umur sebagai faktor kovariat untuk setiap panjang segmen dalam Model 2 KHA, Model 4 TLA, dan Model 6 UALA juga telah dibangunkan. Kovariat lain seperti jantina dan bangsa tidak dimasukkan dalam model ini kerana demografi analisis menunjukkan tidak signifikan dengan pengukuran tinggi di kalangan CP.Persamaan berasaskan KH baru termasuk Model 1KH: $_{Y1}$ = 22.54 +2.679 KH dan Model 2KHA: $_{Y2}$ = 31.5 + 2.11 KH + 1.228A. Model formula persamaan baru berdasarkan TL adalah Model 3TL: $_{Y3}$= 32.18 + 3.139 TL dan Model 4TLA: $_{Y4}$ = 39.905 + 2.417 TL+ 1.31 A. Akhir sekali, Model 5UAL: Y5 = 20.469 +3.83 UAL dan Model 6UALA: Y6 = 33.15 + 2.771 UAL + 1.55A adalah berdasarkan UAL. Dalam Fasa 2, kesemua enam model baru telah disahkan secara ‘cross validation’ untuk mengesahkan penggunaan formula persamaan ramalan. Model 3TL menunjukkan ralat standard terendah (SE), iaitu 1.42 berbanding model lain. Analisis pekali intra-korelasi (ICC) menunjukkan perjanjian yang kukuh antara ketinggian sebenar dan anggaran untuk semua model kecuali Model 1KH dan Model 2KH (0.58). Selain itu, Model 3TL: Y3 = 32.18 + 3.139 TL menunjukkan korelasi yang kuat dengan ketinggian sebenar (^{R2} = 0.834) dan menunjukkan SE yang rendah (1.42) dan ICC tinggi (0.929). Kesimpulannya, enam persamaan baru telah dibangunkan di Fasa 1. Semua model baru telah disahkan dan divalidasi dalam Fasa 2 untuk memastikan ketepatan dan kebolehpercayaan model dalam populasi CP. Semua formula formula persamaanbaru adalah sah untuk digunakan dalam populasi CP Malaysia, bagaimanapun, keputusan pengesahan menunjukkan bahawa Model 3TL adalah formula persamaan ramalan panjang segmen yang paling sesuai untuk digunakan dalam menganggarkan ketinggian kanak-kanak CP berusia dua hingga 18 tahun. Kajian lanjut formula persamaan baru untuk subjek CP di semua wilayah di Malaysia diperlukan supaya penggunaannya dapat diperluaskan secara umum kepada semua kanak kanak CP dalam populasi Malaysia.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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Declaration by Members of Supervisory Committee

This is to confirm that:

- The research conducted and the writing of this thesis was under our supervision;
- Supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

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ARDS	Acute Respiratory Distress Syndrome
AS	Arm Span
BIA	Bioelectric Impedance Analysis
BMI	Body Mass Index
BSA	Body Surface Area
C4D	CBR 4 Division
CAG	CBR Alor Gajah
CBB	CBR Bukit Baru
CBK	CBR Bakri
CBR	Community Rehabilitation Centre
CDC	Centers for Disease Control and Prevention
CG	CBR Gombak
CK	CBR Kajang
CKT	CBR Kem Terendak
CHK	CBR Hulu Klang
CM	CBR Meru
CKS	CBR Klang Selatan
CNI	CBR Nur Iman
CML	CBR Malindo
CNL	CBR Nilai
CP	Cerebral Palsy
CPP	CBR Puchong Perdana
CPY	CBR Penyayang
CS	CBR Semenyih
CSA	CBR Shah Alam
CSB	CBR Seremban
CSN	CBR Senawang
CTG	CBR Tangkak
CV	Coefficient of Variation
CVG	Cross Validation Group
DXA	Dual Energy X-ray Absorptiometry

EDG	Equations Development Group
FFM	Fat Free Mass
GERD	Gastroesophageal Reflux Disease
GFR	Glomerular Filtration Rate
GMFCS	Gross Motor Function Classification System
HKL	'Hospital Kuala Lumpur'
HM	'Hospital Melaka'
HPSF	'Hospital Pakar Sultanah Fatimah'
HTJS	'Hospital Tuanku Ja'afar Seremban'
ICC	Intra Correlation Coefficient
ICU	Intensive Care Unit
KH	Knee Height
KHA	Knee Height and Age
KKM	'Kementerian Kesihatan Malaysia'
LLL	Lower Leg Length
LOA	Limit of Agreement
MLR	Multiple Linear Regression
NMRR	National Medical Research Registration
PBW	Predicted Body Weight
REE	Resting Energy Expenditure
RL	Recumbent Length
SE	Standard Error
SL	Segmental length
SEE	Standard Error of The Estimate
SEM	Standard Error Measurement
SFT	Skinfold Thickness
SMM	Skeletal Muscle Mass
TEE	Total Energy Expenditure
TL	Tibia Length
TLA	Tibia Length and Age
TSF	Triceps Skinfold
UAL	Upper Arm Length
UALA	Upper Arm Length and Gender
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

1.1 Background

Cerebral Palsy (CP) involves a group of chronic movement and posture disorders caused by a non-progressive lesion in an immature brain (Sadowska et al., 2020). It is the most common cause of physical disability in children, with a worldwide incidence of 2.11 per 1000 live births (Oskoui et al., 2013). The prevalence of CP among Asian babies was 1.09 per 1000 live births (Lang et al., 2012). In Malaysia, 12.9% of CP cases were associated with disabilities (Tan & Yadav, 2008) such as mental retardation, visual and hearing impairments, speech and language disorder, and oral motor dysfunction (Araújo & Silva, 2013).

CP can be classified based on levels of motor functions using the Gross Motor Function Classification System (GMFCS). It is a classification system that describes the gross motor function of CP children based on their self-initiated movement on sitting, walking, and wheeled mobility. The GMFCS consists of five levels (I, II, III, IV, and V) with the lower levels corresponding with mild CP and the higher levels indicating severe CP.

Physical growth is essential to determine nutritional status. Physical growth can be reflected by weight or height measurement. However, CP children with motor impairments are predisposed to a high risk of malnutrition. Therefore, CP children often suffer from poor growth due to common nutritional problems such as dysphagia, gastroesophageal reflux, swallowing disorder, vomiting, and chronic constipation, all of which can affect nutritional intake (Calis et al., 2008; Sullivan et al., 2000). Nutritional problems can lead to serious adverse health consequences, especially undernutrition which poses a significant burden on the affected children, families, and society. Additionally, delayed diagnosis of malnutrition may increase the risk of mortality among CP subjects. (Rempel, 2015) A study on the height centile distribution of CP subjects reported that 4.8% of boys and 5.3% of girls in the study were below the 10th percentile of height. Nearly half (47.7%) of male CP children and three-quarters (78.9%) of the females were below the 50th percentile of height (Tomoum et al., 2010). Furthermore, another recent study showed that as high as 80% of CP children in Malaysia were underweight (Rajikan et al., 2017).

Anthropometric measurements can be used to assess CP's nutritional status. According to a scoping review, the anthropometry assessments included weight, height, body composition, and the use of segmental in predictive equations. This study compares the various anthropometry measurements in CP children.

Body composition can be calculated using dual-energy X-ray absorptiometry (DXA), bioelectrical impedance (BIA), or triceps skinfold (TSF) or subscapular skinfold measurements (SFT). TSF was easily measured without causing the CP children any discomfort, but it generally underestimated fat stores because CP causes fat to be stored primarily in the central part of the abdominal cavity. These SFT measurements, however, were not reliable when used alone. Because DXA is expensive, there is a need for a less expensive and more dependable technique, such as anthropometry and BIA. BIA is not only inexpensive, but it is also easy to transport and use in assessing fat stores in children with cerebral palsy (Mokhy et al., 2020).

Height measurement is a vital indicator of nutritional status and growth among children. CP subjects often have poor growth. Standing height or recumbent length (RL) is a gold standard to measure height among children including CP children. However, height assessment in this population is difficult due to several factors such as scoliosis, muscle weakness, spasticity, contractures, bone deformities, lack of subject cooperation, and involuntary movement (Hogan, 1999). Direct measurement of recumbent length or height may be inaccurate and unreliable in children and adults with disabilities such as CP. A study highlighted the inability to obtain the height measurement of more than half of the CP children (52.0%) either through recumbent length or direct measurement (Stevenson, 1995a). Furthermore, the more severe the level of CP (IV and V), the more difficult it is to measure the height of the subject.

A scoping review study shows that predictive equations are the most preferred method to be used to estimate height in CP children (Mokhy et al., 2020). These predictive equations use segmental length (SL) as a reference technique used for height assessment. Even though this technique requires specialised equipment and expertise, it is quick and easy to perform in the clinical setting (Bell et al., 2012; Bell & Davies, 2006). Different SLs such as upper arm length (UAL), ulna length, forearm length, knee height (KH), and tibia length (TL) have been proposed as alternative methods to solve the difficulties in obtaining standing height measurement (Bell & Davies, 2006; Samson-Fang & Bell, 2013). Some researchers developed equations for normal healthy children to measure their segmental height to estimate actual height especially when they were bedridden or amputated.

KH is easy to measure and it has the smallest standard error based on previous studies in United States by Stevenson, 1995 and Chumlea, 1994. It is also the most useful measurement when using a segmometer (Stevenson, 1995). The first study to develop a prediction equation among CP children was in the United States by Stevenson, and he used a segmometer as a tool to measure KH. Studies by Stevenson et al. (1995) showed that height measurement using KH correlated with the stature or length of CP children (r=0.98). Another study by Hogan et al. (1999) echoed this and also found that direct measures of recumbent length were significantly correlated with indirect measures calculated using KH prediction equations (r=0.88). Apart from that, TL is another measurement that can be easily performed with a measuring tape. TL is a reliable index of bone growth and it may also be used as a proxy for stature and height assessment. It can also be estimated among CP subjects with lower limb joint contracture or scoliosis (Kihara et al., 2015).

In addition to using SL as a proxy for a predictive equation when assessing nutritional status, the estimated height obtained from the SL predictive equation can be directly compared with growth charts such as the standard reference growth chart by WHO/CDC or the specific growth chart for CP children. Plotting anthropometric measurements (height/ stature, weight) on the reference growth chart is a fast and effective way to identify any nutritional problems or health concerns (Day et al., 2012).

In summary, height measurement is crucial for clinical assessment and health monitoring, especially in CP children. This study aimed to compare the existing predictive equations used to estimate height among the CP population in Malaysia in previous research and to develop new equations. The validity of the new equation to estimate height would be determined by comparing the estimated height calculation using the new equation with actual height or recumbent length measurement. Standing height and RL measurement are used as the reference technique or gold standard for measuring heights among CP children.

1.2 Problem Statement

Growth and anthropometric assessments are essential to determine nutritional status. Children with CP, especially those with moderate to severe CP, are predisposed to poorer health status and malnutrition (Herrera et al., 2016). General anthropometry measurements including BIA, TSF, SFT, height, and weight are some of the essential measurements to determine if the child suffers from malnutrition. However, it is challenging to obtain the height measurement among CP children because they often have joint contractures and scoliosis, thus making them unable to stand straight (Finbråten et al., 2015).

Several alternative approaches have been proposed to estimate the height of CP children who are unable to stand. This includes measuring SL such as KH, TL, and UAL that are later used as a proxy in the alternative equation to estimate height.

In an earlier study in the United States, involving 172 CP children, aged 2 – 12 years old, Stevenson (1995) developed alternative equations based on KH, TL, and UAL. The gold standard in this study was actual height and RL. Although the correlation coefficient of the equation was good (KH: R=0.98, TL, and UAL: R= 0.97) some limitations remained. Firstly, the study only included diplegia and hemiplegia subjects between 2-12 years old. Diplegia is a form of paralysis that affects similar body parts on both sides of the body, such as both legs or arms. While hemiplegia involves the loss of movement and sensation on one side, meaning that a patient's right arm and right leg may be the only areas affected. Secondly, existing equations by Stevenson (1995) were also reliable and valid to be used only among CP children aged 2-12 years. Thus, it is questionable whether it is reliable to be used for CP children above 12 years old.

As the GMFCS growth chart is designed for children aged 2-20 years, it is vital to obtain accurate estimated height measurements among this population that can be used for plotting the GMFCS growth chart. To date, there is no available equation that can be used to estimate height for CP children between 2 and 18 years of age that is useable for the GMFCS growth chart.

Even though Chumlea et al. (1994) developed an equation to estimate height by using KH, it was mainly used for children aged 6-18 years with healthy development. Chumlea develops an equation for healthy children that can be used for clinical assessments for children who cannot ambulate due to amputation or critically ill children. Furthermore, the Chumlea equations were only based on age and sex and it catered only to children of Caucasian and African ethnicities. Another equation that incorporates age and sex in the equation to estimate height for CP was developed by Gauld et al. (2004). As this equation is meant for children aged 5-19 years, thus it can be used in children above 12 years old. However, it was developed based on healthy children and adolescents in Australia. In Asia, the predictive equation to estimate height was developed among 3647 healthy Chinese children between 3 to 18 years old (Cheng et al., 1998). The predictive equation to estimate height among healthy children that had been developed may not be suitable and accurate for CP children especially for those in levels III, V, and IV. Hence there is a need to develop a predictive equation that can be applied to all levels CP children

Apart from that, studies have also highlighted that racial and ethnic differences can significantly affect anthropometric measurements. One study found that the equation derived from healthy adolescents was not accurate when applied to CP adolescents (Bell et al., 2012). Another study showed that equations derived using a taller population sample (e.g., American Caucasians and Australians) may not be accurate for the shorter Asian population (Shahar & Pooy, 2003).

One large retrospective cohort study in California among 629,542 Asians and 2,109,550 Whites from 1991-2001 investigated demographic factors that influence the risk factor of CP. CP prevalence was lower in Asians than whites (1.09 vs 1.36 per 1000 lives). The study adjusted the maternal age and education, infant gender, and birth weight, however, the risk of CP remained lower in East Asians and this disparity is unexplained. (Lang et al., 2012)

As for SL, a recent study shows that TL demonstrated good intra- and inter-rater reliability and equations using TL have been developed among CP and normal healthy children (Kihara et al., 2015). However, this equation was only suitable for children aged 3-12 years with moderate to severe CP. Moreover, the data were mainly derived from Japanese children in a single center. Thus, these equations may not apply to non-Japanese ethnic groups and further research is warranted (Kihara et al., 2015). One contributing factor that may affect the difference between the Japanese population and other Asian race was Japanese mothers have the highest education which affects the social support for CP growth (Lang et al., 2012; Touyama et al., 2013). Another study also found that Japanese children were shorter than Chinese (Yin et al., 2020). Research suggests that child growth differs among ethnic groups due to genetic factors and environmental factors. Child growth differs among Asian countries. Chinese and Taiwanese children are not smaller than children in Western countries, but Japanese children do tend to be smaller than their Asian and Western counterparts (Kato et al., 2014)

It can be concluded that predictive equations for the CP population are still limited, and the available equations may not be applicable for all ethnicities/nationalities. Furthermore, the existing equations cover a wide range of age groups and special instruments such as segmometers and knee calipers, which can be expensive and are not always available in health care facilities.

CP is a pathological condition that can impair growth in moderately to severely affected children. Before the growth chart for CP children was developed, weight and height centiles were used to assess the development. The classification ranged from fully ambulatory, unable to walk, crawl, or feed themselves, to being fed through a gastrostomy tube and it was performed according to age, gender, and five levels of functional ability (Day et al., 2007).

Based on the Gross Motor Function Classification System (GMFCS), children in levels IV and V (severe) had shorter stature and lower weight than their peers (Rempel, 2015). Stevenson (1995) developed an equation based on UAL, TL, and KH among children with CP up to the age of 12 years old without involving the GMFCS classification. However, it may not suitable equation because it is not applicable for individuals with scoliosis or contractures (Haapala et al., 2015b).

Palisano et al. (1997) pioneered the design of a gross motor function classification system for children with CP that was similar to the staging and grading systems used in medicine to describe cancer and tumor staging. In addition, a review also outlined the concepts and practices in the creation and validation process of the GMFCS, besides reflecting on the development of an ordered, valid, and reliable system to identify the functions of children and adolescents with developmental differences (Rosenbaum et al., 2008).

The GMFCS classification system has been validated and widely used globally. However, the methods to measure stature by Stevenson (1995) for diplegic and hemiplegic CP children have not been established by GMFCS level as this GMFCS level classification only been introduced in 2011. As a result, the current existing predictive equations for CP stature have been established based on the GMFCS standard. Kihara et al. (2015) developed a predictive equation based on TL for growth assessments of CP children, however this equation only in GMFCS levels I, II, and II, aged 3 to 12 years old.. For GMFCS levels I and II, the height estimation can be obtained by standing height however in certain cases such as amputated and critically ill CP patients, height estimation is needed. Therefore, there is a need to develop an equation for height estimation that can be used for all GMFCS levels. This equation will be important in the establishment of a height-for-age growth chart for CP children that have been stratified by the GMFCS level.

This study aimed to compare the existing predictive equations and to determine the best equations to estimate the height of the CP population in Malaysia. We anticipated that all the existing equations would have certain limitations, thus we would develop and validate new equations that are relevant for all GMFCS levels and suitable for CP children aged 2–18 years in Malaysia. To date, this represented the first study to develop and validate predictive CP equations for all GMFCS levels to be used as one of the key anthropometric assessment tools among CP children in Malaysia.

1.3 Significance of the Study

Assessment of physical growth is important to determine the health status of children. It is also used by the physician to screen the endocrine system and general health. In severe brain damage cases, such as cerebral palsy, the neurotransmitter pathways involved in GH control may be impaired, affecting the hormone's normal secretion. 70% of CP children have low levels of growth hormones, which may impair their physical development. (Devesa & Casteleiro, 2010; Uday et al., 2017)

Accurate and appropriate estimation of height is essential as height is an indicator of the nutritional status and energy requirement of children (Bell & Davies, 2006). In Malaysia, 54.5% CP children were spastic quadriplegia and 87% were disabled, making height measurement is difficulty to measure (Zainah et al., 2001). 80% CP children in Malaysia underweight and 60-70% had feeding problems that affect the nutritional status (Rajikan et al., 2017; Zainah et al., 2001) Height and length measurements are frequently used along with body weight to evaluate nutritional status in the clinical setting (Hickson & Frost, 2003). Therefore, this study is essential to provide an accurate anthropometry assessment as part of the clinical assessment of the subject's nutritional status.

Besides, nutritional status is also important in the detection of undernutrition among CP children. It is crucial to detect any deterioration in nutritional status as early as possible so that appropriate dietary intervention can be taken immediately to prevent severe malnutrition. The earlier the malnutrition diagnosis is made, the greater the likelihood of survival due to the maximum opportunity for children to thrive (Kuperminc & Stevenson, 2008).

To apply prediction equations in a particular population, the equations must meet the empirical standards in the assessed culture so that they will be providing accurate quantification of the values of interest. Otherwise, it may lead to an under-or overestimation of the values. Such errors of measurement can be misleading to diagnoses and management plans (Karlijn Van et al., 2008). Furthermore, it is especially important to develop and validate inexpensive and simple tools to estimate the height of children with CP and to serve as a marker of nutritional adequacy since single anthropometric measures are a poor predictor of body fat percentage for children with CP (Gurka et al., 2010).

The outcome of this study will produce validated equations that can be used by the health professionals in Malaysia and nearby regions to accurately assess the nutritional status of CP children. This new prediction equation among CP children will be the first prediction equation that is developed in the Malaysian population. With proper assessment, nutritional intervention can be provided promptly to the vulnerable CP population to address their nutritional issues for them to grow and develop optimally. This prediction equation will be useful in the dietetic field to estimate height among CP children, not only in in-patient but also in out-patient and home visits. This prediction equation will make the nutritional assessment easy and fast. No expensive special equipment or instruments are needed in performing this prediction equation.

1.4 Research Questions

a) Is there a difference in between anthropometric measurements in CP such as? height, KH, TL, UAL and age, gender and races.
b) Are existing predictive equations valid and reliable to estimate height for 2-18 years old children with CP in Malaysia?
c) Which predictive equation is the most suitable and accurate to determine height among 2-18 years old children with CP in Malaysia?
d) Are the new equations to estimate height among 2-18 years old children with CP in Malaysia reliable and valid?
e) Can the new equations be used to determine heights for children with CP in all GMFCS levels?

1.5 Objectives

1.5.1 General Objectives

To develop and validate segmental length equations to estimate heights among 2-18 years old CP children in the Southern and Central Region of Malaysia.

1.5.2 Specific Objectives

The specific objectives of the study included:

Phase 1: Preliminary data collection, assessment of existing equations, and development of new equations among Equation Development Group (EDG)

1. To determine the anthropometric differences according to gender, age, race and level of GMFCS groups among CP Children.
2. To compare the accuracy between existing predictive equations and height measurement to estimate height for subjects.

3. To determine the agreement between actual height or segmental length and estimated height from existing equations among subjects.
4. To develop new predictive equations to estimate height among subjects.

Phase 2: Validation of new equations among CP children based on preliminary data among the Cross -Validation group (CVG)

1. To determine the anthropometric differences according to gender, age, race and level of GMFCS groups among CP Children.
2. To validate the new equations to estimate height for subjects using cross-validation.
3. To determine the most suitable equations to estimate height among subjects.

1.6 Hypotheses

H1. There are significant differences in anthropometric measurements in CP such as height, KH, TL, UAL and age, gender and races
H2. Existing predictive equations are not valid to estimate height for 2-18 years old children with CP in Malaysia
H3. New predictive equations to estimate height among 2-18 years old children with CP in Malaysia reliable and valid
H4. New equations predictive equations can be used in all GMFCS levels.

1.7 Conceptual Framework

According to the previous study, SL has a significant relationship with height estimation in CP. KH, TL, and UAL were the three variables that were reliable and reproducible (Cheng et al., 1998; Chumlea et al., 1994; Kihara et al., 2015; Stevenson, 1995b) The predicted height can be calculated using the prediction equation based on the SL. In some CP children who are unable to stand, the actual and RLs will be calculated using the predicted height measurement. Factors associated with the prediction equation model included segmental length and age. Other factors included GMFCS level, dietary intake, epilepsy and medical chronic illness. Figure 2.2 depicts the conceptual framework for the relationship between variables and estimated actual height in children with CP. In this study we developed new predictive equation in Phase 1 to estimate height using SL (KH, TL and UAL) and age as additional covariate among CP children. Then the new equation were be validated in Phase 2.

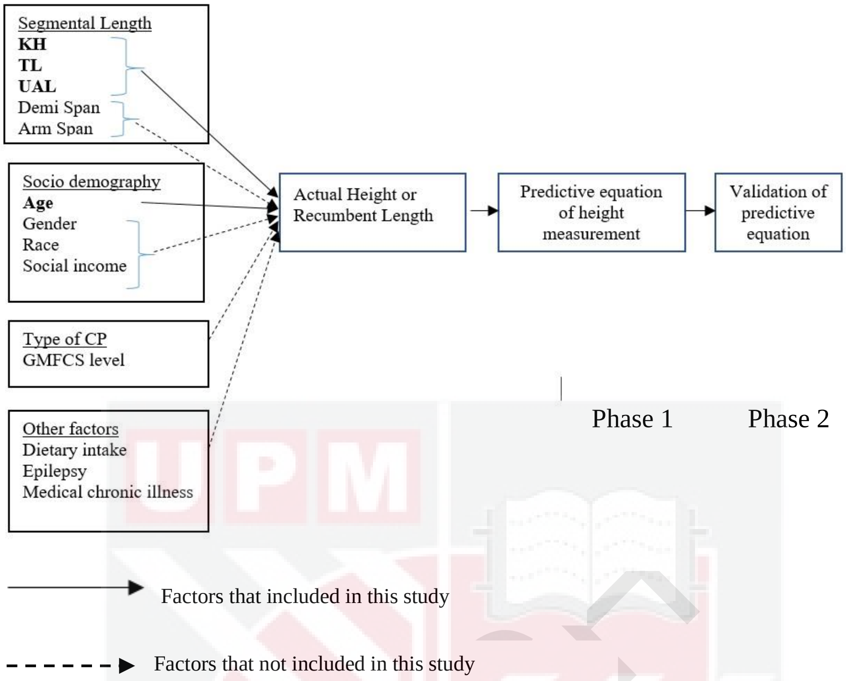

Figure 1.1: Conceptual Framework

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