The predictive validity of Hammersmith Infant Neurological Examination versus Prechtl's General Movement Assessment with the Motor Optimality Score on gross motor outcomes in high-risk infants at 12-15 months corrected age: a descriptive study

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DECLARATION

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ABSTRACT

BACKGROUND

Advances in neonatal and maternal care have caused an increase in survival rate of high-risk infants, however with increased risk for developing adverse neurodevelopmental outcomes such as cerebral palsy (CP). Evidence supports the predictive value of Prechtl's General Movement Assessment (GMA) with Motor Optimality Score (MOS), and the Hammersmith Infant Neurological Examination (HINE) for CP outcome before 5 months corrected age. Exploring usefulness of these measures and understanding how these two compare in predicting gross motor outcome in high-risk infants may enable earlier referrals for all and not just those at risk for developing CP.

OBJECTIVE

To compare the predictive validity of the HINE versus Prechtl's GMA with MOS (measured at 11-16 weeks corrected age) for determining the gross motor outcomes in high-risk infants at 12-15 months corrected age as measured by the Alberta Infant Motor Scale (AIMS).

METHODOLOGY

A longitudinal descriptive study was conducted at Tygerberg Children's Hospital (TCH). All high-risk infants assessed at 11-16 weeks corrected age using Prechtl's GMA with MOS and HINE and whose parents consented to participation were re-evaluated using the AIMS to determine their gross motor outcome at 12-15 months corrected age. Data was analysed using STATA version 16 and IBS SPSS software. HINE and Prechtl's GMA with MOS cut-off scores were determined and ROC curve analysis utilised to determine sensitivity and specificity values for both measures.

RESULTS

The study enrolled 100 infants with a mean birthweight of 1525.6g and a mean gestational age of 31.1 weeks. Fifteen infants scored <5th percentile on the AIMS at 12-15 months corrected age and seven infants were suspected to have CP. The HINE

with a sample specific cut-off score of 62.5 had an area under the curve (AUC) of 0.867 to predict gross motor delay with sensitivity of 87% and specificity of 81%, and positive predictive value (PPV) of 45%, negative predictive value (NPV) of 97%. Prechtl's GMA with the MOS had AUC=0.713 with sensitivity of 47% and specificity of 100%, and PPV of 100%, NPV of 91%. The reflexes and reactions subcategory on the HINE, and the observed postural patterns and fidgety movements subcategories on the MOS were predictive of gross motor outcome. Both HINE and GMA with MOS total scores were more predictive of gross motor outcome than subcategory scores or single items.

CONCLUSION

The results of this study indicate that both the HINE and Prechtl's GMA with MOS are valid measures for predicting gross motor delay as determined by the AIMS in high-risk infants. The HINE, however, is more sensitive to predict gross motor delay than the GMA with MOS. The HINE showed lower PPV to predict gross motor delay compared to the GMA with MOS, however NPV values for both were similar. For both measures total scores were more predictive of gross motor outcome than subcategory or single item scores. The results of our study suggest either HINE or GMA with MOS total scores be used to predict gross motor outcome. However due to small sample size and recruitment from one site this topic warrants further research.

ABSTRAK

AGTERGROND

Vooruitgang in neonatale en moederlike sorg het gelei tot ‘n hoër oorlewingskoers van hoë-risiko babas, maar hierdie babas het steeds ‘n verhoogde risiko vir ongewensde neuro-ontwikkelings uitkoste soos serebrale gestremdheid (SG). Literatuur ondersteun die voorspellende geldigheid van Prechtl se Algemene Bewegings Assessering (GMA) met die Motor Optimaliteit Telling (MOS) en die Hammersmith Baba Neurologiese Assessering (HINE) vir die uitkoms van SG voor 5 maande gekorrigeerde ouderdom. Dit is belangrik om die gebruiklikheid van hierdie twee assesserings te ondersoek en te verstaan hoe dit vergelyk om grof motoriese uitkomste te voorspel.

UITKOMSTE

Om die voorspellende geldigheid van die HINE teen Prechtl se GMA met die MOS (gemeet by 11-16 weke gekorrigeerde ouderdome) om grof motoriese uitkomste van hoë-risiko babas by 12-15 maande gekorrigeerde ouderdom volgens die Alberta Baba Motor Skaal (AIMS) te bepaal.

METODOLOGIE

‘n Longitudinale beskrywende studie is uitgevoer by Tygerberg Kinder Hospitaal (TCH). Alle hoë-risiko babas geasseseer met Prechtl se GMA met die MOS en die HINE by 11-16 weke gekorrigeerde ouderdom, en wie se ouers toestemming gegee het tot deelname in die studie, is her-evalueer deur die AIMS om hulle grof motoriese vaardigheid by 12-15 maande gekorrigeerde ouderdom te bepaal. Data is geanaliseer deur STATA weergawe 16 en IBS SPSS sagteware te gebruik. HINE en Prechtl se GMA met die MOS afsny-punte is bepaal en ROC kurwe analise is gebruik om sensitiwiteit en spesifisiteit waardes te genereer.

RESULTATE

Een honderd babas met ‘n gemiddelde geboortegewig en gestationele ouderdom van onderskeidelik 1525.55g en 31.14 weke is ingesluit in die studie. Vytien babas het by 12-15 maande gekorrigeerde ouderdom <5de persentiel op die AIMS behaal, en sewe

babas is voorwaardelik met SG gediagnoseer. Die HINE, met ‘n afsny-punt van 62.5 het ‘n area onder die kurwe (AUC) van 0.867, sensitiwiteit van 87%, spesifisiteit van 81%, positive voorspellende waarde (PPV) van 45% en negatiewe voorspellende waarde (NPV) van 97% gehad om grof motoriese uItkomste te voorspel. Prechtl se GMA met die MOS het ‘n AUC=0.713, sensitiwiteit van 47%, spesifisiteit van 100%, en PPV en NPV van 100% en 91% gehad. Die reflekse en reaksies subkatagorie van die HINE en die geobserveerde postural patrone en woelige bewegings subkatagorieë van Prechtl se GMA met die MOS was die mees voorspellend van motoriese uitkoms, Beide die HINE en die MOS totale puntetellings was meer voorspellend van grof motoriese uitkoms as subkatagorieë of enkele items.

GEVOLGTREKKING

Die resultate van hierdie studie wys dat beide die HINE en Prechtl se GMA met die MOS geldige assesserings is om grof motoriese uitkomste volgens die AIMS te voorspel in hoë-risko babas. Die HINE is egter meer sensitief as die GMA met die MOS. Die HINE het laer PPV gehad om grof motoriese uitkomste bepaal as die MOS, maar NPV vir beide assesserings was eenders. Vir albei asseserings was die totale puntetellings meer voorspellend van grof motoriese agterstand as subkatagorieë of enkele items. Die resultate dui daarop dat beide die HINE en GMA met MOS assesserings gebruik kan word om grof motoriese uitkomste te bepaal. As gevolg van die klein steekproefgrootte, en beperkte werwings ligging, verg hierdie onderwerp verdere navorsing.

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GLOSSARY

Definitions and terminology

Area under the curve

Statistical measurement obtained from a receiver operating characteristic (ROC) curve. The area under the curve (AUC) is defined as the average value of sensitivity for all the possible values of specificity (Hajian-Tilaki, 2013). An optimal AUC=1.00 (Hajian-Tilaki, 2013).

Chronological age

The time that has passed since birth expressed in days, weeks, months and/or years of age (Blackmon, Batton, Bell, Denson *et al*., 2004).

Corrected age

Age of a child/infant from expected date of delivery. It is calculated by subtracting the number of weeks an infant was born preterm/premature (before 40 weeks of gestation) from the chronological age. As an example: if an infant is now 24 months old and was born at 28 weeks gestational age (thus 12 weeks premature), the corrected age is 21 months: 24 months – [(40 weeks – 28 weeks) x 1 month/4 weeks] (Blackmon *et al*., 2004).

Extremely low birth weight (ELBW)

A birthweight of ≤1000 grams that includes up to and 999 grams (Cheong, Spittle, Burnett, Anderson *et al*., 2020).

Gestational age

The time that has elapsed between the first day of a woman's last menstrual cycle and the day of delivery/birth. This definition can be used to calculate the expected date of delivery of an infant (Blackmon *et al*., 2004).

Post-menstrual age

The time elapsed between the first day of the last menstrual cycle and birth of the infant, plus the time that has elapsed after birth (infant's gestational age). Described in number of weeks (Blackmon *et al*., 2004).

Validity

The extent to which an assessment/tool measures what it is intended to measure, or the extent to which a concept is measured accurately (Heale & Twycross, 2015).

Preterm birth/prematurity

Infants born alive prior to 37 weeks completed gestation or fewer than 259 days since the first day of a woman's last menstrual period. Preterm births can be further classified as extremely preterm (<28 weeks gestation), very preterm (28 to <32 weeks gestation) and moderate to late preterm (32 to <37 weeks gestation) (WHO, 2012).

Very low birthweight (VLBW)

A birthweight of ≤1500 grams, including and up to 1499 grams (Pascal, Govaert, Oostra, Naulauers *et al.*, 2018).

Acronyms and abbreviations

ADHD: Attention deficit hyperactivity disorder

AIMS: Alberta Infant Motor Scale

ATNR: Asymmetric tonic neck reflex

AUC: Area under the curve

CA: Corrected age

CMV: Cytomegalovirus

CP: Cerebral palsy

DCD: Developmental coordination disorder

ELBW: Extremely low birth weight

EPT: Extremely preterm

FAS: Foetal alcohol syndrome

FMs: Fidgety movements

GMs: General movements

GMA: General Movement Assessment

GMFCS: Gross Motor Function Classification System

HIE: Hypoxic-ischemic encephalopathy

HINE: Hammersmith Infant Neurological Assessment

HIV: Human immunodeficiency virus

HNNE: Hammersmith Neonatal Neurological Examination

HREC: Health Research Ethics Committee

ICC: Intraclass correlation coefficient

IUGR: Intrauterine growth restriction

IVH: Intra-ventricular haemorrhage

MOS: Motor Optimality Score

MRI: Magnetic resonance imaging

NICU: Neonatal intensive care unit

NPV: Negative predictive value

NVD: Normal vaginal delivery

PCR: Polymerase chain reaction

PI: Principal investigator

PPE: Personal protective equipment

PPV: Positive predictive value

PVL: Periventricular leukomalacia

RDS: Respiratory distress syndrome

ROC: Receiver operating characteristic

TBM: Tuberculosis meningitis

TCH: Tygerberg Children's Hospital

US: Ultrasound

VLBW: Very low birth weight

VPT: Very preterm

WHO: World Health Organization

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CHAPTER 1

INTRODUCTION

Worldwide, it is estimated that 11.1% of all births are preterm births, and advances in neonatal and maternal care have caused an increase in the survival rate of these infants (de Kleine, den Ouden, Kollée, lsen *et al*., 2007; Pascal, Govaert, Oostra, Naulauers *et al*., 2018). A recent meta-analysis estimated that 20.6% of very preterm born infants (28–31 weeks gestational age), and 44.5% of extremely preterm born infants (<28 weeks gestational age) presented with motor delay at 2 years corrected age (Pascal *et al*., 2018). Neurodevelopmental diagnoses including cerebral palsy (CP) and disorders such as developmental coordination disorder (DCD), attention-deficit-hyperactivity disorder (ADHD), learning disabilities and language disorders have all been reported in premature born infants (Zwicker, 2014).

Prematurity is however not the only risk factor for neurodevelopmental delay in infants, and various perinatal factors and injuries can also cause neurodevelopmental impairment (Novak, Ozen & Burd, 2018). “High-risk” infants refer to those who are at greater risk for morbidity and mortality, and includes preterm born infants, very low birth weight (VLBW)(<1500g) and extremely low birth weight (ELBW)(<1000g) infants, infants with hypoxic-ischemic encephalopathy (HIE), infants with intraventricular haemorrhage (IVH), as well as sepsis and severe jaundice (Chattopadhyay & Mitra, 2015). A review published in 2018 reported 41% of included infants with HIE were diagnosed with CP and that 15% of these infants presented with some degree of developmental delay (Novak, Ozen & Burd, 2018). Literature suggests that CP is also prevalent in infants diagnosed with IVH, and that the prevalence increases with IVH severity with percentages ranging from 18% (grade III IVH) to 40% (grade IV IVH) (Novak, Ozen & Burd, 2018).

CP is defined as a ‘group of disorders affecting the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing foetal or infant brain’ (Bax, Goldstein, Rosenbaum, Leviton *et al*., 2005:571). Of all physical disabilities in children, CP is the most common (Novak, Morgan, Adde, Blackman *et al*., 2017). Over the past few decades, research has focussed on developing methods for earlier and more accurate prediction and

diagnosis of CP. The diagnosis of CP has historically only been made between 12-24 months of age, but experts have proposed that CP can now be accurately predicted prior to 6 months corrected age (Novak *et al*., 2017). This will enable earlier referral and may improve the outcome of these infants (Novak *et al*., 2017). Literature reports the prevalence of CP to be 2.1 cases per 1000 in high-income countries (Novak *et al*., 2017). The rate is higher in low- and middle-income countries (Novak *et al*., 2017). The most recent systematic review on the prevalence of CP in Africa estimated that the prevalence of CP in Africa is much higher (10 per 1000 in Southern Africa) than the 2-2.5 per 1000 as reported in high-income countries (Donald, Samia, Kakooza-Mwesige & Bearden, 2014). It is known that children in low- and middle-income countries have many contributing factors that may increase the risk of developing CP. In Africa, the diagnosis of CP is often delayed, as recognition of disability is most often noticed in older infants by parents or caregivers where routine follow-up is not provided (Donald *et al*., 2014). Early, accurate and time-efficient assessments are therefore needed, to timeously identify those infants at greater risk for neurodevelopmental delay and neurological deficits to ensure early referral for intervention. This is especially true in resource scarce settings and countries such as South Africa that has a struggling health system unable to provide equitable access.

There are currently only a few reliable assessment methods available for the diagnosis and early prognosis of severe neurological disorders in young infants. In a recently published systematic review, Novak *et al.* (2017) concluded that there is high quality evidence to support the predictive value of Prechtl's General Movement Assessment (GMA), Hammersmith Infant Neurological Examination (HINE) and neonatal magnetic resonance imaging (MRI) (sensitivity 98%, 90% and 86-89% respectively) for detecting CP in high-risk infants before 5 months corrected age (Novak *et al*., 2017). It is however costly to perform neonatal MRI's and poses various challenges such as possible need for sedation of the infant to obtain optimal imaging, and this in turn has its own medical risks. In the 1990s, Professor Heinz Prechtl and his colleagues developed a method to assess the developing young nervous system based on the observational assessment of spontaneous movement quality and called it Prechtl's General Movement Assessment (GMA) (Einspieler & Prechtl, 2005). The change in convention to utilise observational assessment of spontaneous movement quality rather than utilising clinical assessment techniques such as responses and reflex

testing, was a significant advance in the functional assessment of the immature nervous system (Einspieler & Prechtl, 2005). Prechtl's GMA is acclaimed for screening for neurological abnormalities due its high predictive power (Einspieler, Bos, Krieber-Tomantschger, Alvarado *et al*., 2019). Studies have reported specificity values ranging from 89-96% and sensitivity values between 95-98% for the prediction of CP (Einspieler *et al*., 2019). The excellent predictive power of GMA is mainly attributable to fidgety general movements, or in short fidgety movements (FMs), which appear from 9 weeks after term and is present till 20 weeks post-term age when voluntary, purposeful movements against gravity become more dominant.

Precthl's GMA has expanded to include the Motor Optimality Score (MOS) that allows assessment of postural patterns and age specific movements (Einspieler *et al*., 2019). The MOS uses scoring based on an optimality concept and is sensitive to detect subtle abnormalities or atypical motor behaviour (Einspieler *et al*., 2019; Salavati, Einspieler, Vagelli, Zhang *et al*., 2017). The MOS does not only allow for the classification of movements as "atypical" or "normal" but has the added benefit of allowing the clinician to assess the quality and quantity of the young infant's movement patterns (Einspieler *et al*., 2019; Salavati *et al*., 2017).

The use of Prechtl's GMA to predict severe neurodevelopmental outcome such as CP is a widely recognised and valid method, but less is known about the predictive validity of the GMA with the MOS for infants' later motor performance. Prechtl's GMA and MOS are easy to perform and is a hands-off assessment. It requires a video recording of an infant observed in supine for 5-10 minutes. Prechtl's GMA and MOS however have the disadvantage that it must be performed by a qualified clinician skilled in interpreting observed results. Completing the Prechtl's GMA training is costly, and the course is mostly presented overseas (General Movements Trust, n.d.).

Another popular and highly recommended neurological assessment utilised in the screening of infants for neurodevelopmental abnormalities and CP is the HINE (Novak *et al*., 2017). The HINE, first developed in 1981 by Dr Lilly and Dr Victor Dubowitz and colleagues at Hammersmith Hospital in London, is an easy-to-use neurological examination of infants between 2 and 24 months of age (Romeo, Cioni, Scoto, Pizzardi *et al*., 2009). This test/outcome measure was standardised in a population of term infants and reported high prognostic power to predict ability to walk at 2 years of age

in very preterm infants (Romeo *et al*., 2009). The literature reports many advantages for using the HINE in any clinical setting. It is easily and freely obtainable and only takes 5-10 minutes to perform (Romeo, Ricci, Brogna, Mercuri, 2016). Research has also recorded good inter-observer reliability, even with users less experienced in performing the examination (Romeo *et al*., 2016).

The aim of this study was to ascertain which of the two neurological assessments, Prechtl's GMA and MOS or the HINE, administrated at 11-16 weeks corrected age, is most predictive of gross motor development at 12-15 months corrected age as assessed with the Alberta Infant Motor Scale (AIMS) in an at-risk group of infants born at Tygerberg Children's Hospital (TCH). According to the literature both the HINE and Prechtl's GMA are regarded as a gold standard in the early detection of CP, and both assessments have been routinely used in Europe, North America and Australia with great success. However, to the researcher's knowledge, there is currently no published or unpublished research comparing the HINE's and Prechtl's GMA and MOS's ability to predict gross motor delays (or atypical gross motor outcomes), besides the diagnosis of CP, in any at-risk group of infants. There are also very few studies investigating the use of Prechtl's GMA, and specifically the MOS, in low or middle-income countries, and none reported in Africa.

Both the HINE and Prechtl's GMA and MOS are currently used to evaluate high-risk infants at the neonatal high-risk outpatient clinic at TCH, one of the largest tertiary hospitals in South Africa. It can be argued that understanding how these two assessments compare in predicting severe neurological disorders such as CP as well as atypical gross motor outcome in any high-risk group of infants living in low- or middle-income countries such as South Africa, will enable more infants at risk of motor delay to be detected early, and thus referred for appropriate intervention. Since a delay in early detection of infants at risk for gross motor developmental delays could result in increased disability and secondary impairments, earlier identification will assist in enhancing the management of these infants and may improve long term outcome (Donald *et al*., 2014; Samuels, Slemming & Balton, 2012).

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

In this chapter Prechtl's General Movement Assessment (GMA) and Motor Optimally Score (MOS) as well as the Hammersmith Infant Neurological Examination (HINE) is discussed with regards to their history and development, ability to predict developmental delay, and assessment of the different sub-categories suggestive of later neurodevelopmental including gross motor delay.

A systematic search was conducted through Stellenbosch University Library services and included the use of the following online databases: CINAHL-EBSCOhost, Cochrane library, Google Scholar, PubMed, Science Direct, and Scopus. To source information regarding Prechtl's GMA and MOS, the General Movement Trust's website (http://general-movements-trust.info) was also utilised. Key search terms such as "motor outcome", "Motor Optimality Score or MOS", "Hammersmith Infant Neurological Examination or HINE", "predictive validity", "neurodevelopment", "Prechtl's General Movement Assessment" and "high-risk infants" were utilised during the search. Articles of interest were selected to provide a detailed overview of available literature.

2.2. NEUROMOTOR ASSESSMENTS IN EARLY INFANCY: AN OVERVIEW

As stated in Chapter 1, several advances in maternal and neonatal care have led to increased survival rates of preterm and low-birthweight infants (Spittle, Doyle & Boyd, 2008). A better preterm survival rate has however, resulted in an increase in the number of infants at risk for developing motor impairments later in life. It is known that these infants are more prone to developing movement disorders such as cerebral palsy (CP) and developmental coordination disorder (DCD) (Spittle, Doyle & Boyd, 2008). In high-income countries, healthcare providers such as neonatologists, are often the first point of contact with these infants at risk for neurological impairment and are therefore essential to aid in the prediction of motor developmental delays/

impairments, and referral for early intervention (Heineman & Hadders-Algra, 2008). Referral for early and appropriate intervention aims to improve functional outcomes in these infants (Heineman & Hadders-Algra, 2008). In low- and middle-income countries such as South Africa however, resource constraints often lead to a lack of sufficient staff at hospitals and clinics to screen these infants. Financial constraints and transport issues also result in infants missing appointments at scheduled follow-up clinics.

A systematic review published in 2014, highlighted the lack of policy in low- and middle-income countries for structured screening for developmental deficits of infants and school-going children (Donald *et al*., 2014). The authors also reported that parents and caregivers in the African setting, are often the first point of contact to identify abnormalities in their children, only seeking assistance at healthcare settings when secondary soft tissue changes such as muscle stiffness and joint contractures have developed (Donald *et al*., 2014). Therefore, early identification of infants at risk for possible neuromotor impairment is very important, as it ensures timeous referral for intervention to enable optimal developmental outcomes. Regular neuromotor assessments serve not only to distinguish between infants with typical and atypical development, but also predict possible later motor impairment (Spittle, Doyle & Boyd, 2008).

According to Kirshner and Guyatt (1985) health measure instruments in the field of neuromotor assessment aim to either distinguish between individuals with neurological impairment (discriminate), and those without; or predict a specific developmental outcome; or to measure change over time. It is therefore important that the correct neuromotor assessment tool is selected for its intended purpose (Heineman & Hadders-Algra, 2008).

To date, only two systematic reviews have been published comparing many available neurological assessments used to predict neurological and motor outcomes in high-risk infants. Spittle *et al.'s* (2008) systematic review aimed to investigate the psychometric properties of standardised assessments utilised in the evaluation and prediction of motor development in infants born preterm (Spittle, Doyle & Boyd, 2008). Their systematic review included nine assessment tools, namely the Alberta Infant Motor Scale (AIMS), Bayley Scale of Infant and Toddler Development - 3rd edition, Prechtl's GMA, Movement Assessment of Infants, Neuro Sensory Motor Development

Assessment, Peabody Developmental Motor Scales - 2nd edition, Posture and Fine Motor Assessment of Infants, Test of Infant Motor Performance, and Toddler and Infant Motor Examination. The authors investigated the clinical utility of each of the selected assessment tools and found the AIMS and GMA to be the shortest in duration to perform and involved minimal handling when compared to other assessments. Reliability of most of the assessment tools were found to be excellent, especially the test-retest ability of the AIMS, with high intra- and interrater reliability of the AIMS, GMA, Motor Assessment of Infants, and Test of Infant Motor. The GMA therefore stands out as a useful, and reliable assessment tool to use however, assessors require specific training to complete assessments such as the GMA. The Toddler and Infant Motor Examination, Peabody Developmental Motor Scales - 2nd edition and Bayley Scale of Infant and Toddler Development - 3rd edition was found to be time-consuming and more complicated to perform, although the authors did conclude that the hands-on approach of the caregiver during the Toddler and Infant Motor Examination evaluation could lead to a more accurate representation of a child's motor ability (Spittle, Doyle & Boyd, 2008).

Overall, the authors of this systematic review highlighted the importance of selecting the correct assessment tool for its intended purpose. Knowledge regarding the predictive validity of the chosen assessment tool is important, as it is essential to identify those infants that are at greater risk of neurological impairment and thus will need earlier referral for intervention. A limitation of this review, however, was that the authors failed to report which assessment tools are most predictive at certain age points for example, which assessment tools are more predictive before 3-4 months corrected age (Spittle, Doyle & Boyd, 2008).

Heineman and Hadders-Algra (2008) also conducted a systematic review that focused on validity and reliability of assessment tools used to predict neurological and motor outcomes in high-risk infants. They included fifteen instruments for assessing neuromotor function in infants between 3-18 months of age and included many of the same neurological assessment tools included in the systematic review by Spittle, Doyle and Boyd (2008). Findings of the two systematic reviews were similar. According to Heineman and Hadders-Algra, (2008), the Touwen Infant Neurological Examination, Amiel-Tison neurological examination, Muscle power (active and passive muscle power as reported by de Groot, Hopkins and Touwen, 1992), HINE,

GMA and Test of Infant Motor Performance all have good predictive validity, with the AIMS, Peabody Developmental Motor Scales - 2nd edition, and Movement Assessment of Infants having moderate predictive validity. Muscle power and GMA had very good construct validity, and the AIMS and GMA were the only two assessments found to have very good intra-observer agreement (Cohen's kappa >80%). Inter-observer agreement for the HINE, Peabody Developmental Motor Scales - 2nd edition, Toddler and Infant Motor Evaluation, AIMS and GMA was also found to be very good (Cohen's kappa >80%). Overall, the authors concluded that GMA and Test of Infant Motor Performance had the highest predictive validity when utilised in the assessment of infants prior to 4 months corrected age. The authors also acknowledge and reiterate the fact that the infant brain is ever developing, and thus infant developmental prediction utilising any outcome measure will never be perfect. Therefore, they advocate for the use of multiple, complementary assessment tools, combined with adequate infant history, neurological and physical examination, and movement quality assessment combined with neuroimaging results, to be able to make the most accurate conclusion of neuromotor impairment (Heineman & Hadders-Algra, 2008).

Many imaging modalities (such as magnetic resonance imaging (MRI) or cranial ultrasound) and clinical assessment tools have been developed over the years with the aim to assist with timeous diagnosis of neurological disorders such as CP (Bosanquet, Copeland, Ware & Boyd, 2013; Heineman & Hadders-Algra, 2008). Medical imaging technology such as MRI and cranial ultrasound are also used for diagnosing CP and other neurological impairments (Bosanquet *et al.*, 2013). MRI findings have been shown to correlate to findings from neurological assessments for diagnosing CP (Novak *et al*., 2017; Morgan, Romeo, Chorna, Novak *et al*., 2019). Prior to- and after 5 months corrected age, MRI findings are 86-89% sensitive to predict later CP (Novak *et al*., 2017). While a systematic review performed by Bosanquet *et al*. (2013) reported an even higher sensitivity and specificity of 86-100% and 87-97% respectively at term age. MRI findings are considered superior to cranial ultrasound findings to diagnose CP in high-risk infants when performed after term age (Bosanquet *et al*., 2013; Novak *et al*., 2017). Imaging modalities such as cranial ultrasound and especially MRI is expensive and not always readily available in resource scarce countries. In settings such as South Africa patients often rely on clinic services rather

than that of secondary and tertiary level hospitals. This is largely due to a lack of access, especially in rural areas. Advanced imaging modalities such as MRI are therefore not always readily available or feasible for use in the South-African context.

Choosing the correct assessment tool for infant evaluations is not always easy, and many factors need to be considered when selecting an assessment tool for a specific purpose. Due to the recent guidelines by Novak et al. (2017) where Prechtl's GMA and HINE were found to be superior to other neurological assessments when utilised in the diagnosis of infants with CP, these two observational assessments and the analysis thereof, will be the focus of this study, and the rest of this literature review**.**

2.3 PRECHTL'S GENERAL MOVEMENT ASSESSMENT (GMA)

2.3.1 History and development of the assessment tool

With the introduction of ultrasound equipment in the 1980's, Professor Heinz Prechtl and his colleagues began to utilise this recent technology by performing a series of longitudinal studies to describe foetal movements, with the aim of developing a neurological assessment method to utilise in the early identification of infants with adverse neurological outcomes (Einspieler, Marschik & Prechtl, 2008). The authors observed side flexion of the head to be the first spontaneously occurring foetal movement at 7.5-8 weeks post-menstrual age. While more complex and generalized movement patterns arise as early as 9-10 weeks post-menstrual age (Einspieler, Marschik & Prechtl, 2008). It was observed that most foetal movements develop during the first half of a pregnancy, and that these movements continue up until term age and beyond (Einspieler, Marschik & Prechtl, 2008). Prechtl suggests that foetal-type movement patterns and behaviour continues for the first two months post-term, and that the greatest change in many neural functions occurs when an infant reaches an age of 3 months post-term age, as this period is characterised by an increase in muscle strength, and thus better movement control against gravity (Einspieler, Prechtl, Bos, Ferrari *et al*., 2004:1). It is remarkable to note that there are barely any changes in the pattern of observed foetal movements in the first weeks following the birth, even though there are extensive changes in the environmental conditions for example a threefold increase in gravity (Einspieler *et al*., 2004:9). Movement patterns may include general movements (GMs), twitches, limb movements occurring in isolation, startles,

yawning and stretches that all start to occur from 9-12 weeks post-menstrual age (Einspieler & Prechtl, 2005).

The term “general movements” (GMs) refers to a wide range of spontaneous foetal and infant movement patterns generated endogenously by the immature human nervous system without an external stimulus (De Vries & Bos, 2011; Einspieler & Prechtl, 2005). Prechtl proposed that direct observation with the unaided eye, is one of the easiest ways to assess the quality and quantity of spontaneously occurring movement in the young infant (Prechtl, 1990). Prechtl’s GMA is based on the visual Gestaldt perception, quoted by Konrad Lorenz to be defined as “the ability to take into account a greater number of individual details and more relationships between these than any rational calculation” (Prechtl, 1990:154). The observation of GMs is considered one of the most effective methods to utilise for the functional assessment of the young nervous system, and it is non-invasive, valid and reliable. The use of GMA is becoming increasingly popular, especially in high income countries (Einspieler & Prechtl, 2005; Zang, Yang, Han, Cao *et al*., 2016).

2.3.2 General movements (GMs) and the developing infant brain

The development of the human brain is a progressive and prolonged process, and the foetal period up to 2 years of age is characterised by rapid neurological development, as this is the time when structural and functional architecture of the brain is put in place (Hadders-Agra, 2018). At 5 weeks post-menstrual age neurological development of the foetus starts with neural tube development, and soon after neuron formation the ventricles follow (Hadders-Agra, 2018). Neurons then migrate to the cortex, and from there differentiate into axons, transmitters, synapses and dendrites (Hadders-Agra, 2018). First generation neurons stop in the cortical subplate, a transient structure in the developing human brain, and these subplate neurons develop synaptic activity by as early as 9-10 weeks post-menstrual age (Hadders-Agra, 2018). Literature suggests that abnormal GMs is the result of neurological damage, especially cortical subplate dysfunction as well as dysfunction of efferent motor connections that transgress the basal ganglia, central grey matter and periventricular white matter (Brogna, Romeo, Cervesi, Scrofani *et al.*, 2013). Foetal brain development continues until the last few weeks of full-term gestation, and premature birth can therefore interfere with critical brain maturation, often resulting in white matter damage, loss of subplate neurons and

axons, and thus impairment of thalamo-cortical connections (Brogna *et al*, 2013). Several studies conclude that normal quality GMs can only occur with intact neurological and brain function and that in turn, abnormal GMs allude to neurological dysfunction (Einspieler & Prechtl, 2005; Einspieler, Marschik & Prechtl, 2008).

2.3.3 Characteristics of normal and abnormal general movements (GMs)

Normal GMs are complex and elegant, involving the whole body in a variable sequence of trunk, neck and limb movements. Prechtl's GMA reports on two types of movement patterns that is observed in infants from term age: writhing movements and fidgety movements (FMs). Writhing movements are the first GMs to occur from term age until 6-9 weeks post-term age (Brogna *et al*., 2013; Einspieler *et al*., 2004:10). They are characterised by slow to moderate speed and a small to moderate amplitude of movement (Einspieler & Prechtl, 2005). They wax and wane in force, and speed and are elliptical in form, which creates the impression of a writhing quality. Writhing movements gradually disappear by 6-9 weeks post-term age to make way for the observation of fidgety movements. Fidgety movements are GMs that are present from seven up until 20 weeks post-term age, when intentional, and anti-gravity movements become apparent, and are characterised as being small in amplitude, and moderate in speed (Brogna *et al*., 2013; Einspieler & Prechtl, 2005). Fidgety movements also consist of trunk, neck and limb movements with continuous, multidirectional and variable acceleration in an infant that is awake (Einspieler & Prechtl, 2005).

As mentioned earlier, it is suggested in the literature that GMs are generated by the cortical subplate and that the quality is modulated by reticulospinal or corticospinal pathways. Damage or impairment of these structures can therefore lead to an abnormal repertoire of GMs (Einspieler & Prechtl, 2005). Abnormal GMs are without a complex, elegant, fluent and variable character (Einspieler & Prechtl, 2005). Abnormal GMs in the writhing period are described as poor repertoire, cramped-synchronised or chaotic, and fidgety movements are described as abnormal or absent (Einspieler & Prechtl, 2005). Abnormal fidgety movements are defined as fidgety movements with exaggerated speed, jerkiness, and amplitude (Einspieler & Prechtl, 2005). When fidgety movements are not observed from 9-20 weeks post-term age, they are classified as "absent" fidgety movements (Einspieler & Prechtl, 2005). The

significance of absent and abnormal fidgety movements for later prediction of motor delay will be discussed later in this chapter.

2.3.4 Prechtl's General Movement Assessment (GMA) and the Motor Optimality Score (MOS)

Prechtl's GMA has recently been expanded to include a more detailed evaluation of the quality of observed infant movements namely the motor optimality concept. Prechtl proposed that it would be worthwhile to not only assess GMs, but also to further examine concurrent motor repertoire, thus movements that occur together with GMs (Einspieler *et al*., 2004:27) The Motor Optimality Score (MOS) therefore allows the examiner to describe movements and postural patterns that occur in conjunction with fidgety movements between 9-20 weeks post-term age such as hand-to-hand, foot-to-foot, hand-to-mouth, swipes and leg lifting movements. The MOS also describes the quality of the movement character, for example: smooth and fluent movements or monotonous, jerky and/or stiff co-current movement patterns (Einspieler *et al*., 2019).

To date only a few studies have been published utilising both Prechtl's GMA with the additional MOS to study and predict motor performance and possible neurological impairments such as CP, and to the authors knowledge, none to date in Africa. There is, however, an emerging body of evidence that suggests that a low MOS score observed in infants at 3-5 months corrected age is suggestive of poor motor performance and cognitive function later in life (Bruggink, Einspieler, Butcher, Van Bracckel *et al*., 2008; Fjørtoft, Grunewaldt, Lohaugen, Morkved *et al*., 2013). The detailed scoring of motor repertoire using the motor optimality concept has also been shown to have a high inter-rater reliability with intraclass correlation coefficient (ICC) ranges between 0.80 and 0.94 (Zang *et al*., 2016).

Recent studies using Prechtl's MOS have also distinguished a relationship between MOS and cognition, as well as speech and language outcomes (Salavati *et al*., 2017). Literature now suggests that assessment of early movement repertoire with Prechtl's GMA and MOS in infants can predict later cognitive outcome (Kodric, Sustersic & Paro-Panjan, 2010; Salavati *et al*., 2017). This poses an interesting concept for further research into and will be briefly discussed in the latter part of this chapter, but an in-depth examination regarding this field falls outside of the scope of the present study.

2.4 THE HAMMERSMITH INFANT NEUROLOGICAL EXAMINATION (HINE) FOR THE NEURODEVELOPMENTAL ASSESSMENT OF THE HIGH-RISK INFANT

2.4.1 History and development of the Hammersmith Infant Neurological Examination (HINE)

The HINE was developed in 1981 by Dr Lilly and Victor Dubowitz at Hammersmith Hospital in London (Haataja, Mercuri, Regev, Cowan *et al*., 1999). The HINE was derived from the standard infant neurological examination and has undergone several modifications since its first introduction. The original neurological assessment proforma was developed in 1981 with the examination of the newborn infant in mind and was subsequently adapted to develop a comparable neurological examination that could be utilised in infants from 2-24 months of age (Haataja *et al*., 1999). The authors aimed to develop a neurological assessment tool that would be both practical and objective when monitoring the neurological status of young infants, as well as provide a baseline for the longitudinal neurological examination of developing infants and toddlers (Dubowitz, Dubowitz, Palmer & Verghote, 1980).

The authors believed, that at the time, except for Prechl's examination of the developing infant, other early neurological examinations of young infants were based on primitive reflexes and tone only, thus not good indicators of higher cerebral functioning and upper motor neuron impairment (Dubowitz *et al*., 1980). The authors also noted an increasing need for the development of a neurological examination that could be conducted by staff that did not necessarily have any expertise in neonatal neurology, and that would be applicable in both preterm and term infants and beyond, to allow for early detection in neurodevelopmental pattern changes in these infants (Dubowitz *et al*., 1980). The authors also noted that previously proposed neurological examinations were deemed to be too time-consuming and aimed to develop an accurate assessment tool that could be performed within 10-15 minutes (Dubowitz *et al.*, 1980).

The authors modified their original assessment to include items assessing active and passive movements, cranial nerve function, spontaneous movements, reflexes, and protective reactions. The HINE was also adapted to include the examination of specific

age-dependent items reflective of gross and fine motor development (Haataja *et al*., 1999). Researchers have also developed HINE optimality scores based on the frequency distribution of neurological findings, which has been standardised in both term and preterm infants (Haataja *et al*., 1999).

2.5 PREDICTIVE VALIDITY OF OBSERVATIONAL NEUROLOGICAL ASSESSMENTS TO DETERMINE MOTOR IMPAIRMENT AND DISABILITY IN HIGH RISK-INFANTS

In this section the predictive validity of Prechtl's GMA and the MOS in comparison to the predictive validity of the HINE will be discussed with regards to their ability to determine later motor impairment and disability in high-risk infants. Both examinations have been applied and studied in cohorts of high-risk infants, and aim to identify neurological impairments, as well as provide insight as to possible functional outcomes and limitations in this population.

2.5.1 Prechtl's General Movement Assessment (GMA) and the Motor Optimality Score (MOS)

Researchers have shifted their attention to the value of observing quality of movement and postural patterns for predicting later neurological outcome (Hitzert, Roze, van Braeckel & Bos, 2014). Recently there has been an increase in research aimed at investigating factors for the early prediction of severe neurological disorders such as CP and research has shown observation and assessment of early spontaneous infant movements to be a good predictor thereof (Kwong, Fitzgerald, Doyle, Cheong *et al*., 2018).

In 2017, many international experts systematically reviewed available evidence for the accurate and early diagnosis of CP, and subsequently developed an international practice guideline (Novak *et al*., 2017). Six systematic reviews and two evidence based clinical guidelines with high methodological quality were analysed to develop consensus on the best neurological assessments and imaging modalities to use for the early detection of CP. Prechtl's GMA, the HINE and MRI were found to have the highest predictive validity for CP diagnosis prior to 5 months corrected age (Novak *et al*., 2017). Prechtl's GMA was found to be superior with sensitivity of 95-98% to predict

CP prior to 5 months corrected age. Ideally, it is suggested that Prechtl's GMA be conducted, and the results interpreted in combination with MRI findings to further validate congruent findings (Novak *et al.*, 2017). A systematic review previously published and included in the study conducted by Novak *et al*. (2017), also found similar pooled sensitivity (98%) and specificity values (91%) of GMs to predict later CP (Bosanquet *et al.*, 2013).

Kwong *et al*. (2018) conducted a systematic review to assess the predictive validity of different neurological assessments based on the observation of spontaneous early infant movements. They reviewed forty-seven studies describing Prechtl's GMA, GMs according to Hadders-Algra's classification, HINE, movement assessment of infants (MAI), and the Hammersmith Neonatal Neurological Examination (HNNE). Fidgety movements according to Prechtl's classification had the highest sensitivity (97%) and specificity (89%) for the prediction of CP (Kwong *et al*., 2018). Analysing fidgety movements also had a lower rate of false negative results, with negative predictive values (NPV) ranging from 80-100% (Kwong *et al*., 2018). Overall, it was concluded that fidgety movements according to Prechtl's GMA had the highest predictive validity for later CP, compared to the other included neurological assessments (Kwong *et al*., 2018). The authors only evaluated articles including Prechtl's GMA but did note, that combining the presence of poor limb movement and asymmetrical/abnormal postures as is done in Prechtl's GMA with the additional MOS, may even further increase the predictive validity of the assessment.

In 2019, also with mention to the recently published guidelines by Novak *et al*. (2017), Einspieler *et al.* (2019) performed an observational study with a large, worldwide cohort of 468 high risk infants that aimed to identify specific markers for ambulation, gross-motor function and type and topography of CP (Einspieler, *et al*., 2019). This study used a novel approach by combining Prechtl's GMA with the MOS to gain insight into the severity of the infants' later motor function. Infants were assessed utilising Prechtl's GMA with the MOS at 3-5 months post-term age and re-evaluated at a median age of 3.5 years to determine motor function, CP diagnosis and functionality according to the Gross Motor Function Classification System (GMFCS). The GMFCS is used to classify the severity of motor disability (mobility function) in children with CP (Palisano, Rosenbaum, Walter, Russell *et al*., 1997). Einspieler *et al*. (2019) concluded that a low MOS score, especially in infants with severe brain lesions, is predictive of

CP. The authors however caution that MOS alone cannot yet be used in isolation to predict a CP diagnosis and should thus be combined with neuroimaging results such as MRI (Einspieler *et al*., 2019). A MOS score of ≤14, absent fidgety movements and a cramped synchronised movement character were found to warrant early intervention, as they are all indicators of a likely poor neurodevelopmental and motor outcome, while a MOS score of <8 was found to be suggestive of severe functional limitations (Einspieler *et al*., 2019). This was a big study with a suitable large sample of children diagnosed with CP, but due to a lack of related studies investigating the ability of the MOS to predict later motor delays or atypical motor outcomes (and not only CP) in infants, further research and publication of articles investigating this topic is warranted.

The international guidelines proposed by Novak *et al.* (2017) advocate for the use of neurological assessments in combination with neuro imaging findings. In keeping with this guideline, Morgan *et al*. (2019) performed the first study investigating the pooled diagnostic accuracy of neuroimaging, GMs, and neurological examination to predict CP in a cohort of high-risk infants. Eighty two percent (82%) of infants classified as “normal” and without disability also had normal writhing movements, and 100% of infants without disability had normal fidgety movements (Morgan *et al*., 2019). In infants that had absent fidgety movements at 3 months corrected age, 95% later developed CP, and in children classified with mild disability, 70% had normal fidgety movements, while only 24% had absent fidgety movements. The authors concluded that the pooled sensitivity and specificity of neuroimaging and neurological assessments together were higher than when they are used in isolation. However, they highlighted that Prechtl’s GMA with fidgety movements had the highest accuracy of 96,49% to predict CP diagnosis when considered in isolation, especially if fidgety movements were abnormal or absent at 3 months corrected age.

It is worth mentioning, that although of high quality, all the previously mentioned studies were conducted by authors from high-income countries. Burger, Frieg and Louw (2011) published the first study regarding GMA in the African context. They investigated the ability of GMs to predict neurological outcome in very low birth weight infants (VLBW) and extremely low birth weight infants (ELBW) in a middle-income country, specifically in South Africa. The authors reported a significant relationship between the absence of fidgety movements at 3 months and later motor outcome at

12 months in a cohort of 115 preterm born infants (Burger, Frieg & Louw, 2011). The authors reported sensitivity values of ≥71%, specificity ≥89%, positive predictive value (PPV) of ≥80% and NPV of ≥96% of fidgety movements to predict CP and later motor outcome in this group (Burger, Frieg & Louw, 2011). These findings again emphasize the value of GMA and fidgety movements in predicting later neurological function and motor performance, especially in infants with minor neurological disfunctions (Burger, Frieg & Louw, 2011).

In a study set in a low-and middle-income country, investigators aimed to determine if Prechtl's GMA and the MOS performed on infants at 3 months of age could be associated with motor development in preterm born infants at 12 months in India (Adde, Thomas, John, Oommen *et al*., 2016). The authors aimed to determine if Prechtl's GMA and the MOS could also be feasible in a cohort of infants in a low-and middle-income country, as there are little to no studies reporting on the differences of GMs when assessed in a variety of ethnic groups (Adde *et al*., 2016). The cohort presented a low prevalence of absent or abnormal fidgety movements, but results showed that when fidgety movements were abnormal or absent, it was associated with significantly reduced total motor and gross motor scores as per Peabody Developmental Motor Scales - 2nd edition (Adde *et al*., 2016). The authors also found a strong association between the observed infant motor repertoire, and later gross motor development, again suggesting that the quality and quantity of observed GMs and the concurrent motor repertoire have a significant association with later fine and gross motor development (Adde *et al*., 2016). This was the first attempt to utilize Prechtl's GMA and the MOS to predict fine and gross motor outcome, and not only severe neurological disorders such as CP, in a lower middle-income country. These results suggest the GMA and the MOS is suitable for neurological assessment of infants from different ethnic groups in both high, and low-middle income settings.

It is evident from the literature that Prechtl's GMA has a high predictive validity of CP, and that research concerning Prechtl's GMA, especially with the MOS to predict other motor impairments in high-risk infants other than CP in low- and middle-income countries is currently lacking.

2.5.2 Predictive validity of the Hammersmith Infant Neurological Examination (HINE)

The HINE is widely recognised as one of the finest neurological assessment tools utilised in diagnosis of severe neurological impairments such as CP. International guidelines as proposed by Novak *et al.* (2017) suggest that the HINE is 90% accurate to predict CP after 5 months corrected age (Novak *et al*., 2017). Prior to 5 months corrected age, Prechtl's GMA is superior with regards to predictive validity, but the authors also advocate for the use of the HINE during this period, especially if an GMA is not possible and MRI neuroimaging is unavailable. A HINE score of <57 at 3 months corrected age was found to be 96% predictive of CP (Novak *et al*., 2017). When predicting CP after 5 months corrected age and utilising a standardised neurological assessment, the authors suggest that HINE scores of <73 at 6, 9, and 12 months corrected age is considered high-risk for development of CP, and that HINE scores of <40 at these specified age ranges, almost always indicates a CP diagnosis (Novak *et al*., 2017).

Romeo *et al*. (2016) conducted the only known systematic review to date exclusively investigating the value of the HINE to identify early signs of neurological impairment, as well as prognostic validity to identify CP diagnosis in infants (Romeo *et al*., 2016). The authors suggested that the HINE is a useful neurological assessment tool to predict, as well as to describe severity of later CP (Romeo *et al*., 2016). The authors included ten studies in their review and determined that infants with global HINE scores of ≤56 at 3 months corrected age, and ≤65 at 12 months of age had a sensitivity and specificity of 90% to accurately predict CP (Romeo *et al*., 2016). Furthermore, the authors concluded that a HINE score of <40 accurately predicts severe CP, and that identification of certain clinical patterns indicative of abnormal outcome may also be able to predict later functional levels such as ability to sit or ambulate (Romeo *et al*., 2016). When compared to a detailed assessment of movement such as Prechtl's GMA and the MOS, the value of assessing movement quality and quantity utilising the HINE is limited, but that it is none the less predictive of motor outcome in high-risk infants when utilised as part of a general assessment, considering various aspects of neurological functioning (Romeo *et al*., 2016).

The systematic review by Kwong *et al*. (2018), found that Prechtl's GMA is superior to HINE and other neurological assessments in the classification and prediction of CP. The authors, however, also found a strong relationship between the HINE score at 3 months corrected age to predict later CP (Kwong *et al*., 2018). The review reports on the study conducted by Romeo *et al.* (2008a), that concluded that in a large cohort of preterm infants, both abnormal GMs and low HINE scores observed and recorded at 3 months of age were highly predictive of a later diagnosis of CP (Romeo, Guzetta, Scoto, Cioni *et al*., 2008a). These findings are relevant to that of this Masters' thesis study, as Prechtl's GMA with MOS and HINE scores were reviewed at this specific time range of 11-16 weeks corrected age. While the study conducted by Romeo *et al.* (2008a) is one of the only studies comparing the GMA (without the MOS) to another neurological examination (HINE) to predict neurological outcome (similar as to what the author aimed to do in this study), the authors only reported on presence of disability and CP diagnosis and did not describe the degree of functionality and gross motor outcome (Romeo *et al*., 2008a).

In another study by Romeo *et al*. (2009), the authors also concluded that the HINE scores performed as early as 3 months corrected age can be used to accurately predict motor outcome of preterm infants at 2 years corrected age (Romeo *et al*., 2009). Morgan *et al*. (2019) also concluded that at 3 months of age, the HINE is highly accurate to detect CP with a sensitivity of 59.18% and specificity of 98,64% (utilising a HINE cut-off score of 57). Of the infants assessed, 82% were correctly classified with CP diagnosis utilising HINE scores alone at 3 months. It is therefore suggested that there is a high correlation between a low HINE score and later CP diagnosis.

In a systematic review, Bosanquet *et al*. (2013) concluded that neurological examinations such as the HINE, Touwen Infant Neurological Examination and Lacey Assessment of Preterm infants are less valuable at preterm age but may be highly accurate to predict CP diagnosis and neurological impairment after preterm age. These earlier findings by Bosanquet *et al*., (2013) are again in support of the findings later published by Novak *et al*. (2017) stating that the HINE is highly sensitive (with 90% accuracy) for the prediction of CP before 5 months corrected age.

It is therefore also evident from studying the literature that the HINE scores at all prescribed ages, but especially from 5 months corrected age is accurate to predict

later CP. The use of the HINE in the literature to determine infants with possible later gross motor delay other than CP is however limited, and it can be argued that it warrants further study and investigation.

2.6 PREDICTING TYPE AND SEVERITY OF CEREBRAL PALSY (CP) AND DEGREE OF MOTOR IMPAIRMENT

The observation of quality and quantity of movement has been found to be accurate to detect major, as well as minor neurodevelopmental problems, as well as to aid in the diagnosis of CP (Hitzert *et al*., 2014). In this section, the ability of Prechtl's GMA and MOS, as well as the HINE will be discussed with regards to determining the severity of motor impairment and functional limitations.

2.6.1. Prechtl's General Movement Assessment (GMA) and Motor Optimality Score (MOS)

The first studies published as early as the 1990s already commented on the predictive value of abnormal GMs to predict later neurological impairment and proposed that the presence of cramped-synchronized GMs is highly predictive of a poor neurological outcome (Einspieler *et al*., 2004:40; Einspieler & Prechtl, 2005). The presence of constant cramped-synchronised GMs can be utilised to predict both spastic diplegia and tetraplegia (Einspieler & Prechtl, 2005). Children that later developed hemiplegia, are often observed as having absent fidgety movements and a decrease in the observation of segmental unilateral body movements at 3 months post-term age (Cioni, Bos, Einspieler, Ferrari *et al*., 2000; Ferrari, Cioni, Einspieler, Roversi *et al*., 2002; Einspieler & Prechtl, 2005). From 2-5 months post-term age, children who later develop dyskinetic CP are observed as having a poor repertoire of GMs with monotonous, "circling" arm movements with subsequent finger spreading (Einspieler *et al*., 2004:43; Einspieler & Prechtl, 2005). A lack of movement towards the midline, such as with hand-to-hand and foot-to-foot contact, especially from 3 months of age and onwards, has also been shown to be indicative of possible later dyskinetic CP (Einspieler & Prechtl, 2005). The absence of fidgety movements, as well as anti-gravity movements such as "lifting of legs" at 3-5 months post-term age has also been shown to be suggestive of both dyskinetic, as well as spastic CP (Einspieler *et al.,* 2004:44).

When all is taken into consideration, it is suggested in the literature that the absence of fidgety movements is more predictive of CP, and thus a poorer neurological outcome compared to the observation of abnormal fidgety movements (Einspieler *et al*., 2004:44).

A large worldwide, multicentre study conducted by Einspieler *et al*. (2019) found that overall MOS scores in high-risk infants tested between 9-22 weeks post-term age had a strong association with motor outcome according to the GMFCS, with a Spearman rank-correlation order of rho= -0.66 ($p<0.001$) (Einspieler *et al*., 2019). MOS scores of >14 were associated with GMFCS levels I-II, and a MOS score of <8 was strongly associated with GMFCS levels IV-V (Einspieler *et al*., 2019). Increased scores in MOS sub-categories of quality of movement patterns, age adequate movement patterns, postural patterns and movement character were associated with improved functional outcomes according to GMFCS levels, and thus increased scores in these specific categories were linked with improved gross motor outcomes (Einspieler *et al*., 2019). Furthermore, the authors found a correlation between atypical mouth movements, atypical foot-to-foot contact and atypical arching with GMFCS level III-V and diagnosis of bilateral CP (Einspieler *et al*., 2019). Circular arm movements were also found to be predictive of a GMFCS level of III-V, and was indicative of bilateral, non-spastic CP (Einspieler *et al*., 2019). Overall, it was concluded that infants with a MOS of ≤14 and absent fidgety movements were at high risk for functional abnormalities, and warrant early referral for intervention (Einspieler *et al*., 2019).

2.6.2 Hammersmith Infant Neurological Examination (HINE)

When utilising the HINE, cut-off scores may be used to predict motor severity of CP. HINE cut-off scores of 50-73 at 3, 6, 9, or 12 months indicates a high probability of unilateral CP, whereas HINE scores <50 likely indicate bilateral CP (Novak *et al.*, 2017). HINE scores of 40-60 at 3-6 months corrected age is indicative of GMFCS I-II, and a score of <40 will likely indicate a GMFCS of III-IV (Novak *et al*., 2017).

In a retrospective study, Romeo, Cioni, Scoto, Mazzone *et al*. (2008b) compared the neuromotor development of children with confirmed cerebral palsy (CP) with their HINE scores at 12 months of age. The authors concluded that the HINE scores can distinguish infants with diplegia from infants with quadriplegia. Decreased scores in tone and the posture subsections on the HINE correlated well with the functional level

as determined by the GMFCS, with p<0.000 (Romeo *et al*., 2008b). In this study infants with diplegia, at all ages, scored significantly lower for every subsection on the HINE, than infants with hemiplegia. Infants with quadriplegia also scored much lower on the HINE compared to infants with hemiplegia. Similarly, HINE scores were also found to be strongly associated with GMFCS levels, and thus functional outcomes recorded at 2 years. Pizzardi *et al*. (2008) also concluded that single items of the HINE at 3, 6, 9, and 12 months corrected age are accurate to predict motor performance at 2 years of age (Pizzardi, Romeo, Cioni, Romeo *et al*., 2008).

HINE sub-category scores and single items have also been found to be useful to predict later motor impairment. In a study performed by Romeo *et al.* (2009), the authors listed the most and least predictive items of the HINE for predicting later locomotor function at 2 years corrected age. When preterm born infants were assessed at 3 months corrected age, the authors found movement quality, movement quantity, feet posture, arm supination and pronation, scarf sign and lateral tilting to be the sub-categorical items most predictive of motor performance. Furthermore, the authors concluded that arm protection, visual response, popliteal angle, forward parachute, leg posture, trunk posture in sitting and ankle dorsiflexion to be least predictive of motor performance at 2 years corrected age. These findings are correlate to that of Pizzardi *et al.* (2008) where observation of upper limb items was found to be more predictive of motor function than assessment of reflexes and reactions (Pizzardi *et al*., 2008). The authors concluded that the HINE had a constant high predictive value throughout assessment in the first year of life and suggested that the HINE's effectiveness may be attributed to its effective combination of the assessment of observed items for each age period (Romeo *et al*., 2009).

2.7 Prechtl's General Movement Assessment (GMA) and Motor Optimality Score (MOS) versus Hammersmith Infant Neurological Examination (HINE) to predict minor and major neurological impairments.

Motor abnormalities often present as more subtle deviations of movement and posture. In the literature, a large body of research has focussed only on the early identification and prediction of children at risk for development of severe neurological

impairments such as CP. However, less has been reported on the early identifiers of infants for development of other motor deficits or disorders, for example developmental coordination disorder (DCD) (Sustersic, Sustar & Paro-Panjan, 2012). Mild movement deficits or disorders may range from decreased physical fitness, impaired coordination, and poor posture. These deficits may persist and not resolve over time (Sustersic, Sustar & Paro-Panjan, 2012).

A systematic review and meta-analysis published in 2020 analysed the ability of Prechtl's GMA, to predict minor neurological dysfunction after 12 months of age (Pires, Marba, Caldas & Stopiglia, 2020). The analysis yielded low sensitivity and specificity results in all but one study, but it is worth noting that the authors were only able to include three articles for analysis, and it can be argued that a larger number of studies is needed to obtain a more accurate result. One of the studies investigated was that of Sustersic, Sustar and Paro-Panjan (2012). They conducted a study to determine the predictive value of Prechtl's GMA performed at term age and 9-20 weeks post-term age to identify preterm infants at later risk for minor neurological deficits at 5-6 years of age. From a sample of 41 children, seven were identified as having a definite motor problem or borderline characteristics of DCD. Study findings suggested that abnormal fidgety movements may be indicative of later motor abnormalities, as all the study participants with definite motor abnormalities had abnormal fidgety movements at 9-20 weeks post-term age. GMs in the fidgety stage were therefore found to be more sensitive to detect later motor abnormalities than at term corrected age. Study results however, showed that GMs at both term and 9-20 weeks post-term age had a low specificity to predict normal motor outcome (Sustersic, Sustar & Paro-Panjan, 2012). Prechtl's GMA with assessment of quality of motor repertoire at 3-5 months has also been found to identify later motor, and even cognitive deficits in children without a definitive CP diagnosis (Fjørtoft *et al.,* 2013).

Another study included in the review by Pires *at al.*, (2020) was that of Spittle *et al.* (2013). The authors found GMs when performed at 3 months corrected age to be predictive of moderate to severe motor impairment when assessed at 2 years of age with 70% sensitivity and 85% specificity respectively (Spittle, Spencer-Smith, Cheong, Eeles *et al*., 2013). They also found GMs to have moderate sensitivity (70%) and high specificity (85%) to predict moderate to severe cognitive impairment at 2 years of age (Spittle *et al*., 2013). GMs were less sensitive to predict cognitive impairment at 4 years

of age (42%) but had a high specificity (88%). The authors concluded that analysing GMs at 3 months corrected age can therefore be predictive of a range of neurodevelopmental outcomes in children aged 2 years old and up. The previously mentioned studies investigated GMs in the fidgety and writhing stage only and did not investigate GMA with concurrent motor repertoire and MOS. Bruggink *et al.* (2008) conducted a study to determine the predictive power of the quality of early motor repertoire to determine minor neurological dysfunction in previously preterm infants when they reach school going age. They aimed to determine the extent to which the assessment of the quality of fidgety movements as well as the concurrent motor repertoire at 6-24 weeks post-term age in a cohort of 82 infants could predict minor neurological deficits in children aged 7-11 years. The authors found the presence of abnormal fidgety movements at 11-16 weeks post-term age to predict later complex minor neurological dysfunction in 64% of cases, and that the quality of fidgety movements at 11-16 weeks post-term age could also be strongly related to overall neurological status (Bruggink *et al*., 2008).

A motor repertoire considered as “normal’ at this age, was also able to successfully distinguish between infants that later developed adverse neurological conditions such as CP or complex minor neurological dysfunction, and those who did not. The quality of observed fidgety movements, as well as the quality of the concurrent motor repertoire had high prognostic value in the prediction of later complex minor neurological dysfunction at 11-16 weeks post-term age (Bruggink *et al*., 2008). These findings suggest that a smooth concurrent motor repertoire in combination with normal fidgety movements at 11-16 weeks post-term age can provide an insight into early central nervous system development. A smooth motor repertoire may also be needed for proper infant development through play and exploration, as a monotonous, jerky movement repertoire may lead to a decreased ability of an infant to interact with the environment and develop appropriate movement strategies (Bruggink *et al*., 2008).

In a study performed by Fjørtoft *et al.* (2013) the authors found that when studying the concurrent motor repertoire of previous high-risk infants at a mean age of 14 weeks post-term age, it had a sensitivity of 91% to detect motor abnormalities and 90% to detect cognitive dysfunction in these children at 10 years of age. In 86% of study participants an abnormal motor repertoire at 14 weeks post-term age could predict a poor motor and cognitive outcome at ten years of age, and 59% of children with normal

fidgety movements and an abnormal infant motor repertoire had a motor outcome deficit. The authors were able to conclude that the presence of fidgety movements, together with an abnormal motor repertoire may be beneficial when used to predict possible motor deficits in children with diagnosis other that CP.

Adde *et al*. (2016) conducted a study with the aim to investigate the early motor repertoire in VLBW infants in India. The authors reported a significant association between the observed infant motor repertoire and later gross motor development at 12 months post-term age. Abnormal fidgety movements, abnormal quality of concurrent motor repertoire as well as absent or reduced age-adequate movements was found to be associated with poorer gross motor performance. Their findings suggest that the quality and quantity of observed GMs and the concurrent motor repertoire therefore have a significant association with later fine and gross motor development (Adde *et al*., 2016).

While literature regarding the ability of the HINE to predict CP and severe neurological outcomes are readily available, literature on the use of the HINE to detect minor neurological impairments in infants, is currently scarce. Romeo *et al.* (2016) found suboptimal global HINE scores in infants to be indicative of minor neurological impairment, or impaired psychomotor development, even in the absence of a CP diagnosis (Romeo *et al*., 2016). Studies also report on the high sensitivity and specificity of HINE optimality scores for predicting walking in infants at 2 years corrected age (Romeo *et al*., 2016). HINE score of <40 is highly indicative of poor motor performance, while scores of 41-60 have been shown to indicate motor impairments that are less severe (Ricci, Cowan & Pane, 2006). Infants that score in this range have been shown to be able to sit independently at 2 years corrected age but were often shown to not be able to walk at this age (Ricci, Cowan, Pane, 2006).

The potential application of the GMA with the MOS, and the HINE to predict outcomes other than severe neurological disorders such as CP, is an exciting prospect and therefore warrants further research and investigation.

As previously reported earlier in this review, studies published regarding Prechtl's GMA and MOS, as well as the HINE to predict neurological disorders in infants other than CP in low- to middle-income countries are scarce. Differences in socioeconomic status could possibly translate into inequities in infant and child development.

Literature investigating the influence of socioeconomic status on later infant development is however conflicting, with some research suggesting that there may be a correlation between acquirement of adequate gross motor skills and socioeconomic status (Kwon & O'Neill, 2020). It is not the opinion of the researcher that utilising these assessment tools in low-to middle income countries will result in largely different results to those found in studies done in high income countries, but rather that it will provide a unique perspective as to some of the challenges that high-risk infants born into these societies face.

2.8 CONCLUSION

While extensively researched with regards to predicting CP diagnosis, literature supporting the use of Prechtl's GMA and HINE to determine motor outcomes other than CP in high-risk infants is lacking. There is also currently a lack of studies reporting on which neurological assessment is best to use at which period in high-risk infants. To date, no study has been performed in high or low-and middle-income countries, including Africa, investigating the ability of Prechtl's GMA with the additional MOS or the HINE to determine motor outcomes (especially outcomes other than just CP) in an at-risk group of infants.

This descriptive study was conducted at Tygerberg Children's Hospital (TCH), a large tertiary hospital in Cape Town, South Africa and aimed to ascertain which neurological infant assessment (Prechtl's GMA with MOS or HINE) is most predictive of not only severe gross motor outcomes (such as CP), but also delayed or atypical gross motor outcomes in a subset of high-risk infants. In the following chapter, the study research question, study aims and objectives as well as the study methodology will be discussed.

CHAPTER 3

METHODOLOGY

This chapter outlines the research methods that were followed in the study. The research question, study objectives, study design, study population, sample size and sampling method, as well as the instrumentation used in this study is described. The study procedure, data analysis and lastly, the ethical issues that were considered are also described.

3.1 RESEARCH QUESTION

What is the predictive validity of the Hammersmith Infant Neurological Examination (HINE) versus Prechtl's General Movement Assessment (GMA) with the Motor optimality Score (MOS), administrated at 11-16 weeks corrected age, on gross motor outcomes in high-risk infants, followed up at the neonatal high-risk clinic of Tygerberg Children's Hospital (TCH) at 12-15 months corrected age?

3.2 STUDY OBJECTIVES

The primary objectives of the study were:

- To describe the gross motor outcomes of high-risk infants at 12-15 months corrected age using the Alberta Infant Motor Scale (AIMS).
- To establish the predictive validity of the HINE versus Prechtl's GMA with the MOS at 11-16 weeks corrected age in determining severe or atypical gross motor development[1] in high-risk infants at 12-15 months corrected age.
- To describe outcomes on the different subcategories of the HINE and Prechtl's GMA with the MOS in high-risk infants at 11-16 weeks corrected age.

[1] Severe and atypical gross motor development is defined as scoring <5th percentile on the AIMS

The secondary objectives of the study were:

- To determine which subcategories and/or items of Prechtl's GMA with the MOS and the HINE were most predictive of severe or atypical gross motor development at 12-15 months corrected age.
- To determine the validity of the HINE versus Prechtl's GMA with the MOS at 11-16 weeks corrected age to predict a provisional diagnosis of cerebral palsy (CP) at 12-15 months corrected age.

3.3 STUDY DESIGN

A longitudinal correlational descriptive study was conducted to answer the research question.

3.4 STUDY SETTING

The study was conducted at TCH which is a tertiary institution and one of the main teaching hospitals affiliated to Stellenbosch University's Faculty of Medicine and Health Sciences. The hospital is the largest public hospital in the Western Cape, and services a wide variety of patients from many different areas and backgrounds. TCH has a routine follow-up neonatal outpatient high-risk clinic, where all infants deemed as high risk for neurodevelopmental delays/disabilities are screened. These infants usually presented with one of the following conditions, and were thus deemed as high risk for neurological impairment and developmental delay: hypoxic ischaemic encephalopathy (HIE) and received cooling post birth, prematurity with birthweight <1500g, intraventricular haemorrhage (IVH) (grades III and IV), meningitis, or severe neonatal jaundice. The neonatal high-risk clinic routinely conducts follow-up assessments of these infants at 3 months, 12-15 months, and 3 years corrected age. The HINE and Prechtl's GMA with the MOS are routinely done as part of the screening at 3 months corrected age. Infants with detected developmental delay, disabilities or any neurological concerns are more frequently followed up and referred for appropriate intervention.

3.5 STUDY POPULATION

The study population included all high-risk infants admitted to the neonatal wards of TCH (born in 2019/2020) that were later followed up as outpatients at the neonatal high-risk clinic.

3.6 STUDY SAMPLE

The study sample consisted of all high-risk infants fitting the inclusion criteria that had both HINE and Prechtl's GMA with the MOS assessments done at 11-16 weeks corrected age and then attended the 12-15 month corrected age follow-up assessments at the neonatal high-risk clinic at TCH in 2021.

3.7 SAMPLING METHOD

Successive sampling was used to assemble an appropriate study sample. High-risk infants who presented at their 12-15 months follow-up appointment at the neonatal high-risk clinic of TCH from February till the end of August 2021 were identified by the primary researcher with the assistance of a medical doctor[2] and recruited for inclusion in the study.

3.8 SAMPLE SIZE

To the knowledge of the researchers, there are currently no available studies on the validity of Prechtl's GMA with the MOS versus the HINE to predict motor outcome in high-risk infants. An interim power calculation was therefore performed on a subset of 40-50 infants to determine whether we needed to enrol more infants. The results of the initial analysis yielded that a sample of 50 infants would be sufficient to answer the study question, but it was suggested to continue with data collection until at least 80 infants were included in the study in order to try and include more infants that would have a possible gross motor delay. The principal investigator (PI) therefore initially included all eligible infants that followed up at the neonatal high-risk clinic at 12-15

[2] Dr JI van Zyl: Medical Doctor at TCH's neonatal high-risk clinic with multiple years' experience evaluating infants with both the HINE and Prechtl's GMA with the MOS. Study consultant to the PI.

months corrected age between the time periods of 1 February and 31 August 2021. A total of 100 infants were included in the final study sample.

3.9 INCLUSION CRITERIA

To be included in the study, participants had to comply with the following:

- High-risk infants who had completed the HINE and Prechtl's GMA with the MOS assessments at 11-16 weeks corrected age, and that attended the follow-up assessment at 12-15 months corrected age between the time periods of February and August 2021.
- The following infants at risk for neurodevelopmental disorders were eligible for inclusion:
    - Infants weighing <1500g at birth. The neonatal high-risk clinic at TCH only routinely follows up preterm infants or infants with intrauterine growth restriction with a birth weight of ≤ 1499g.
    - Preterm and/or term infants with moderate to severe HIE, cooled or not.
    - Infants with congenital cytomegalovirus (CMV) infection.
    - Infants with grade III or IV IVH.
    - Infants with cystic periventricular leukomalacia (PVL).
    - Preterm and/or term infants with severe neonatal jaundice requiring exchange infusion.
    - Infants with neonatal bacterial meningitis (acquired within first 28 days of life).

3.10 EXCLUSION CRITERIA

The following exclusion criteria applied:

- Infants with known foetal alcohol syndrome (FAS).
- Infants with known congenital disorders or malformations of the central nervous system.
- Infants with known chromosomal defects (for example Down syndrome).
- Infants without written consent for inclusion in the study by legal guardians or parents.

- Infants with recurrent/prolonged hospital admissions after the 11-16 weeks corrected age assessment.
- Infants at 12-15 months corrected age fitting the inclusion criteria, but who were too upset or uncooperative during evaluations to obtain an accurate AIMS score.
- Infants that contracted diseases after the 11-16 weeks corrected age assessment that could influence neurological outcome for example meningitis/tuberculosis meningitis (TBM).

3.11 INSTRUMENTATION

In this study, Prechtl's GMA with the MOS, as well as HINE were conducted prior to assessment of motor development at 12-15 months corrected age. Routine HINE and GMA with MOS assessments were performed on all high-risk infants at 11-16 weeks corrected age. The PI then performed the AIMS assessment on the same subset of infants at their 12-15 months corrected age follow-up visit at the neonatal high-risk clinic to determine their gross-motor development.

3.11.1 Justification for the use of Alberta Infant Motor Scale (AIMS) to determine neurodevelopment at 12-15 months corrected age

In this thesis, the principal investigator (PI) had to select an outcome measure to determine the presence/absence of gross motor delay in the sample of high-risk infants. The Bayley Scales of Infant and Toddler Development is often used as the gold standard tool in AIMS, as well as other assessment tool validation studies. Both the AIMS and Bayley Scales of Infant and Toddler Development are frequently used in the literature in studies aimed at identifying gross motor delay in especially high-risk infants (Albuquerque, Guerra, Lima & Eickmann, 2018; Almeida, Dutra, Mello, Reis *et al*., 2008). While considered to be the gold standard, the Bayley Scales of Infant and Toddler Development has the disadvantage that it is lengthy to perform, and it requires assessors to be trained prior to the application of the tool. The AIMS is highly sensitive to predict gross motor delay, especially in preterm infants (Albuquerque *et al*., 2018; Almeida *et al*., 2008). Studies have found the predictive power of both the AIMS and the Bayley Scales of Infant and Toddler Development (3rd and 2nd versions) to be

similar when utilized to detect gross motor delay in preterm infants (Albuquerque *et al*., 2018, Almeida *et al*., 2008), suggesting that detection of developmental delays with the AIMS compares well to that of the Bayley Scales of Infant and Toddler Development.

For the purposes of this study, the AIMS was chosen as the tool of choice to establish the presence/absence of gross motor delay in our study sample of high risk-infants. The AIMS is a norm-referenced and performance-based assessment utilised to screen infants for gross motor developmental delays from birth to 18 months of age (Darrah, Piper & Watt, 1998). The AIMS assessment involves observation of the infant and is minimally invasive to perform. The screening tool consists of 58 items tested in various positions of typical gross motor development namely, prone (21 items), supine (9 items), sitting (12 items), standing (16 items). Every included item is representative of a gross motor movement/activity that is normally observed in typically developing infants (Darrah, Piper & Watt, 1998; Pin, de Valle, Eldridge & Galea, 2010; Piper & Darrah, 1994:186). Testing is quick, usually takes 10-15 minutes to complete. Total infant scores are calculated and plotted on a norm-based graph and infants scoring below the 5th percentile are classified as having severe and atypical gross motor delay (Darrah, Piper & Watt, 1998).

A pilot study performed by Manual, Burger and Louw in 2012, investigated the use of the AIMS to assess gross motor development of South African infants in the Cape Metropole. The study found that at 4 months corrected age, the South African infants scored higher than their Canadian counterparts (p=0.01), but that there was no significant difference between the two groups when tested at 8 and 12 months corrected age (Manual, Burger & Louw, 2012). The study also reported excellent interrater reliability scores for the AIMS as scored by two therapists for assessments at various intervals of 4, 8 and, 12 months corrected age. The authors reported a Intraclass Correlation Coefficient (ICC) of 0.995, 0.8 and 0.98 at 4, 8 and 12 months respectively. ICC=0.8 (Manual, Burger & Louw, 2012). Pin, de Valle and Eldridge (2010) also concluded that the AIMS has a high interrater reliability (ICC=0.85-0.98) when performed on preterm infants.

We deemed the AIMS appropriate because it is norm referenced, had good interrater reliability and has been validated for 12-month-old infants in a South African

population. Evaluating infants with a lengthy assessment tool (such as the Bayley Scales of Infant and Toddler Development 2nd/3rd edition) would not have been feasible for the purposes of this study, as infants already received an extensive and lengthy assessment by a medical doctor prior to their assessment by the PI for this study. The PI was also not trained in the application of the Bayley Scales of Infant and Toddler Development but was well trained in the application of the AIMS.

3.11.2 Justification for the use of HINE and Prechtl's GMA with the MOS at 11-16 weeks corrected age

The psychometric properties of both the HINE and Prechtl's GMA with the MOS have already been thoroughly described in Chapter 2 of this dissertation. Both Prechtl's GMA, as well as the HINE are considered as a gold standard for the detection of neurological deficits such as CP, and there is emerging evidence to suggest that it is also useful to protect minor neurological deficits in high-risk infants.

High inter-scorer reliabilities have been suggested in the literature for Prechtl's GMA with Cohen Kappa scores in range of 0.88-0.92 (Einspieler *et al*., 2019). Prechtl's GMA also has a high predictive power with sensitivity ranging from 95-98%, and specificity from 89-96% in high-risk cohorts (Einspieler *et al.*, 2019). Intra-observer reliability is also high with ICC ranging from 0.80-0.98 (Einspieler *et al*., 2019). Literature validates the use of the HINE for the detection of CP, as well as predicting developmental delay. Research suggests abnormalities detected when utilising the HINE can not only predict the development of CP but also provide an estimate of gross motor functional level of infants, including predicting independent siting, ambulatory ability, and subsequent milestones (Romeo *et al*., 2016).

3.12 PROCEDURE

Following approval by the Health Research Ethics Committee (HREC) of Stellenbosch University (S20/07/163) (Addendum A) participants were recruited into the study and assessed (Figure 3.1).

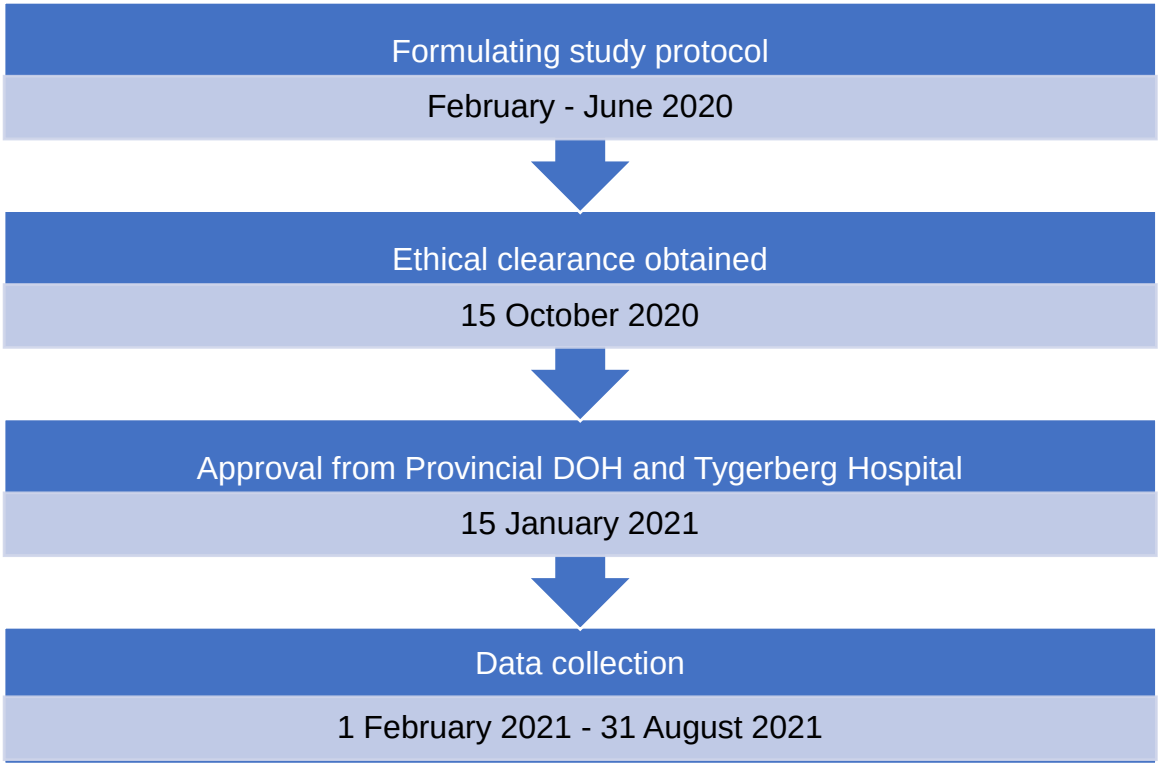

Figure 3. 1 Study procedure and timelines

3.12.1 Recruitment of study participants

Recruitment of infants for inclusion in this study was done in collaboration with the study consultant[2] at the neonatal high-risk clinic of TCH. The neonatal high-risk clinic initiated regular follow-up and screening of high-risk infants and utilises both Prechtl's GMA with the MOS and the HINE to assess and monitor neurodevelopment of these infants. The PI worked closely with the study consultant[2] to monitor infants' eligible to participate in the study. The PI monitored the appointment book to determine which infants are due for 12-15 month corrected age follow up screening in the period that data collection took place.

[2] Dr JI van Zyl: Medical Doctor at TCH's neonatal high-risk clinic with multiple years' experience evaluating infants with both the HINE and Prechtl's GMA with the MOS. Study consultant to the PI.

3.12.2 Procedure for obtaining informed consent

At the 12–15-month follow-up appointment, parents of eligible infants were approached after their infant's consultation with the treating medical doctor and verbally informed regarding the purpose of the study and the procedure to follow. Parents were given a printed consent form in their language of choice (Afrikaans, English, isiXhosa) and allowed sufficient time to properly read the documentation prior to signing consent for their infants to participate in the study. Parents/caregivers were encouraged to ask the PI questions if information was unclear and reminded that participation in the study is entirely voluntary. Parents that agreed to participate in this study were asked to provide written, informed consent (Addendum C), then the neurodevelopmental assessment was done utilising the AIMS. A tri-lingual research assistant (she speaks isiXhosa, English and Afrikaans) with more than ten years' experience assisted the PI to explain the study procedure to exclusively Xhosa speaking mothers (if translation was required). She also assisted with explaining information on consent forms, as well as assisted with translation during infant assessments with the AIMS where needed.

If parents failed to bring their infants for the 12–15-month follow-up appointment, the treating medical doctor sent them a SMS reminder and rescheduled their appointment for the following week (COVID-19 lockdown facility regulations permitting).

3.12.3 Procedure for the neurodevelopmental assessment using the HINE at 11-16 weeks corrected age

The HINE forms part of a standard neurodevelopmental assessment procedure at the neonatal high-risk clinic. The HINE assesses various aspects of neurodevelopment, including posture, cranial nerve function, quality and quantity of movement, reflexes, and muscle tone (Maitre, Chorna, Romeo, & Guzetta, 2016). The assessment is divided into 26 items (Maitre *et al*., 2016). For the study, all infants eligible for participation had a completed and scored HINE assessment on file. The HINE examination was performed by the treating medical doctor, who has multiple years of experience assessing infants with this tool. All infants were observed and scored for each item by obtaining a mark of either 0, 1, 2 or 3 with total scores ranging from 0-78. Each item on the HINE assessment sheet was scored separately, and the total

scores then added to obtain an optimality score. The HINE was analysed retrospectively for those infants whose parents/caregivers consented to participation in the study and allowed the PI to evaluate their infants utilising the AIMS assessment at 12-15 months corrected age. The PI was therefore blinded to the HINE scores (obtained by the infant's doctor at 11-16 weeks corrected age) prior to assessing the infants using the AIMS and only obtained access to the completed HINE score sheets after the assessment of the infant with the AIMS was completed at 12-15 months follow-up. All HINE assessments were completed by a medical doctor[2], and the PI was not present or involved in these assessments.

An initial total HINE cut-off score of 40 to predict later gross motor delay on the AIMS was utilised to generate a receiver operating characteristic (ROC) curve. Thereafter data was re-analysed to obtain a sample specific HINE total cut-off score in order to predict infants with a gross motor delay according to the AIMS. The cut-off used to determine gross motor delay on the AIMS was the 5th percentile. A HINE cut-off score of 40 is reported in the literature to be 100% predictive of CP at 3 months corrected age (Pizzardi *et al*., 2008; Romeo *et al*., 2008a; Romeo *et al*., 2016).

3.12.4 Procedure for videotaping and scoring of Prechtl's GMA with the MOS at 11-16 weeks corrected age

Prechtl's GMA with the MOS at 11-16 weeks corrected age forms part of a standard neurodevelopmental assessment procedure at the neonatal high-risk clinic. The study consultant[2] made video recordings of the infant's general movement patterns in compliance with the standardized protocol according to the General Movements Trust (General Movement Trust, n.d.). Recordings were made with a high-quality camera phone. All infants were recorded in a supine position and were suitably dressed to ensure comfort but allow for free unrestricted movement. Infants were filmed for a period of 5-8 minutes. The temperature of the room was maintained at 22-25° Celsius, and noise levels were kept to the minimum to reduce external factors that could distract the infant. External stimulation by caregivers (use of pacifiers or toys while the infant was being filmed) was not allowed. If the infant started to hiccup, fuss, or cry during the video recording, the recording was temporarily paused, and the caregiver had the opportunity to console the infant before resuming the recording.

The assessments of the video recordings utilising Prechtl's GMA with the MOS can only be conducted by assessors with an advanced GMA qualification from the General Movement Trust (www.general-movements-trust.info/). At TCH, two medical doctors[2,3] and a paediatric physiotherapist[4] are qualified to perform GMA screening. The video recordings of the GMs were independently scored by three assessors. Any conflicts in scores were resolved by a senior licensed Prechtl GMA tutor[5]. All video recordings and Prechtl's GMA with the MOS scoring were performed prior to commencement of data collection by the PI. All assessors, except one, were blinded to the infants' medical history and their developmental outcome. The PI was blinded to GMA and MOS scores until screening with the AIMS was completed at 12-15 months corrected age. The data was thus analysed retrospectively for those infants whose parents/caregivers consented to participation in the study and allowed the PI to evaluate their infants utilising the AIMS assessment at 12-15 months corrected age.

The MOS evaluations were scored as follows:

- Temporal organisation and quality of fidgety movements, scored as either normal, abnormal, exaggerated, or absent (scores 12, 4 and 1 respectively).
- Quality of movement patterns other than fidgety movements, scored as predominantly normal, equal number of normal and atypical patterns, or predominantly atypical (scores 4, 2 and 1 respectively).
- Age-adequate movement repertoire, scored as present, reduced, or absent (scores 4, 2 and 1 respectively).
- Postural patterns, scored as predominantly normal, equal number of normal and atypical patterns, or predominantly atypical (scores 4, 2 and 1 respectively).
- Movement character, scored as smooth and fluent, monotonous and/or jerky, stiff, tremulous, slow/fast or cramped-synchronised (Scores 4, 2 or 1 respectively).

[2] Dr JI van Zyl: Medical Doctor at TCH's neonatal high-risk clinic with multiple years' experience evaluating infants with both the HINE and Prechtl's GMA with the MOS. Study consultant to the PI.
[3] Dr M du Preez: Neonatologist at TCH.
[4] Ms Marlette Burger: senior lecturer at Stellenbosch University, Division of Physiotherapy and paediatric physiotherapist.
[5] Prof Christa Einspieler, Research Unit iDN, Interdisciplinary Developmental Neuroscience, Institute of Physiology, Center for Physiological Medicine, Medical University of Graz, Graz, Austria.

A MOS was deemed as optimal when it ranged from 25-28 (minimum score 5, maximum score 28) and a score of <25 was regarded as less optimal or reduced (Einspieler *et al.,* 2019). The infant's MOS was categorized as follows: optimal score ≥25; mildly reduced: 20-24; moderately reduced 9-19, and severely reduced ≤8. An initial MOS cut-off score of 8 to predict a gross motor delay on the AIMS was utilised to generate a ROC curve, whereafter a study sample specific MOS cut-off score could be determined to identify infants with gross motor delays (the cut-off score for gross motor delay on the AIMS was the 5th percentile). Literature reports that a MOS total score of <8 is associated with GMFCS levels IV and V, thus indicating severe functional and gross motor impairment (Einspieler *et al*., 2019).

3.12.5 Procedure for Neurodevelopmental Scoring at 12-15 months corrected age using the Alberta Infant Motor Scale (AIMS)

The PI was responsible for assessing the infants at 12-15 months corrected age using the AIMS. Assessment took place in a quiet, well-lit and clutter free area in TCH. A therapy mat was placed on the floor for the infant to freely move around without risk of injury. All surfaces were thoroughly sterilised and cleaned between infant evaluations. Toys were placed strategically or utilised to entice infant participation and were sterilised with 70% alcohol solution after each new infant evaluation. Parents/caregivers were also encouraged to use their own babies' toys where possible, to ensure health and safety of all infants evaluated. The infant was then observed from a distance, and only prompted into positions where needed. The duration of the evaluation performed was no longer than 15-30 minutes.

The PI observed the infant in prone (21 items), supine (9 items), sitting (12 items) and standing (16 items) and observed the least to most mature gross motor items as demonstrated by the infant. A window of movement repertoire was then created between the least and most observed items. Total AIMS scores were calculated by crediting each item below the least mature observed item with one point, as well as all the items observed within the window. A maximum total score of 58 could be achieved (Darrah, Piper & Watt, 1998). The PI utilised a standardised table of AIMS percentile ranks (where percentile ranks have been averaged over an entire age month) to determine each infants percentile ranking according to their AIMS total score (Piper & Darrah, 1994:48). The percentile ranking allocated indicates what proportion of the

norm-referenced sample of infants in the same age group attained a similar AIMS score. A higher AIMS percentile ranking indicates a decreased likelihood for gross motor delay (Piper & Darrah, 1994:49). An AIMS total score of ≤35 indicated that an infant scored ≤1st percentile on the AIMS percentile reference table, and a maximum AIMS score of 58 indicated that an infant scored >77th percentile on the AIMS (Piper & Darrah, 1994:204).

It is stated in the literature that a cut-off AIMS percentile of 5th percentile is to be utilised for infants >8 months corrected age to maintain the highest specificity values (Darrah, Piper & Watt, 1998). Infants in our study were classified as having a severe or atypical gross motor delay if they scored <5th percentile on the AIMS.

As part of the routine 12-15 month follow up assessment, the study consultant[2] also performed a complete neurological examination and infants were classified as normal, suspect, or abnormal. The severity of motor disability of those infants falling in the abnormal group was then classified in accordance with the GMFCS for children with CP (Palisano *et al.*,1997). Infants were classified as follows:

Level I - Infant was able to pull to stand and take steps holding on to furniture. And/or able to crawl on hands and knees. And/or able to sit independently on the floor with both hands free to manipulate toys and was able to move in and out the sitting position.

Level II - Infant crept on stomach or crawled on hands and knees. And/or maintained the floor sitting position but needed to use hands for support to maintain balance.

Level III - Infant rolled and crept forward on the stomach. And/or only maintained floor sitting position when the low back was supported.

Level IV - Infant was able to roll from prone to supine. And/or had head control, but full trunk support was needed for floor sitting.

Level V - Infant was unable to maintain head and trunk control in the puppy prone position as well as in the floor sitting position. Infant required assistance to roll from prone to supine or supine to prone.

3.12.6 Data management and storage

All data was managed confidentially utilising a coding system. Names of infants were replaced by a unique code, and the full names and details of infants was only known to the PI, and the study consultant[2] that performed the neurological examination (HINE and Prechtl's GMA with the MOS). All confidential documents (consent forms/assessment sheets/copies) were securely locked away either at Stellenbosch University, Division of Physiotherapy, 4th Floor Clinical Building, or at the high-risk neonatal clinic of TCH, C3A, at the office of the study consultant.

3.12.7 Infant information collected

The following additional information was collected from medical records of each infant, as well as part of the verbal interview with their parents/caregiver and logged onto an excel spreadsheet:

- Birth weight (grams)
- Apgar score at birth
- Small for gestational age vs intrauterine stunted growth
- Gender
- Gestational age (weeks)
- NICU admission/stay: length of hospitalisation, ventilation/oxygen therapy administered
- Surgical procedures performed
- Periventricular leukomalacia (PVL Grade I-IV)
- Delivery method: normal vaginal delivery (NVD) vs caesarean section
- Morbidities and/or disease: e.g., meningitis
- Birth complications: intraventricular haemorrhage (IVH Grade I-IV)
- Diagnosis of and/or exposure to human immunodeficiency virus (HIV) (if information was available)
- Reasons for hospitalisation after initial neonatal intensive care unit (NICU) discharge
- Information regarding any birth complications
- Information regarding recent hospital admissions of infant and current medication use

- Demographic information regarding care of the infant at home as well as social circumstances: parent's level of education, employment details, marital status, use of a baby walker in infancy, practice of carrying the infant on the caregivers back

3.12.8 Personal protection and safety during evaluation/testing

The global COVID-19 pandemic brought about additional concerns regarding physical and close contact with others and required additional safety measures to be implemented for the duration of this study. During evaluation of all infants with the HINE and Prechtl's GMA with the MOS (at 11-16 weeks corrected age) and AIMS (at 12-15 months corrected age) the PI and treating medical doctor wore appropriate personal protective equipment (PPE) as needed when examining infants (surgical mask, gloves, protective eye wear) to avoid possibility of disease transmission to others, as well as to protect the PI/treating medical doctor from possible infection. Infants and/or parents that displayed flu-like symptoms or had a history of being in close contact with a person confirmed with COVID-19 (positive polymerase chain reaction (PCR) test) were kindly requested to not attend the follow up evaluation session and referred for further investigation/assistance as needed. Parents of infants were requested to wear a fabric mask and to practice good hand hygiene principals. All surfaces and toys were thoroughly sterilised and cleaned with 70% alcohol solution after each new infant evaluation.

3.13 STUDY LIMITATIONS

Due to infant follow up being limited to 12-15 months corrected age and not beyond, study results are limited in their ability to predict long term neurological outcomes in these at-risk infants.

3.14 STATISTICAL ANALYSIS

Stata version 16 software was utilised for data analysis. The outcomes of interest with regards to the MOS and HINE were analysed both as continuous and categorical variables. Linear regression and correlation were considered for the continuous

version of the variables while ordinal logistic regression and Chi-square test of association was used for the categorical version of the outcomes. Level of significance to interpret Chi-square test results was set at $p<0.05$. Exact-2-sided significance was used to interpret p-values where appropriate. A cut-off score of the 5th percentile on the AIMS was used to identify infants with a gross motor delay (Darrah, Piper & Watt, 1998). Categorical variables were summarized and are presented using frequencies and percentages. Continuous variables are presented using means and standard deviations or median with interquartile range, when not distributed normally.

ROC curves were generated to determine sensitivity and specificity values, and area under the curve (AUC) was statistically generated. A ROC curve is generated to show the relationship between the clinical sensitivity and specificity of a test for all possible test cut-off scores. It also allows the researcher to determine test specific cut-off scores from the curve with optimal sensitivity and specificity values. The x-axis of the ROC curve represents 1- specificity, or the false positive fraction. The y-axis on the ROC curve indicates sensitivity, or the true positive fraction (Hajian-Tilaki, 2013). The closer the ROC curve lies in proportion to the left upper hand corner of the graph (see Chapter 4 for examples of graphs), the greater the discriminatory capacity of the test measured (Hajian-Tilaki, 2013).

The area under the curve (AUC) is a statistical measurement obtained from the ROC curve. The area under the curve (AUC) is defined as the average value of sensitivity for all the possible values of specificity and it therefore gives an overview of the accuracy of the tests that it measures (Hajian-Tilaki, 2013). The AUC can be seen as a combination between sensitivity and specificity values that describes the inherent validity of the tests it measures (Hajian-Tilaki, 2013). An optimal AUC=1.00, thus the closer the AUC value generated is to 1.00, the more accurate the diagnostic probability of the test (Hajian-Tilaki, 2013).

3.15 ETHICAL CONSIDERATIONS

Ethical approval was obtained from The Health Research Ethics Committee (HREC) of the University of Stellenbosch order to conduct this study. The Declaration of Helsinki and South African Guideline for Good Clinical Practice have established

ethical guidelines and standards that are internationally accepted, and this study was conducted in accordance thereof. Furthermore, permission was obtained from the Western Cape Department of Health, Superintendent of Tygerberg Hospital (Addendum B) and departmental chairperson/head of Paediatrics (Addendum B) for the study to be conducted at TCH.

The following ethical topics was considered when conducting this study:

3.15.1 Consent: Parents/legal guardians of all infants eligible for inclusion in the study had to provide written informed consent (Addendum C) prior to the PI being able to evaluate their infants using the AIMS assessment tool.

3.15.2 Assessment of patient records: Infants medical records were accessed, and data processed after consent was obtained from the infant's parents/legal guardians. Patient records were accessed in line with the guidelines stipulated by Protection of Personal Information Act (2020) of South Africa, and stored on a password protected laptop, as well as on password protected cloud storage.

3.15.3 Voluntary Participation: Parents/legal guardians had the choice to either except, and/or decline participation and/or withdraw their infant/(s) at any given point in time, should they wish to do so, without it affecting further treatment/ management at TCH.

3.15.4 Confidentiality: All personal information and data collected was managed confidentially. Participants each had a unique code (baby 1-100). Parents/legal guardians were assured that all data/information collected, and all results/data published would be done anonymously.

3.15.5 Remuneration: Parents/legal guardians were expected to travel to TCH to bring their infants for follow up assessment with a medical doctor[2], whereafter they were evaluated by the PI utilising the AIMS. Since the 12-15 month follow up procedure forms part of the standard follow up of high-risk infants, travel costs were not reimbursed. The parents/legal guardians and their infants did however receive a healthy snack as a small token of appreciation for taking part in the study.

3.15.6 Risks: This study was deemed to be low-risk, and no adverse events or risks occurred during its implementation. Follow up assessments at 12-15 months corrected age were conducted at TCH's neonatal high-risk clinic, C3A and there were qualified

medical and nursing staff on site to intervene/assist in emergency situations where needed.

3.15.7 Clinical implication of assessment: All infants identified as having a gross motor delay on assessment with the AIMS at 12-15 months corrected age were either already receiving outpatient physiotherapy/occupational therapy due to prior referral for intervention by the medical doctor (in the cases of infants already suspected with severe/evolving CP) or were appropriately referred for therapy after assessment and in consultation with the doctor in charge at the neonatal high-risk clinic. Parents of infants with possible developmental delay were informed and educated on the assessment findings, and appropriate developmental exercises and advice were given to parents and caregivers where appropriate.

The study results will be presented in Chapter 4.

CHAPTER 4

RESULTS

The following chapter provides an overview of the study sample size, participant demographics, presence of perinatal factors, as well as predictive validity outcomes and subcategory analysis of the Hammersmith Infant Neurological Examination (HINE) and Prechtl's General Movement Assessment (GMA) with Motor Optimality Score (MOS). Numbers are rounded off to two decimal points (where applicable), and a significance level of 5% ($p<0.05$) was selected to identify significant results.

4.1 SAMPLE SIZE

One hundred (n=100) infants fitting our inclusion criteria attended their 12-15 month scheduled follow-up appointment at the neonatal high-risk clinic during the data collection period of February the 1st and the 31st of August 2021. We utilised opportunistic sampling and therefore consented all infants fulfilling the inclusive criteria during the data collection period.

4.2 DEMOGRAPHIC PROFILE OF THE SAMPLE

4.2.1 Gender, gestational age, birth weight

Fifty-five infants included in our study were female, and 45 infants were male (Table 4.1). Table 4.1 also shows that of the 100 enrolled participants, 54 were infants of black ethnicity and 46 of coloured ethnicity. No Caucasian or Indian infants were enrolled in this study. Gestational age ranged from 27-41 weeks with a mean gestational age of 31.14 weeks (Figure 4.1). Infants had a mean birthweight of 1525.55g (ranging from 790g to 4250g) (Figure 4.2). Table 4.2 provides a further description of the distribution of infants that were classified as extremely low-birth weight (ELBW), very-low birth weight (VLBW), and either preterm or term born. Majority of the infants included in the study were born preterm, with 17% of infants being extremely preterm (EPT), 57% very preterm (VPT), 9% late-to-moderate preterm and 17% full-term infants. Twenty-one percent (21%) of infants were classified

as being ELBW and 60% of infants had a VLBW. Of the infants that scored <5th percentile on the Alberta Infant Motor Scale (AIMS), 20% were ELBW and 53,33% were VLBW. More than seventy percent (73.3%) of the infants that scored <5th percentile on the AIMS were born very preterm, and 26.67% were born at term.

Table 4.1 Infant gender and ethnicity (n=100)

		COUNT	%
Gender	Female	55	55.0%
	Male	45	45.0%
Ethnicity	Black	54	54.0%
	Coloured	46	46.0%

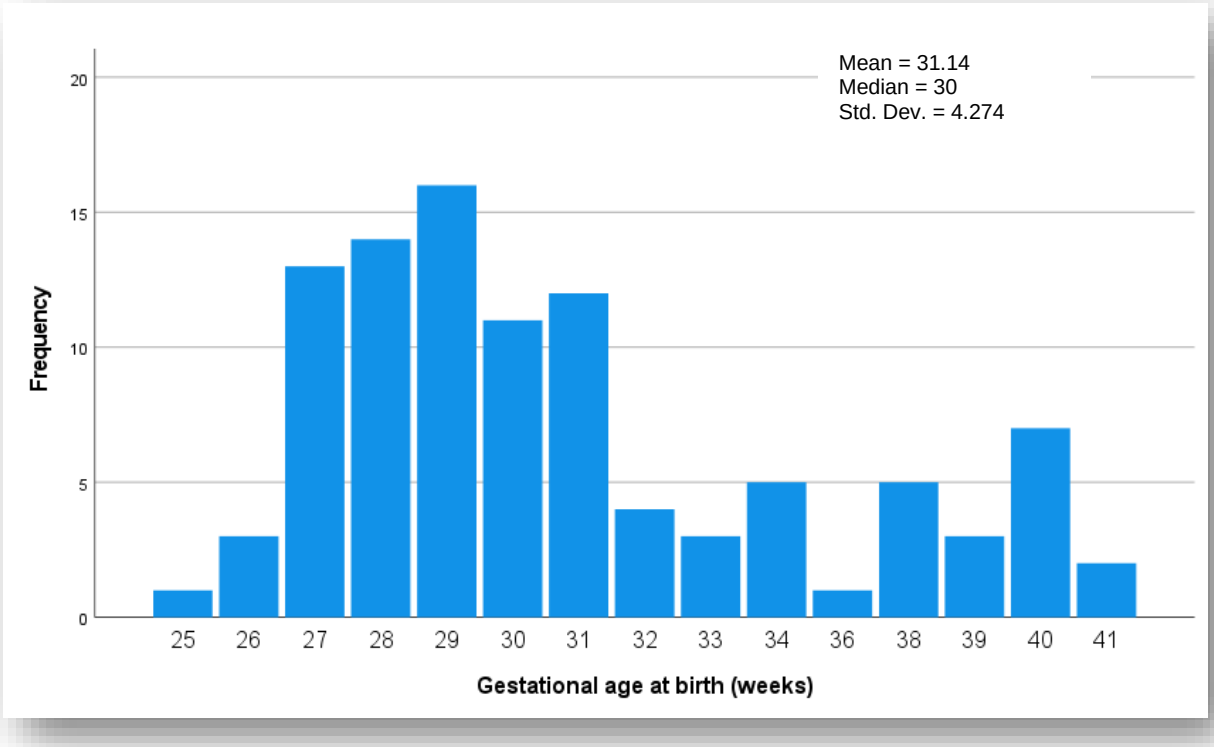

Figure 4.1 Frequency distribution of gestational age of infants

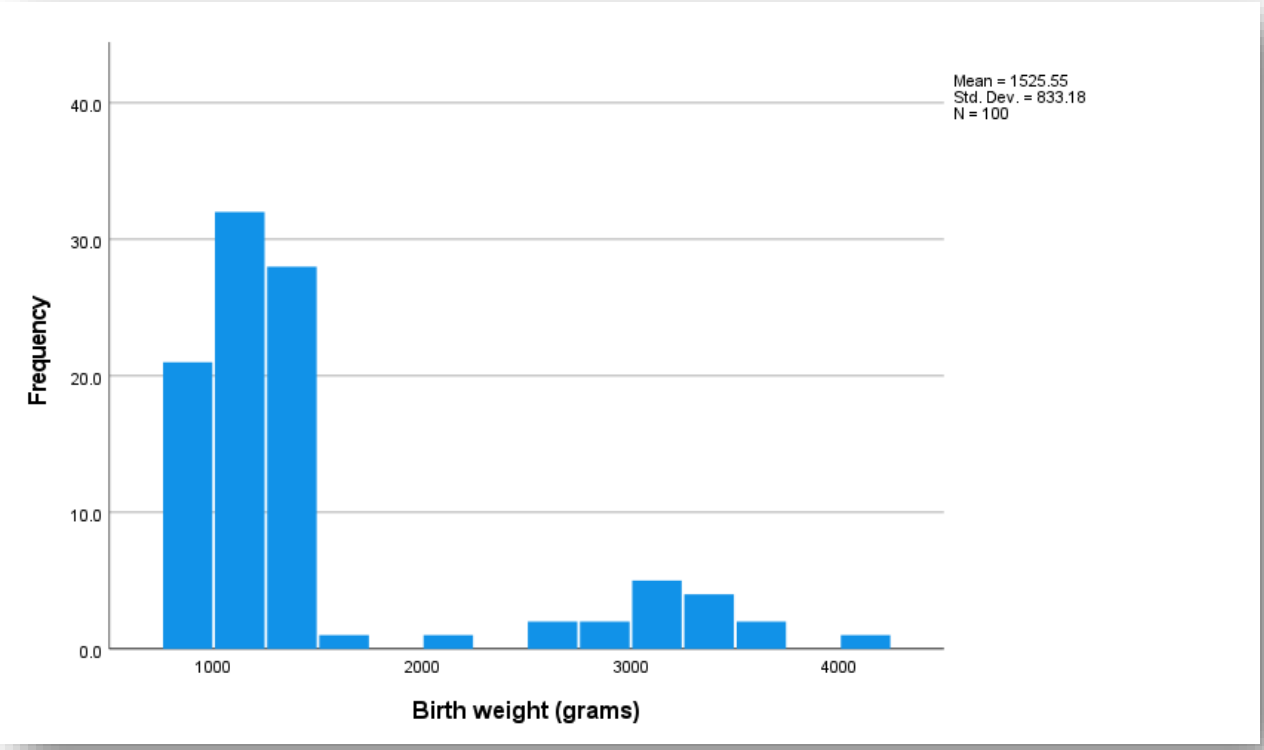

Figure 4.2 Frequency distribution of birth weight of infants

Table 4.2 Distribution of birthweight of infants (n=100)

	COUNT	%
ELBW	21	21.00%
VLBW	60	60.00%
Extremely preterm	17	17.00%
Very preterm	57	57.00%
Late/Moderate preterm	9	9.00%
Full-term	17	17.00%

ELBW: Extremely low birth weight; VLBW: Very low birth weight

4.2.2 Perinatal risk factors of infants

Table 4.3 shows the distribution of perinatal risk factors and illness information of the high-risk infants included in our study. The majority of infants were diagnosed with respiratory distress syndrome (RDS) post-birth. Sixty-seven percent (67%) of infants with RDS also had hyalin membrane disease (HMD). Infants were prone to develop jaundice (55%), sepsis (28%), hypoxic-ischaemic encephalopathy (HIE) (17%), anaemia (13%) and seizures (12%). All of the infants with HIE were born at term and had a normal birthweight (Table 4.4). The ability of infants that scored <5th percentile on the AIMS to roll, sit, and walk at 12-15 months corrected age is also portrayed in Table 4.4. None of the infants that were classified with a gross motor delay were able to walk at 12-15 months corrected age, and the majority of these infants were unable to roll or sit independently.

Table 4.3 Perinatal risk factors of high-risk infants

	COUNT	%
Sepsis	28	28.00%
Meningitis	4	4.00%
IVH	1	1.00%
Anaemia	13	13.00%
Jaundice	55	55.00%
RDS	95	95.00%
HMD	67	67.00%
Reflux	2	2.00%
MRSA	4	4.00%
NEC	5	5.00%
Abnormal CUS	4	4.00%
HIE	17	17.00%
Seizures	12	12.00%
Congenital syphilis	1	1.00%
PDA	2	2.00%

IVH: Intra-ventricular haemorrhage; RDS: Respiratory distress syndrome; HMD: Hyalin membrane disease; MRSA: Methicillin-resistant Staphylococcus aureus; NEC: Necrotizing enterocolitis; CUS: Cranial ultrasound; HIE: Hypoxic ischemic encephalopathy; PDA: Patent ductus arteriosus

Table 4.4 Characteristics and motor ability of infants scoring <5th percentile on the AIMS (n=15)

		COUNT	%
Birthweight	ELBW	3	20.00%
	VLBW	8	53.33%
	Normal BW	4	26.67%
Gestational age	Extremely preterm	0	0.0%
	Very preterm	11	73.33%
	Moderate/late preterm	0	0.0%
	Term	4	26.67%
HIE	Yes	4	26.67%
	No	11	73.33%
Rolls independently (12-15 months CA)	Yes	8	53.55%
	No	7	46.66%
Sits independently (12-15 months CA)	Yes	9	60.00%
	No	6	40.00%
Walks independently (12-15 months CA)	Yes	0	0.0%
	No	15	100.0%

ELBW: Extremely low birth weight; VLBW: Very low birth weight; HIE: Hypoxic ischemic encephalopathy; CA: Corrected age

4.3 DEMOGRAPHIC INFORMATION OF INFANT CAREGIVERS

Maternal age at birth ranged from 15 to 40 years of age with a mean age of 28 years. Mothers attended school to a mean grade of eleven, and 59% of mothers completed their high school education (grade 12). Fifty-six percent (56%) of mothers were unemployed, and 8% were still in school with 36% of mothers employed in the formal or informal sector. Seventy-five percent (75%) of families earned less than R5000 per month. The socio-economic circumstances and demographic information of caregivers are further described in Table 4.5.

Table 4.5 Demographic and social information of infant caregivers

		MEAN (Range)	COUNT	%
Maternal age at birth		28 (15-40)		
Education grade		11 (4-12)		
Total pregnancies	1		27	27.00%
	2-4		60	60.00%
	>5		13	13.00%
Employed	Yes		36	36.00%
	No		56	56.00%
	Student		8	8.00%
Marital status	Married		36	36.00%
	Single		31	31.00%
	In relationship		33	33.00%
Monthly household income	≤ R5000		75	75.00%
	R5000-R10 000		16	16.00%
	≥R10000		9	9.00%

4.4 TEST SCORE RESULTS AT 12-15 MONTHS CORRECTED AGE

4.4.1 Gross motor outcomes according to the Alberta Infant Motor Scale (AIMS) at 12-15 months corrected age (CA)

The mean total AIMS score (out of a total of 58) and AIMS percentile ranking at 12-15 months corrected age was 49.05 and 33.83 respectively (Table 4.6). Total AIMS scores ranged from 7-58 while AIMS percentile rankings ranged from 1 to ≥77th percentile. An AIMS percentile ranking of <5th percent is equated to a severe or atypical gross motor development. Fifteen infants in our study scored below the 5th percentile on the AIMS.

Table 4.6 Descriptive statistics of AIMS scores of high-risk infants (n=100)

	COUNT	AIMS TOTAL	AIMS PERCENTILE
N		100	100
Mean		49.05	33.83
Median		52.00	28.00
SD		11.76	24.81
Skewness		-2.45	.477
Std. Error of Skewness		.241	.241
Minimum		7	1
Maximum		58	77
AIMS <5th percentile	15		
AIMS 10th – 5th percentile	3		

AIMS: Alberta Infant Motor Scale; SD: Standard deviation

Table 4.7 provides an overview of the outcomes on each of the AIMS subcategories for all high-risk infants. Infants that scored <5th percentile on the AIMS mostly scored poorly in the standing subcategory of the AIMS.

Table 4.7 Outcomes on AIMS subcategories for total sample of infants (n=100) versus infants scoring <5th percentile on the AIMS (n=15)

	AIMS TOTAL		PRONE		SUPINE		SITTING		STANDING	
	Total infants	<5th percentile AIMS	Total infants	<5th percentile AIMS	Total infants	<5th percentile AIMS	Total infants	<5th percentile AIMS	Total infants	<5th percentile AIMS
Mean	49.05	24.86	19.05	9.13	8.47	6.13	11.04	6.20	10.63	3.73
Median	52	27.00	21.00	8.00	9.00	7.00	12.00	8.00	10.00	3.00
SD	11.76	13.77	4.78	5.91	1.37	2.41	2.60	4.17	3.96	2.63
Range	7 - 58	7 - 46	3 - 21	3 - 21	2 - 9	2 - 9	1 - 12	1 - 12	1 – 16	1 - 10

AIMS: Alberta Infant Motor Scale; SD: Standard deviation

Figure 4.3 and Figure 4.4 below illustrate the frequency distribution of both the total AIMS scores, as well as the AIMS percentile rankings for all the infants assessed. The mean age total score was 49.05 (Table 4.3), and the mean AIMS percentile 33.83 (Table 4.4).

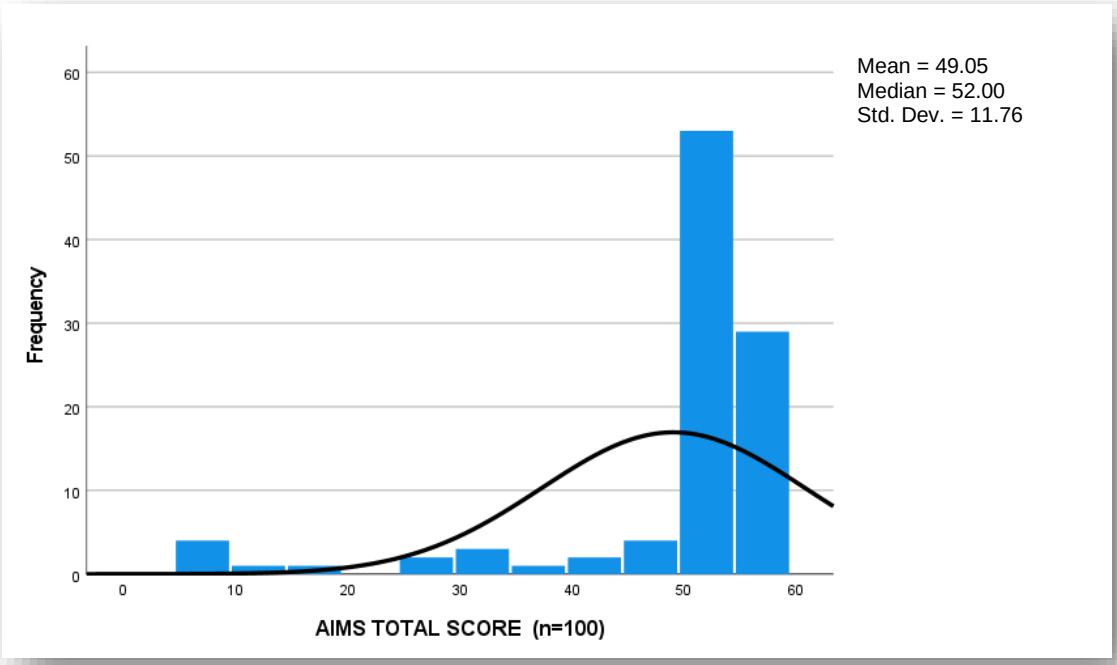

Figure 4.3 Frequency distribution of AIMS total scores at 12-15 months corrected age

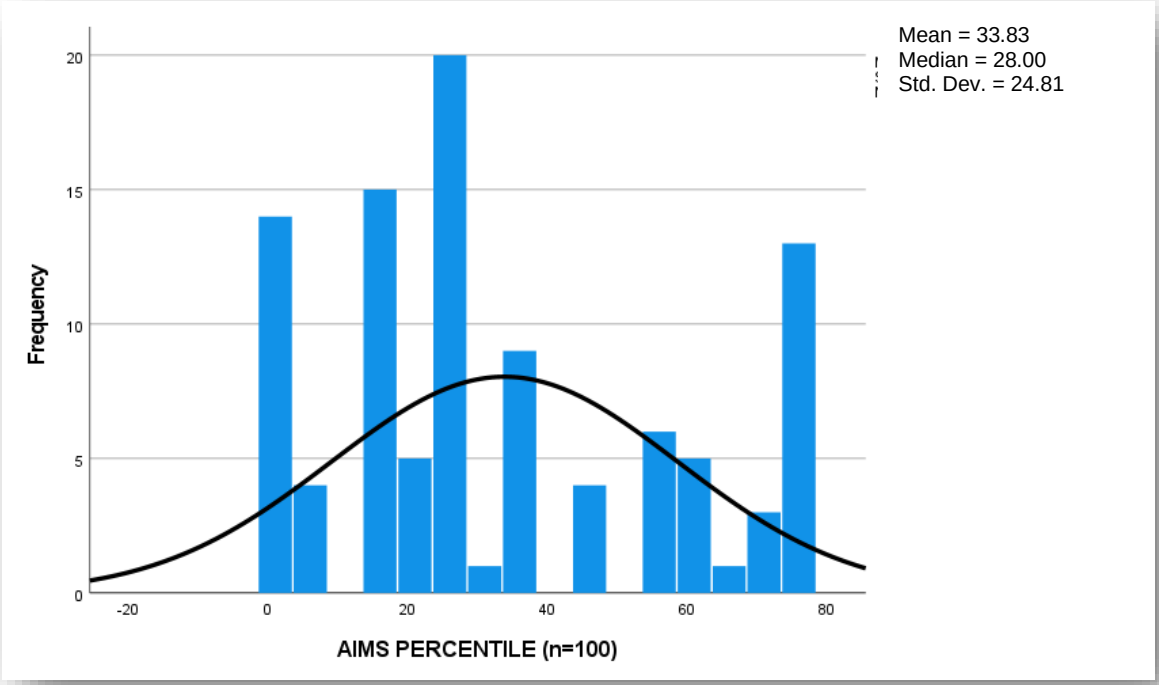

Figure 4.4 Frequency distribution of AIMS percentile rankings at 12-15 months corrected age

4.5 DESCRIPTION OF INFANTS WITH CEREBRAL PALSY (CP)

Table 4.8 provides a description of the infants in our study provisionally diagnosed with cerebral palsy (CP) at 12-15 months corrected age. Seven infants (7%) out of our total sample of 100 infants were diagnosed with CP. Five of the seven infants had spastic-quadriplegic CP, one infant was classified with suspected evolving spastic diplegic CP, and one infant with right-sided hemiplegia. Four infants were female, and three infants were male. Five infants were provisionally classified as Level V on the Gross Motor Function Classification System (GMFCS), thus indicating that they are severely limited in gross motor and functional ability. Two infants were classified as level III on the GMFCS. Four infants were born at term, and three infants were born preterm.

Table 4.8 Description of infants diagnosed with CP at 12-15 months corrected age

PROPOSED CP DIAGNOSIS AT 12-15 MONTHS CA	GMFCS AT 12-15 MONTH CA	FM AT 11-16 WEEKS CA	GENDER	BW (g)	GESTATION (weeks)	APGAR 1	APGAR 5	APGAR 10
Evolving spastic diplegic CP	III	Absent	Female	2830	40	2	7	7
Spastic right hemiplegia	III	Normal	Male	1380	29	2	6	8
Spastic Quadriplegia	V	Absent	Female	3255	40	3	4	5
Spastic Quadriplegia	V	Absent	Male	1225	30	6	8	9
Spastic Quadriplegia	V	Absent	Female	1290	29	7	8	8
Spastic Quadriplegia	V	Absent	Female	3100	40	2	7	8
Spastic Quadriplegia	V	Absent	Male	2020	38	0	3	4

BW: Birth weight; CA: Corrected age; CP: Cerebral palsy; FM: Fidgety movements; GMFCS: Gross Motor Function Classification System

4.6 PREDICTIVE VALIDITY OF TESTS TO DETERMINE GROSS MOTOR OUTCOMES AT 12-15 MONTHS CORRECTED AGE

4.6.1 Outcomes of infants on the Hammersmith Infant Neurological Examination (HINE)

Table 4.9 provides a visual representation of outcomes of all the infants according to the HINE. The mean total HINE score (highest possible total 68) was 63.18 with a range of 21 – 71. Infants scored well in the cranial nerve, posture, movement and tone subcategory, and had poorer scores in the reflexes and reactions subcategory of the HINE.

Table 4.9 Outcomes of infants according to the HINE total score and subcategories (n=100)

	HINE SUBCATERGORIES					
	HINE TOTAL	**CRANIAL NERVES**	**POSTURE**	**MOVEMENT**	**TONE**	**REFLEX AND REACTIONS**
Mean	63.18	13.81	13.42	5.82	21.54	8.7
Median	64.50	15.00	14.00	6.00	22.00	9.00
SD	6.71	1.43	1.33	0.92	2.51	2.25
Range	21 - 71	8 - 15	7 - 16	0 - 6	4 - 24	0 - 12

HINE: Hammersmith Infant Neurological Examination; SD: Standard deviation

Table 4.10 Outcomes on the HINE of infants scoring <5th percentile on the AIMS (n=15)

	HINE TOTAL	**CRANIAL NERVES**	**POSTURE**	**MOVEMENT**	**TONE**	**REFLEX AND REACTIONS**
Mean	54.20	12.80	12.10	4.93	18.70	5.66
Median	60.00	13.00	12.00	6.00	22.00	6.00
SD	12.68	2.04	2.23	2.21	5.12	2.76
Range	21 - 71	8 - 15	7 - 16	0 - 6	4 - 24	0 - 12

HINE: Hammersmith Infant Neurological Examination; SD: Standard deviation

4.6.2 Predictive validity of the Hammersmith Infant Neurological Examination (HINE)

Figure 4.5 demonstrates the predictive validity of the HINE done at 11-16 weeks corrected age to determine the gross motor outcomes on the AIMS at 12-15 months corrected age. The results show that the HINE was a good predicter of gross motor outcome on the AIMS with an area under the curve (AUC) of 0.867. The AUC is a statistical measurement defined as the average value of sensitivity for all the possible values of specificity. It provides an overview of the diagnostic accuracy of a test. An optimal AUC=1.00, thus the closer the AUC value generated is to 1.00, the more accurate the diagnostic probability of the test (Hajian-Tilaki, 2013). The HINE had good specificity (100%), but poor sensitivity (13%) to predict later gross motor delay on the AIMS. PPV was 100%, and NPV was 87%.

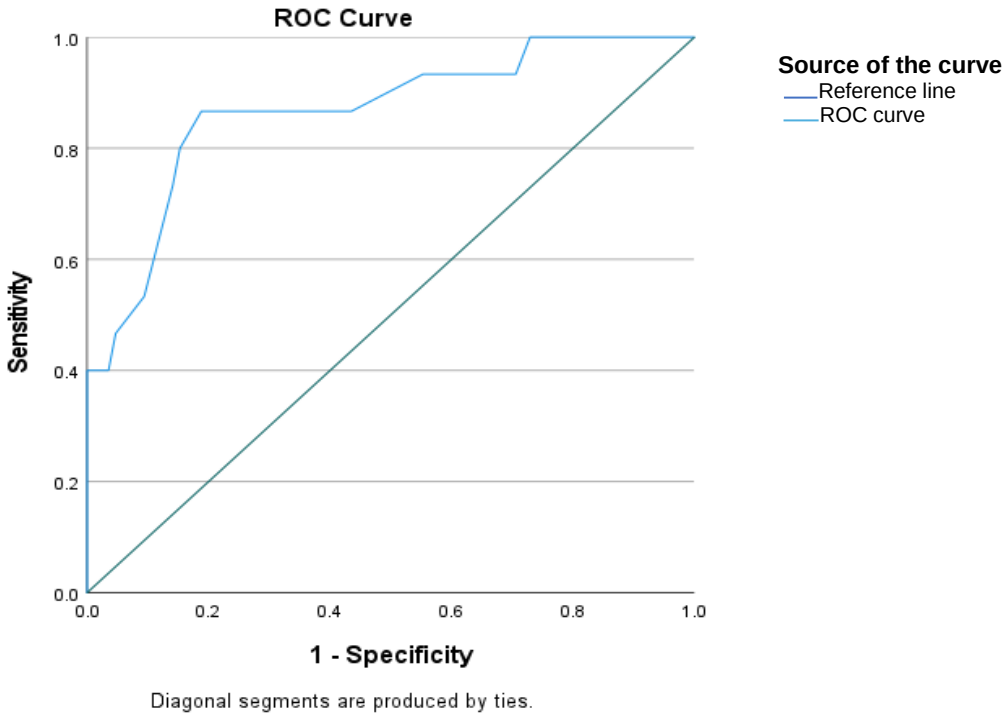

Figure 4.5 Predictive validity of HINE to determine gross motor outcome on AIMS at 12-15 months corrected age.

A HINE total cut-off score was determined and related to gross motor outcomes of infants on the AIMS. The aim was to determine a HINE cut-off score that would be able to identify infants that scored less than the 5th percentile on the AIMS (thus having a severe gross motor delay such as CP, but also to identify infants with atypical gross motor delays). Utilizing receiver operating characteristic (ROC) curve analysis, a proposed HINE cut-off score of 62.25 was identified with a sensitivity and specificity of 87% and 81% respectively, with PPV=54% and NPV=97% to identify infants scoring less on the 5th percentile on the AIMS.

4.6.3 Outcomes of infants on Prechtl's General Movement Assessment (GMA) with the Motor Optimality Score (MOS)

Table 4.11 provides an overview of general outcomes of infants according to Prechtl's GMA with the MOS. The mean MOS total score was 25.05 (maximum score 28) and ranged from 5-28. The mean score for MOS subcategories including fidgety movements, observed movement patterns, age-adequate movement repertoire, observed postural patterns, and movement character were 11.34 (maximum score 12), 3.89 (maximum score 4), 2.60 (maximum score 4), 3.47 (maximum score 4) and 3.75 (maximum score 4) respectively.

Table 4.11 Outcomes of infants on Prechtl's GMA with MOS (n=100)

	MOS TOTAL SCORE	FMs	OBSERVED MOVEMENT PATTERNS	AGE-ADEQUATE MOVEMENT REPERTOIRE	OBSERVED POSTURAL PATTERNS	MOVEMENT CHARACTER
Mean	25.05	11.34	3.89	2.60	3.47	3.75
Median	26.00	12.00	4.00	2.00	4.00	4.00
SD	4.57	2.62	.549	1.31	1.02	.687
Range	5 - 28	1 - 12	1 - 4	0 - 4	1 - 4	1 - 4

FM: Fidgety movements; MOS: Motor Optimality Score; SD: Standard deviation

Table 4.12 on illustrates outcomes on Prechtl's GMA with the MOS of infants that scored less than the 5th percentile on the AIMS, and thus had a severe or atypical gross motor delay at 12-15 months corrected age. The mean MOS total score in thus subgroup (n=15) of infants with gross motor delay was significantly lower than that of the total sample of infants (n=100). The mean MOS total score was 19.00 and ranged from 5-28. The mean score for the fidgety movements, observed movement patterns, age-adequate movement repertoire, observed postural patterns, and movement character subcategories of the MOS was 7.6 (maximum score 12), 4.40 (maximum score 4), 2.20 (maximum score 4), 2.53 (maximum score 4) and 3.26 (maximum score 4) respectively.

Table 4.12 Outcomes of infants on Prechtl's GMA with MOS that scored <5th percentile on the AIMS (n=15)

	MOS TOTAL SCORE	FMs	OBSERVED MOVEMENT PATTERNS	AGE-ADEQUATE MOVEMENT REPERTOIRE	OBSERVED POSTURAL PATTERNS	MOVEMENT CHARACTER
Mean	19.00	7.6	4.40	2.20	2.53	3.26
Median	25.00	12.00	4.00	2.00	2.00	4.00
SD	9.07	5.57	1.24	1.37	1.45	1.09
Range	5 - 28	1 - 12	1 - 4	0 - 4	1 - 4	1 - 4

FM: Fidgety movements; MOS: Motor Optimality Score; SD: Standard deviation

4.6.4 Predictive validity of Prechtl's General Movement Assessment (GMA) with Motor Optimality Scale (MOS) of gross motor outcomes on Alberta Infant Motor Scale (AIMS) at 12-15 months corrected age

The median MOS total score was 26.00. The sensitivity and specificity of Prechtl's GMA with MOS (utilising a MOS cut off score of 8) to predict gross motor delay on the AIMS (utilising an AIMS cut-off score of the 5th percentile) is depicted in Figure 4.6. Prechtl's GMA with MOS had a sensitivity and specificity of 20% and 100% respectively. Area under the ROC curve was 0.713 with PPV of 100% and NPV of 88%.

Utilizing ROC curve analysis, we again proposed a new MOS cut-off score of 20.5 after further analysis of data again with the aim to establish if a customised cut-off score specific to our sample would better predict gross motor outcomes alone, and not only severe neurological deficit. A MOS cut-off score was determined to predict infants that would have a severe or atypical gross motor delay on the AIMS at 12-15 months corrected age, thus infants that would score <5th percentile on the AIMS. A cut-off MOS score of 20.5 had a sensitivity and specificity of 47% and 100% respectively, with PPV=100% and NPV=91%.

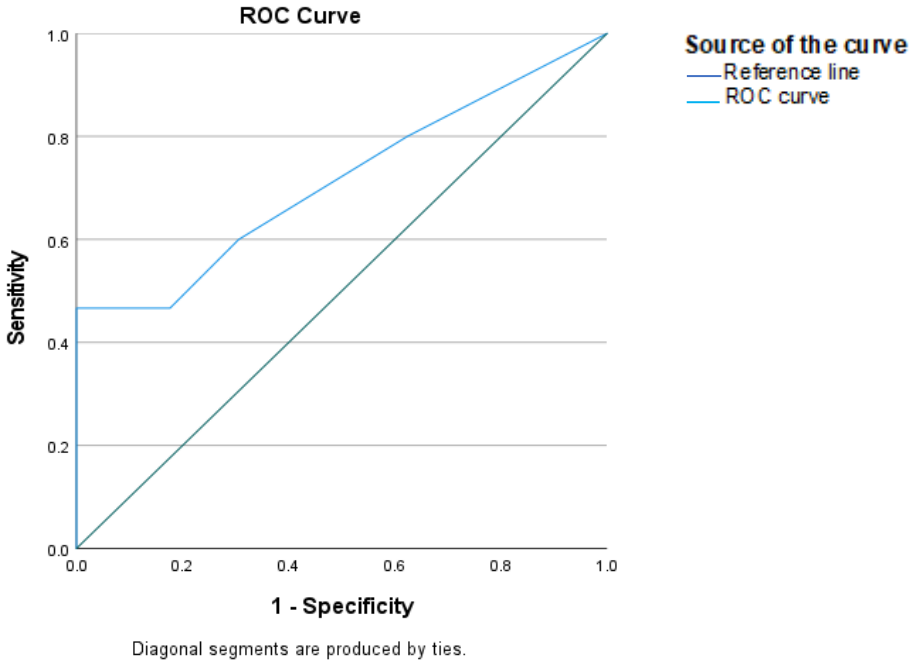

Figure 4.6 Predictive validity of Prechtl's GMA with MOS of gross motor outcomes on the AIMS (n=100)

4.7 PREDICTIVE ABILITY OF TEST SUB-CATAGORIES AND SINGLE ITEMS OF THE HINE AND PRECHTL'S GMA WITH THE MOS TO DETERMINE GROSS MOTOR OUTCOME AT 12-15 MONTHS CORRECTED AGE

4.7.1 Predictive validity of HINE subcategories of later gross motor function of infants at 12-15 months corrected age

HINE subcategory scores were more predictive of severe and atypical gross motor outcomes (defined as infants scoring <5th percentile on the AIMS) than any single item on the HINE assessment tool. The assessment of reflexes and reactions subcategory had the biggest AUC (0.875) and was therefore deemed to be most predictive of gross motor outcome on the AIMS (Figure 4.7). Interestingly, the reflexes and reactions subcategory were more predictive of gross motor delay than the total HINE score (AUC=0.867), but only marginally.

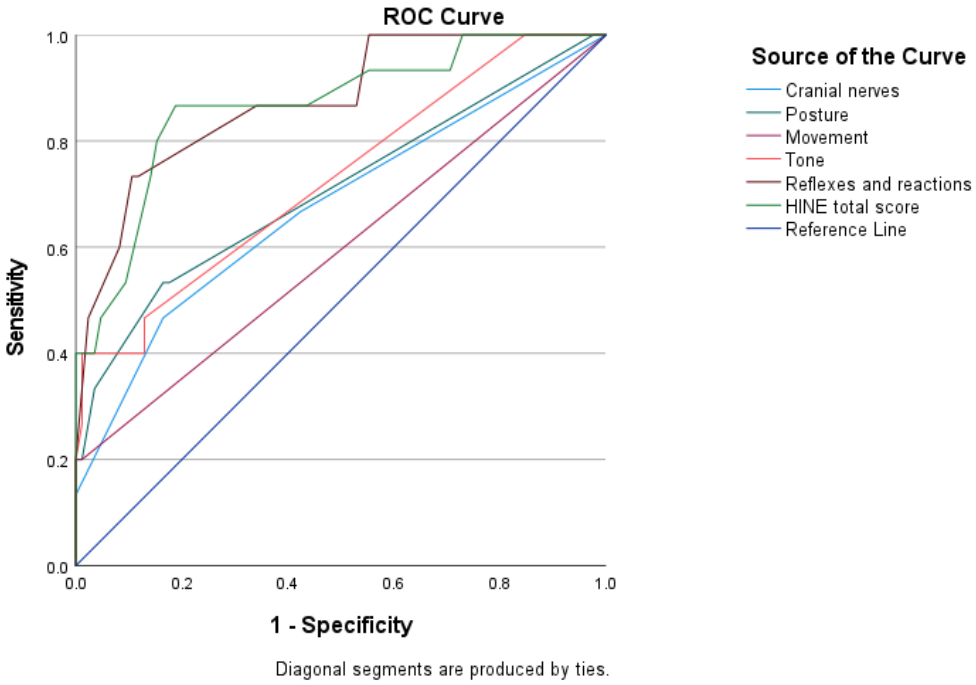

Figure 4.7 Predictive ability of HINE subcategories to determine gross motor outcome on AIMS at 12-15 months corrected age (n=100)

4.7.2 Predictive validity of HINE single items of later gross motor function of infants at 12-15 months corrected age

Further analysis of reflexes and reactions subcategory of the HINE found lateral tilting (Figure 4.8) to be most predictive of severe or atypical gross motor outcome on the AIMS (defined as infants scoring <5th percentile on the AIMS) with AUC=0.802. The other single items had an AUC ranging from 0.706 to 0.780, thus indicating that they were all good indicators of later gross motor delay on the AIMS. The tone subcategory of the HINE was also shown to be predictive of gross motor delay on the AIMS (Figure 4.7). Ventral suspension (Figure 4.9) was the only single item under the assessment of tone subcategory that showed a good correlation to later gross motor development (AUC=0.700)

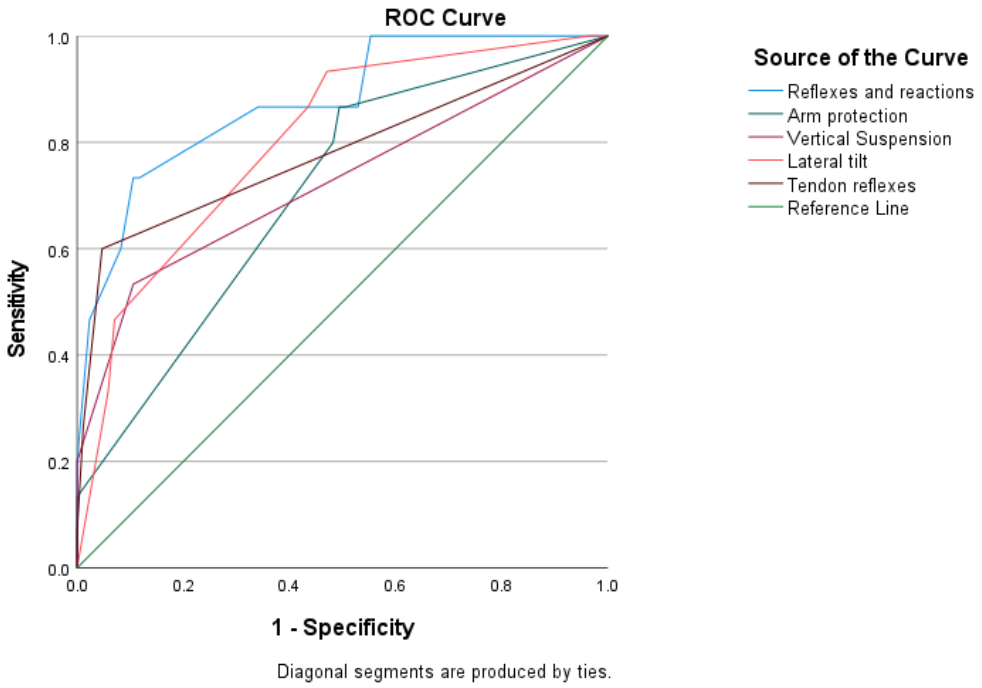

Figure 4.8 Predictive validity of HINE single items under reflexes and reactions subcategory

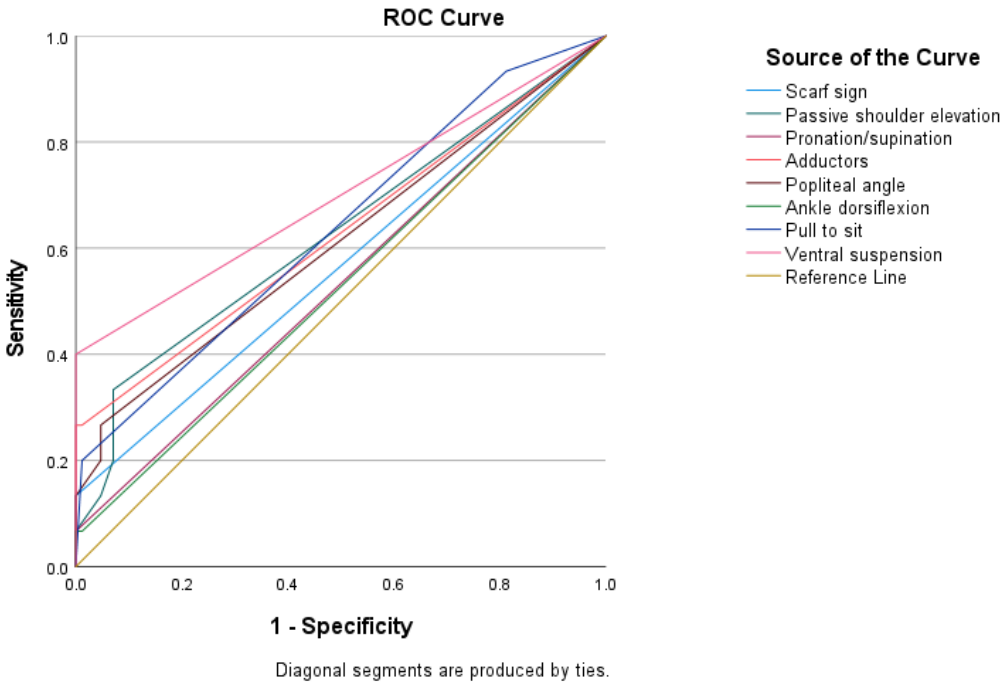

Figure 4.9 Predictive validity of HINE single items under assessment of tone subcategory

4.7.3 Predictive validity of Prechtl's General Movement Assessment (GMA) and Motor Optimality Score (MOS) subcategories of later gross motor function of infants at 12-15 months corrected age on the Alberta Infant Motor Scale (AIMS)

Figure 4.10 depicts the sensitivity and specificity of Prechtl's GMA and MOS subcategories to predict later gross motor outcomes in our group of high-risk infants. Fidgety movement's and observed postural patterns had an AUC of 0.700 and 0.708 respectively, therefore being good predicters of infants that scored <5th percentile on the AIMS. Age-adequate movement repertoire, movement character and observed movement patterns were shown to have poor predictive ability with AUC ranging from 0.595 to 0.628. Table 4.13 depicts the influence of absent or normal fidgety movements at 11-16 weeks corrected age on gross motor and CP outcomes in our sample of infants at 12-15 months corrected age. Fidgety movements were absent in 40% of the infants that scored less than the 5th percentile on the AIMS and absent in 85.71% of infants later diagnosed with CP.

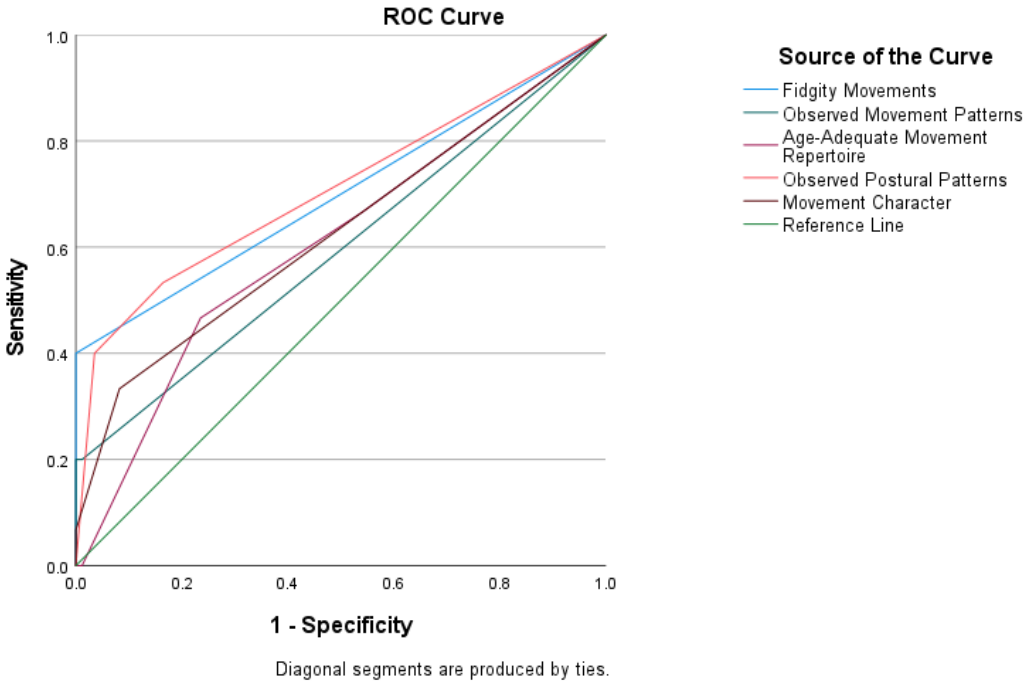

Figure 4.10 Predictive validity of Prechtl's GMA and MOS single items of gross motor outcomes according to the AIMS

Table 4.13 Fidgety movements at 11-16 weeks and later neurodevelopmental outcomes in infants

		AIMS PERCENTILES										CP			
		>50th PERCENTILE		>10th TO 50th PERCENTILE		10 TO 5th PERCENTILE		<5th PERCENTILE		TOTAL		NO CP		CP	
		Count	%	Count	%			Count	%	Count	%	Count	%	Count	%
FMs	Absent	0	0.0%	0	0.0%	0	0.0%	6	40.00%	6	6.00%	0	0.0%	6	85.71%
	Normal	29	100%	53	100%	3	100%	9	60.00%	94	94.00%	93	100%	1	14.29%
	Total	29	100%	53	100%	3	100%	15	100%	100	100%	93	100%	7	100%

AIMS: Alberta Infant Motor Scale; CP: Cerebral palsy; FM: Fidgety movements

4.7.4 Predictive validity of Prechtl's General Movement Assessment (GMA) with Motor Optimality Score (MOS) single items observed at 11-16 weeks corrected age of later gross motor function of infants at 12-15 months corrected age on the Alberta Infant Motor Scale (AIMS)

Table 4.14 on pages 67 and 68 illustrates the presence or absence of MOS single items for infants in each percentile grouping on the AIMS. Of the infants that scored <5th percentile on the AIMS, 73.3% did not have hand-to-mouth or hand-to-hand contact at 11-16 weeks corrected age. Forty-six point seven percent (46.7%) of infants that scored <5th percentile on the AIMS did not have foot-to-foot contact at 11-16 weeks corrected age. A leg lift was not observed in 40% of infants that scored less than the 5th percentile on the AIMS. Body symmetry was abnormal in 93.3% of the infants that had severe or atypical gross motor delay at 12-15 months corrected age on the AIMS (thus scoring <5th percentile). One infant that scored lower than the 5th percentile on the AIMS had a cramped-synchronised movement pattern, and 26.7% of infants with a monotonous movement character were later classified as having a severe or atypical gross motor delay (thus scoring <5th percentile on the AIMS).

Although observed as not being present in most infants with a severe gross motor delay, hand-to-mouth contact, hand-to-hand-contact and foot-to-foot-contact were not found to be significant to predict adverse neurological outcomes (p=0.28, p=1.79, p=0.24 respectively). A monotonous movement character was found to be significant to predict severe or atypical gross motor delay on the AIMS with p=0.02 (Table 4.14).

Table 4.14 Outcomes of high-risk infants on MOS subcategories and single items

		>50TH PERCENTILE		10TH TO 50TH PERCENTILE		<10TH TO 5TH PERCENTILE		<5TH PERCENTILE		TOTAL			NO CP		CP	
	A	N	%	N	%	N	%	N	%	N	%	p value	N	%	N	%
Fidgety		0	0.0%	0	0.0%	0	0.0%	6	40.0%	6	6.0%	0.00	0	0.0%	6	85.7%
movements	N	29	100%	53	100%	3	100%	9	60.0%	94	94.0%		93	100%	1	14.3%
Observed	N<A	0	0.0%	0	0.0%	0	0.0%	3	20.0%	3	3.0%	0.00	0	0.0%	3	42.9%
movement	N=A	1	3.4%	0	0.0%	0	0.0%	0	0.0%	1	1.0%		1	1.1%	0	0.0%
patterns	N>A	28	96.6%	53	100%	3	100%	12	80.0%	96	96.0%		92	98.9%	4	57.1%
Hand-to-	N	13	44.8%	24	45.3%	0	0.0%	4	26.7%	41	41.0%	0.28	40	43.0%	1	14.3%
mouth	NO	16	55.2%	29	54.7%	3	100%	11	73.3%	59	59.0%		53	57.0%	6	85.7%
contact																
Hand-to-hand	N	15	51.70%	19	35.8%	0	0.0%	4	26.7%	38	38.0%	1.79	37	39.8%	1	14.3%
contact	NO	14	48.30%	34	64.2%	3	100%	11	73.3.%	62	62.0%		56	60.2%	6	85.7%
Foot-to-foot	N	18	62.1%	28	52.8%	0	0.0%	8	53.3%	54	54.0%	0.24	52	55.9%	2	28.6%
contact	NO	11	37.9%	25	47.2%	3	100%	7	46.7%	46	46.0%		41	44.1%	5	71.4%
Legs lift	N	23	79.3%	37	69.8%	1	33.3%	9	60.0%	70	70.0%	0.27	67	72.0%	3	42.9%
	NO	6	20.7%	16	30.2%	2	66.7%	6	40.0%	30	30.0%		26	28.0%	4	57.1%
Age-	N<A	4	13.8%	13	24.5%	2	66.7%	7	46.7%	26	26.0%	1.67	21	22.6%	5	71.4%
adequate	N=A	9	31.0%	16	30.2%	1	33.3%	3	20.0%	29	29.0%		28	30.1%	1	14.3%
	N>A	16	55.2%	24	45.3%	0	0.0%	5	33.3%	45	45.0%		44	47.3%	1	14.3%
Observed	N<A	1	3.4%	2	3.8%	0	0.0%	6	40.0%	9	9.0%	0.00	4	4.3%	5	71.4%
postural	N=A	2	6.9%	9	17.0%	0	0.0%	2	13.3%	13	13.0%		12	12.9%	1	14.3%
patterns	N>A	26	89.7%	42	79.2%	3	100%	7	46.7%	78	78.0%		77	82.8%	1	14.3%
Head centred	A	3	10.3%	5	9.4%	0	0.0%	4	26.7%	12	12.0%	0.23	9	9.7%	3	42.9%

Table 4.14 continued

	N	26	89.7%	48	90.6%	3	100%	11	73.3%	88	88.0%		84	90.3%	4	57.1%
Body	A	14	48.3%	30	56.6%	1	33.3%	14	93.3%	59	59.0%	0.17	53	57.0%	6	85.7%
symmetry	N	15	51.7%	23	43.4%	2	66.7%	1	6.7%	41	41.0%		40	43.0%	1	14.3%
ATNR	A	0	0.0%	1	1.9%	0	0.0%	0	0.0%	1	1.0%	1.00	1	1.1%	0	0.0%
	N	19	100%	52	98.1%	3	100%	15	100%	99	99.0%		92	98.9%	7	100%
Movement	N<A	0	0.0%	0	0.0%	0	0.0%	1	6.7%	1	1.0%	0.04	0	0.0%	1	14.3%
character	N=A	2	0.0%	6	11.3%	1	33.3%	4	26.7%	11	11.0%		8	8.6%	3	42.9%
	N>A	29	100%	47	88.7%	2	66.7%	10	66.7%	88	88.0%		85	91.4%	3	42.9%
Smooth and	N	29	100%	46	86.8%	2	66.7%	9	60.0%	86	86.0%	0.00	83	89.2%	3	42.9%
fluent	NO	0	0.0%	7	13.2%	1	33.3%	6	40.0%	14	14.0%		10	10.8%	4	57.1%
Monotonous	A	0	0.0%	4	7.5%	0	0.0%	4	26.7%	8	8.0%	0.02	5	5.4%	3	42.9%
	NO	29	100%	49	92.5%	3	100%	11	73.3%	92	92.0%		88	94.6%	4	57.1%
Cramp	NO	29	100%	53	100%	3	100%	14	93.3%	100	100%	NV	93	100%	7	100%
synchronised	A	0	0.0%	0	0.0%	0	0.0%	1	6.7%	1	1.0%		93	100%	1	14.3%
MOS group	Severely reduced	1	3.4%	1	1.9%	0	0.0%	3	20.0%	5	5.0%	0.00	2	2.2%	3	42.9%
	Moderately reduced	0	0.0%	0	0.0%	0	0.0%	3	20.0%	3	3.0%		0	0.0%	3	42.9%
	Mildly reduced	2	6.9%	12	22.6%	1	33.3%	1	6.7%	16	16.0%		16	17.2%	0	0.0%
	Normal	26	89.7%	40	75.5%	2	66.7%	8	53.3%	76	76.0%		75	80.6%	1	14.3%

A: Abnormal; AIMS: Alberta Infant Motor Scale; ATNR: Asymmetric tonic neck reflex; MOS: Motor Optimality Score; N: Normal; NO: Not observed; NV: No value

4.8 PREDICTIVE VALIDITY OF THE HAMMERSMITH INFANT NEUROLOGICAL EXAMINATION (HINE) AND PRECHLT'S GENERAL MOVEMENT ASSESSMENT (GMA) WITH THE MOTOR OPTIMALITY SCALE (MOS) OF INFANTS WITH CEREBRAL PALSY (CP)

Figure 4.11 illustrates the sensitivity and specificity of the HINE to predict the outcome of CP in our sample of infants. The HINE total score at 11-16 weeks corrected age was very predictive of later CP diagnosis at 12-15 months corrected age with an AUC 0=0.927. The HINE (cut-off score of 40) had a sensitivity of 29% and a specificity of 100% to identify infants with CP, with PPV=100% and NPV=95%.

Figure 4.12 on page 70 depicts an ROC curve demonstrating the sensitivity and specificity of Prechtl's GMA with the MOS (cut-off MOS score of 8) done at 11-16 weeks corrected age to predict later CP diagnosis in our sample of high-risk infants. As was the case with the HINE, the MOS total score was also very predictive of later CP outcome with an AUC=0.966. The MOS had a sensitivity of 43% and specificity of 100% to predict CP with PPV=100% and NPV=96%.

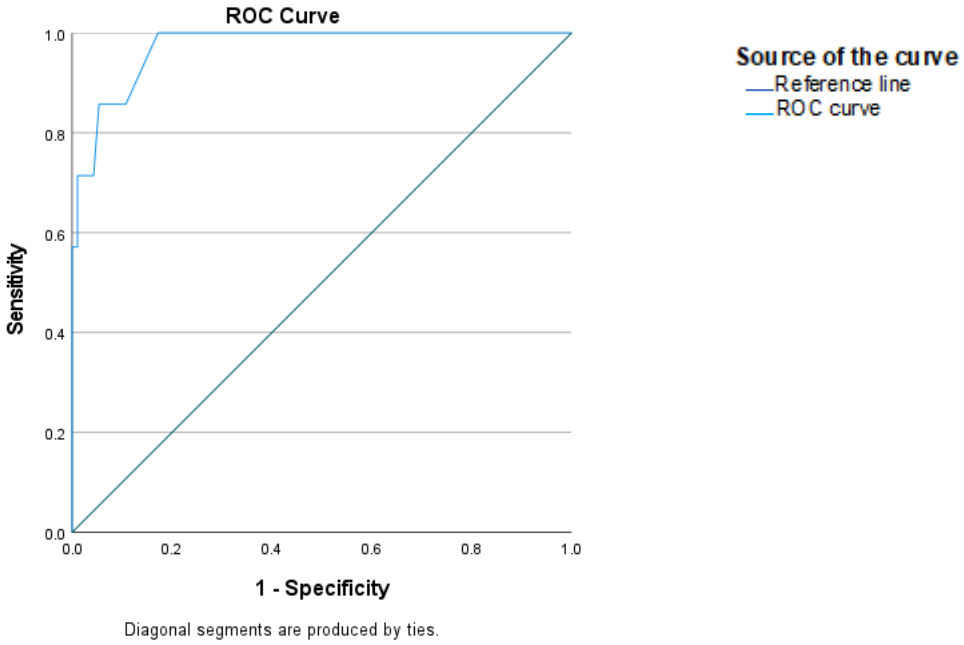

Figure 4.11 Predictive validity of HINE total scores for CP

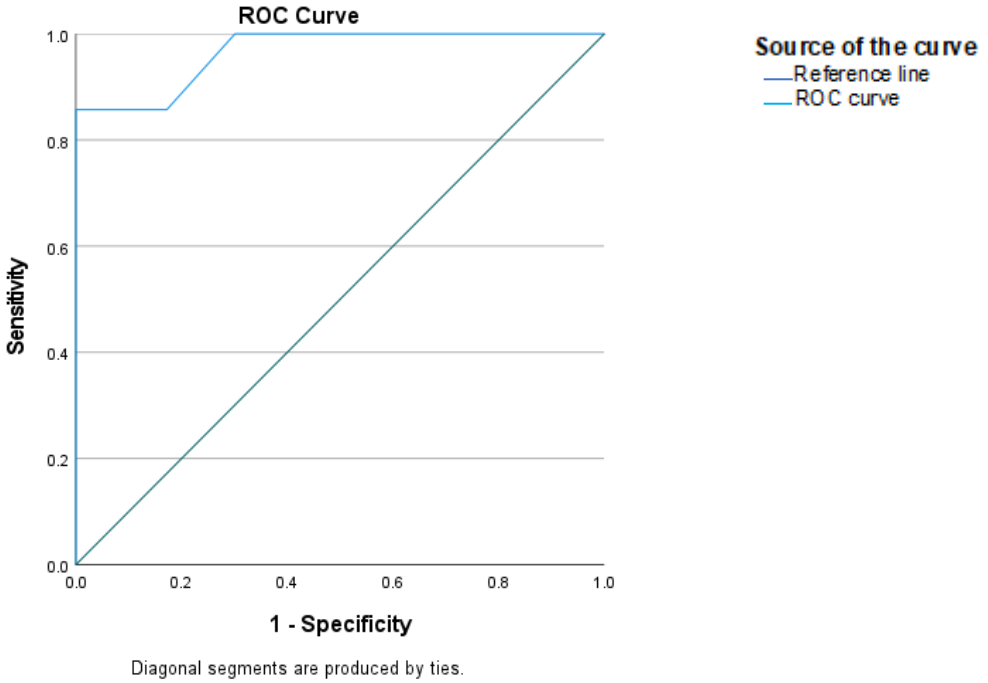

Figure 4.12 Predictive validity of MOS total scores of later CP outcome in high-risk infants

In summary, our study results showed that the HINE, performed at 11-16 weeks corrected age, had a higher sensitivity than Prechtl's GMA with the MOS to predict severe or atypical gross motor delay on the AIMS at 12-15 months corrected age. Prechtl's GMA with the MOS had a higher specificity and PPV to predict severe or atypical gross motor outcome than the HINE, but NPV were similar for both assessment tools. The reflexes and reactions subcategory of the HINE had the best predictive ability to identify severe or atypical gross motor delay on the AIMS, while fidgety movements and observed postural patterns were found to be the most predictive subcategories on the MOS. Both HINE and MOS assessment total scores were more predictive of severe or atypical gross motor outcome than subcategory scores, or single items on assessments. In the next chapter, a discussion of observed results will be provided with further interpretation of findings.

CHAPTER 5

DISCUSSION

5.1 INTRODUCTION

The Hammersmith Infant Neurological Examination (HINE) and Prechtl's General Movement Assessment (GMA) with the Motor Optimality Scale (MOS) have both been recognised to be a gold standard in the prediction of cerebral palsy (CP) in at risk infants (Novak *et al*., 2017). While extensively researched with regards to predicting CP diagnosis, literature supporting the use of Prechtl's GMA with the MOS and HINE to determine delayed or atypical gross motor outcomes other than CP in high-risk infants is lacking. To our knowledge, no study has been performed in Africa, or in the rest of the world, investigating the ability of Prechtl's GMA with the additional MOS or the HINE to determine delayed gross motor outcomes (especially outcomes other than CP) at 12 months corrected age in an at-risk group of infants.

The purpose of this study was to ascertain which neurological observational infant assessment (HINE or Prechtl's GMA with MOS) was most predictive to determine later severe or atypical gross motor delay in a subset of high-risk infants as assessed by the Alberta Infant Motor Scale (AIMS). Our study results showed that the HINE had a higher sensitivity than Prechtl's GMA with the MOS to predict severe or atypical gross motor delay on the AIMS at 12-15 months corrected age. Prechtl's GMA with the MOS had a higher specificity and positive predictive value (PPV) to predict gross motor outcome than the HINE, but the negative predictive values (NPV) were similar for both assessment tools. The HINE and MOS total scores were more predictive of gross motor outcome than any subcategory score or single items on either of the assessment tools.

In this discussion, we further interpret study findings regarding the demographic representation of infants, gross motor outcomes according to the AIMS, predictive validity of the HINE and Prechtl's GMA with MOS, as well as predictive validity of HINE and MOS subcategory and single items. We also discuss outcomes of infants

provisionally diagnosed with CP and further classification according to the Gross Motor Function Classification System (GMFCS).

5.2 DEMOGRAPHIC REPRESENTATION

5.2.1 Gender

Our study sample included 45 males and 55 females. We included all infants meeting our inclusion criteria and that attended their 12-15 months follow-up appointment at the high-risk clinic at Tygerberg Children's Hospital (TCH), and therefore the difference could be of interest. The discrepancy in gender could therefore be attributed to a better follow-up by parents of female rather than male infants. The discrepancy could also simply be a chance finding, due to our systematic enrolment strategy. The discrepancy could also imply that there was a better survival rate of high-risk female rather than male infants at TCH in 2019 and 2020. It is known in the literature that male infants in general have a poorer survival rate than female infants, with male infants also being more susceptible to premature death, intrauterine growth restriction (IUGR), prematurity, respiratory morbidity, and infections (Aghai, Goudar, Patel, Saleem, 2020; Peacock, Marston, Marlow, Calvert *et al*., 2012; Pongou, 2013). As our study sample consisted of high-risk infants, many of which were born prematurely and had many neonatal risk factors, the above could possibly provide the best explanation for the discrepancy in gender. Our study findings therefore likely support what is reported in the literature that female infants have a higher survival rate compared to male infants.

It was not within the scope of this study to investigate the difference in gross motor outcomes between male and female infants specifically.

5.2.2 Ethnicity and social circumstances of infants

Fifty-four percent (54%) of the infants in our study were black, and 47% were coloured. There were no white or Asian infants in our sample. TCH serves a wide catchment area within the Western Cape, and these groups are representative of the population often living in poorer socio-economic circumstances. The majority of parents of infants were unemployed or received a very low monthly income. This observation is

expected, given that TCH is a public tertiary hospital that predominantly services lower socio-economic regions.

Research has shown that infant neurodevelopment may be influenced by physical, emotional, and environmental factors, and that a combination of any of these factors may have a significant impact on ongoing brain development (Laughton, Springer, Grove, Seedat *et al*., 2010; Samuels, Slemming & Balton, 2012). Previous studies by Adnams, Kodituwakku, Hay, Laughton *et al.* (2001), Molteno, Hollingshead, Moodie, Bradshaw *et al*. (1991) and Samuels, Slemming and Balton (2012) have all shown that children living in low socio-economic circumstances in South Africa have significantly poorer developmental outcomes compared to expected norms. Although social and environmental information such as education level of mothers, average monthly family income and employment status of caregivers were collected in this study and portrayed in Table 4.5, it was not within the scope of this study to try and distinguish the relationship between these factors and later gross motor outcome in our sample of infants.

5.2.3 Perinatal risk factors of infants

The average birthweight of all infants included in our study was ±1.5kg, with the median birthweight being 1.2kg. More than 80% of the infants in our study sample were born preterm, with only 16% of infants born at term age. Of all the preterm infants included in this study, two thirds were very low-birthweight (VLBW) infants, 20% were extremely low birth weight (ELBW), and 19% of infants had a normal birth weight. The most prevalent perinatal risk factors in our study sample were respiratory distress (RDS), hyaline membrane disease (HMD), jaundice, anaemia, and hypoxic-ischaemic encephalopathy (HIE) (refer to Table 4.3).

It was not part of the scope of this study to investigate the effect of specific perinatal risk factors on later gross motor delay, but some of our subsequent study findings may be of interest. Of the 15 infants classified as being delayed with their gross motor development according to the AIMS scoring <5th percentile, eight were VLBW, three were ELBW, and four had a normal birthweight. Eleven of the infants with severe gross motor delay were born preterm, and all the term infants with gross motor development had severe HIE at birth. Studies report that there is a correlation between a severe HIE score at birth and the acquirement of later gross motor delay and neurological

impairment (Kali, Martinez-Biarge, van Zyl, Smith *et al*., 2016; Stark, van der Vyver & Gretschel; 2020).

It is well reported in the literature that premature infants are at greater risk for neurodevelopmental delay and morbidity compared to infants born at term. Although most of the infants that presented with gross motor delay at 12-15 months corrected age were indeed born preterm, 73% of all the preterm infants included in this study had a typical gross motor outcome on the AIMS. Majority preterm infants in our study did therefore not present with gross motor and neurodevelopmental delay. These study findings differ to that found in a systematic review by Pascal *et al.* (2018) where the authors investigated the motor development of high-risk infants in low- and middle-income countries, as premature birth and low birth weight were often found to be the main contributing factors to later poor developmental outcomes (Pascal *et al*., 2018). It is however important to note, that all studies included in the study by Pascal *et al*. (2018) investigated motor and neurodevelopmental outcomes in VLBW and very preterm infants only, whereas our study comprised of a “mixed” group of infants with varying birthweight and gestational age. Another explanation for this discrepancy could simply be attributed to the post-natal care that these infants received in the neonatal intensive care unit (NICU) and high care units at TCH, resulting in better motor developmental outcomes.

5.3 GROSS MOTOR OUTCOMES ACCORDING TO THE ALBERTA INFANT MOTOR SCALE (AIMS)

In this study, only 15% of the 100 infants assessed scored lower than the 5th percentile on the AIMS, therefore classifying them as having a severe or atypical gross motor delay. Three infants scored between the 10th and 5th percentile on the AIMS, classifying them as being at risk for later neurodevelopmental delay (Darrah, Piper & Watt, 1998). Our results mirror that reported in other studies by Spittle, Lee, Spencer-Smith, Lorefice *et al*., (2015), Burger, Frieg and Louw (2011) and Wang, Howe, Hinojosa and Hsu (2010) where 36%, 19% and 16.1% of their infants scored below the 5th percentile on the AIMS respectively. Sample sizes were similar across all studies (n=97, n=115, n=105 respectively). The higher rates of infants with a significant gross motor delay on the AIMS in other studies compared to ours, can be explained

by the fact that the authors only included preterm born infants in their studies, whereas term born infants were also included in our study if they met our inclusion criteria. It is well known that premature infants, especially extremely- and very premature infants, are at greater risk for adverse neurodevelopmental outcomes (Fuentefria, Silveira & Procianoy, 2017).

Infants identified as having a gross motor delay at 12-15 months corrected age all scored poorly in the sitting and standing subcategories on the AIMS. According to the World Health Organization (WHO) Multicentre Growth reference study group (2006), children with typical development should sit independently by 5-8 months, stand without support at 9-13 months and walk independently by 10-14 months. Of the 100 infants evaluated in this study 65% were unable to walk at least four steps independently at 12-15 months corrected age. In contrast, only 6% of infants were unable to sit unassisted at this age, and all the infants who were unable to sit unassisted at this age were diagnosed with CP. It is well reported that premature born infants are often delayed in the onset of walking, and that preterm infants exhibit different gross motor developmental trajectories in comparison to infants born at term (Haastert, De Vries, Helders, Jongmans, 2006; Nuysink, van Haastert, Eijsermans, Koopman-Esseboom *et al*., 2013). Most of the infants included in this study were born preterm, thus providing an explanation for the large percentage of infants not yet walking at 12-15 months corrected age. In a study performed by Nuysink *et al*. (2013) in a population of preterm (<30 weeks gestational age), low-birth weight infants, the median age of walking was 15.7 months corrected age. The authors however excluded infants with medical illnesses that could further impair their gross motor development, unlike our study where these high-risk infants were included (Nuysink *et al.*, 2013).

AIMS total scores of the participants in our study ranged from 7-58 and a score of ≤ 46 was always associated with the occurrence of gross motor delay at 12-15 months corrected age. This correlates to the study findings of Su, Jeng, Hsieh, Tu *et al*. (2017) as they found that AIMS total scores of >52.8 (28th percentile on the AIMS at 12 months corrected age) and <33.1 (<1st percentile on the AIMS at 12 months corrected age) were associated with normal and delayed gross motor outcomes respectively. Their study however only evaluated very low birthweight (VLBW) infants with the AIMS at 12 months corrected age, whereas our study also included term infants with normal birthweight (Su *et al*., 2017).

Haastert *et al*. (2006) found that AIMS total scores were significantly lower in preterm infants (born <32 weeks GA) compared to infants born at term with a mean total AIMS score of 48.8. This mean AIMS score correlates to that found in other studies of Jeng Tsou Yau, Chen, Hsiao (2000a) and Jeng, Tsou Yau, Liao, Chen, *et al.* (2000b) where mean total AIMS scores at 12-13 months corrected age were reported as 49.7 and 48.7 respectively. It is important to note that both studies published by Jeng *et al*. (2000) only included premature, and VLBW infants in their study. The mean total AIMS score in our study was 49.05, thus correlating to that found in the aforementioned studies. Our study did however include a "mixture" of extremely preterm, very preterm and term born infants and not only preterm and VLBW infants as was in the case in the studies by Haastert *et al*. (2006), Jeng *et al.* (2000a), and Jeng *et al.* (2000b), however the similarity in results could be explained by the fact that most infants in our study were also born preterm (83%) and VLBW (60%).

5.4 PREDICTIVE VALIDITY OF HAMMERSMITH INFANT NEUROLOGICAL EXAMINATION (HINE) VS PRECHTL'S GENERAL MOVEMENT ASSESSMENT (GMA) WITH MOTOR OPTIMALITY SCORE (MOS) TO PREDICT GROSS-MOTOR OUTCOMES

5.4.1. Outcomes on the Hammersmith Infant Neurological Examination (HINE)

Literature reports a HINE total score at 3 months corrected age to be optimal if it is equal to, or more than 73 (Romeo *et al*., 2009). In our study, none of the participants had an optimal score (≥73) at 11-16 weeks corrected age. It is worth noting that HINE optimality scores were standardized in a group of low-risk infants, and as our study specifically included infants at high risk for developmental delay, this may provide an explanation as to why none of our infants had HINE scores regarded as optimal.

Allocating appropriate HINE cut-off scores to predict gross motor outcomes in our study proved to be difficult, as HINE cut-off scores were developed with the intent to identify those infants at risk of severe neurological deviations such as cerebral palsy (CP). An initial HINE cut-off score of 40 was chosen to run analyses as this is regarded in the literature to be 100% predictive of later CP diagnosis (Novak *et al*., 2017; Pizzardi *et al.*, 2008; Romeo *et al*., 2009; Romeo *et al*., 2016). A need for a HINE cut-

off score that was more sensitive and specific to predict not only CP, but also atypical gross motor delay was identified, as initial ROC curve analysis showed that a low cut-off score of 40 resulted a low sensitivity of 13%.

Using receiver operating characteristic (ROC) curve analysis, we proposed that a new cut-off HINE score of 62.25 deemed more appropriate to predict gross motor delay (thus infants that would score <5th percentile on the AIMS) in our included sample of infants. A cut-off score with a higher sensitivity is important if a screening tool is being evaluated as a public health measure, as this results in more at-risk infants being identified for follow up to monitor future motor development. This could cause less infants “falling through the cracks” and not being identified for regular screening and follow up when they truly need it, bearing in mind that a higher sensitivity may also include a higher number of false positive results. Although the new proposed cut-off score of 62.25 resulted in a decreased PPV of 45% compared to a cut-off of 40, it resulted in an increased NPV of 97%. A high NPV implies that false negative results are minimized. It can be argued that this is clinically relevant to health care workers (especially in resource restricted and over-burdened healthcare settings such as TCH), as a higher NPV indicates that a greater portion of infants screened to not have a risk of developmental delay and thus not warranting further follow up, will indeed not develop a gross motor delay. This would cause a decrease in infants “lost to follow up” and developing adverse outcomes.

At 11-16 weeks corrected age, the HINE showed good predicative validity to predict gross motor outcomes with an area under the curve (AUC) of 0.867 and a sensitivity and specificity of 87% and 81% with a sample specific HINE cut-off score of 62.25. Romeo *et al.* (2009) found similar results reporting that the HINE had good predictive power at 3 months corrected age to predict locomotor function at 2 years of age with a sensitivity and specificity of 93% and 100% respectively and AUC=0.98 (Romeo *et al.*, 2009). It has been suggested that the high predictive value of the HINE during the first year of life can be attributed to the effective combination of distinct groups of items for each key period of age (Romeo *et al*., 2009). Sample sizes in both the study by Romeo *et al*. (2009), and our study were similar (n=103), however the authors used a HINE cut-off score of 50 at 3 months corrected age, and only included very preterm infants (born <32 weeks gestation) in their analysis, whereas our study included

preterm and term born infants. This could explain the higher sensitivity and specificity percentages reported by Romeo *et al*. (2009) compared to our study.

Various studies have reported on the high predictive validity of the HINE to predict later CP diagnosis with sensitivity and specificity values ranging from 59.18% to 100% across different studies (Bosanquet *et al*., 2013; Kwong *et al*., 2018; Morgan *et al*., 2019; Novak *et al*., 2017; Romeo *et al*, 2016). It is difficult to compare our study findings specifically evaluating the ability of the HINE to predict gross motor delay to that available in the literature, as the majority of available studies only focused on the predictive validity of the HINE to predict a diagnosis of CP, and not on the ability to predict gross motor delays. Irrespective of this point, sensitivity and specificity values produced in our study mirror that suggested in other research and again support the HINE as being very predictive of later gross motor outcome. The sensitivity and specificity values of the HINE to predict gross motor outcome portrayed in our study is lower than what is reported in the literature when the HINE is used with the intent to predict CP. In our study, the HINE (with cut-off score of 40) had a sensitivity and specificity of 29% and 100% respectively, with AUC=0.927 and PPV=100% and NPV=95% to predict CP. In contrast when utilising the same HINE cut-off score as proposed in the literature to be 100% predictive of CP, the HINE had a sensitivity and specificity of 13% and 100% respectively to predict gross motor delay (infants scoring <5th percentile on the AIMS). Our study findings therefore suggest that the HINE with a cut-off score of 40 is more predictive of CP diagnosis rather than simply predicting atypical gross motor delay. In our study sample, a higher HINE cut-off score was more predictive of a gross motor delay on the AIMS. It is however important to note that the group of infants identified as having a gross motor delay in our study (n=15) also included infants later diagnosed with CP.

In summary, evaluating the validity of the HINE for predicting gross motor delay in infants depends on the research. Higher values of sensitivity and specificity are more important when researchers want to ascertain how well a test performs in a population, for example if a screening tool is being evaluated for implementation as a screening tool in a public health setting. The HINE (adjusted cut-off score of 62.5) had a high sensitivity and specificity to predict gross motor delay on the AIMS at the neonatal outpatient high-risk clinic of TCH, therefore ticking this box. On the other hand, when evaluating a patient at a specific point in time, it would be less important how well a

test performs in a population (thus sensitivity and specificity values) and more important to know if their infant truly has a gross motor delay/risk of CP or not. In this case the NPV and PPV could be seen as more clinically relevant. The HINE had a poor PPV, but high NPV. The decrease in PPV could have been the result of increasing the cut-off score to 62.5 in order to improve sensitivity of the test.

5.4.2. Outcomes on Prechtl's General Movement Assessment (GMA) with Motor Optimality Score (MOS)

ROC curve analysis with an initial cut-off score of 8 for the MOS in this group of infants showed an excellent predictive value with a sensitivity and specificity of 20% and 100% respectively to predict infants that would score <5th percentile on the AIMS. The PPV and NPV was high with percentages of 100% and 88% respectively. Utilising ROC curve analysis, a new proposed cut-off score of 20.5 showed improved predictive validity with a sensitivity of 47% and a specificity of 100% to predict infants with a gross motor delay (thus scoring <5th percentile on the AIMS). The PPV and NPV was again high with values of 100% and 91% respectively. This can again be resultant of the fact that MOS cut-off scores currently proposed in the literature (thus total MOS cut-off score of 8) were specifically chosen with the aim of identifying those infants at risk of CP, and not those at risk for atypical gross motor delay. It is however important to note that our study sample of infants that scored <5th percentile on the AIMS also included infants later diagnosed with CP, and that infants with CP were not excluded from data analysis. Örtqvist, Einspieler & Ådén (2021) also proposed a revised cut-off value of a <21 after ROC curve analysis on the MOS while investigating a sample of 42 extremely preterm infants for later neurodevelopmental delay. In the current study cut-off scores of 9 and 20.25 had excellent PPV=100%, as well as NPV=88% and 91% respectively, thus indicating that Prechtl's GMA with the MOS is a very good predictor of those infants that will truly either present with gross motor delay, or typical outcome.

Literature reports a MOS of 25 to 28 to be optimal, while a score of 20 to 24 is considered mildly reduced, a score of 9 to 19 as moderately reduced, and from 5 to 8 as severely reduced (Einspieler *et al*., 2019). MOS scores in our sample of infants ranged from 5-28. In the group of infants with gross motor delay, the mean and median MOS score was 19.00 and 25.00 respectively. Örtqvist, Einspieler and Ådén (2021) found absent fidgety movements and a MOS score of ≤21 at 3 months corrected age

is indicative of future impaired neurodevelopment. Children with a neurodevelopmental delay had a median MOS of 17.5, while children with a normal outcome had a median score of 21.0 (Örtqvist, Einspieler & Ådén, 2021). The difference in the values between the current study can be explained by the difference in sample size between the studies. We included a mixture of 100 preterm and full-term infants while Örtqvist, Einspieler and Ådén (2021) included 42 extremely low birth weight infants. Extremely preterm born infants also often demonstrate greater deviation of movement and postural patterns and are more often likely to have absent fidgety movements and a poor quality of early motor repertoire compared to infants born at term, thus resulting in poorer total MOS subcategory scores. This could explain the difference in MOS scores between the groups (Fjørtoft, Evensen, Øberg, Songstad *et al*., 2016).

It is well reported in the literature that the Prechtl's GMA has a high predictive validity for detecting CP in infants (Novak *et al*., 2017). Prechtl's GMA was specifically developed to identify those infants at risk for severe neurodevelopmental impairment. ROC curve analysis in our study showed that that Prechtl's GMA with the MOS had a sensitivity and specificity of 43% and 100% respectively, with AUC=0.996 and PPV and NPV values of 100% and 96% respectively to identify infants with CP. Sensitivity and specificity, as well as PPV and NPV values are therefore higher when a MOS cut-of score of 8 is used to identify infants with CP, compared to using the same cut-off score to identify infants with gross motor delay (thus scoring <5th percentile on the AIMS).

Various systematic reviews have been published investigating the predictive validity of Prechtl's GMA to detect CP with Bosanquet *et al*. (2013), Novak *et al*. (2017) and Kwong *et al*. (2018) reporting sensitivity and specificity values of 98% and 91%, 98% and 95% and 97% and 89% respectively. None of the studies included in the abovementioned systematic reviews included the MOS, and could thus not report on the predictive validity of the MOS to predict CP. To the best of our knowledge, currently no studies exist that state the sensitivity and specificity of the MOS to predict CP. This makes interpretation of our study results difficult, as no studies exist to compare our study findings with. Furthermore, our study also had a low number of infants diagnosed with CP (n=7) and atypical gross motor delay (n=15). The lower rate of sensitivity of the MOS to predict CP can be attributed to the low number of infants diagnosed with

CP in our study, and it can be argued that a larger sample of participants with CP included in our study could have yielded higher sensitivity values. Interestingly, the results of our study showed that the MOS had a higher specificity to predict CP compared to Prechtl's GMA alone as reported by Bosanquet *et al*. (2013), Kwong *et al*. (2018) and Novak *et al*. (2017). This poses an interesting question to be evaluated in further studies, and further research is warranted before a valid conclusion can be made.

In summary, evaluating the cut-off scores for valid prediction of motor delay in infants when using Prechtl's GMA with the MOS depends on whether the purpose is to ascertain how well a test performs in a population (for example as a screening tool) or whether you want to predict a single infant's risk for developing motor delay. The MOS (adjusted cut-off score of 20.5) had a low sensitivity and high specificity to predict gross motor delay as measured by the AIMS. Our study results therefore suggest that in a population, the MOS assessment done at 11-16 weeks corrected age will miss a large proportion of infants that will later develop a gross motor delay. It can be argued that for a parent of an infant, or a clinician evaluating a patient at a specific point in time, it would be less important how well a test performs in a population (thus sensitivity and specificity values) and more important to know if their infant truly has a gross motor delay/risk of CP or not. In this case the NPV and PPV could be seen as more clinically relevant. The MOS had a high PPV and NPV, thus indicating that a large proportion of infants identified as having a gross motor delay/or not, will truly either have normal gross motor development or a significant delay.

5.5 SUBCATAGORY OUTCOMES ON HAMMERSMITH INFANT NEUROLOGICAL EXAMINATION (HINE) AND PRECHTL'S GENERAL MOVEMENT ASSESSMENT (GMA) WITH MOTOR OPTIMALITY SCORE (MOS) TO PREDICT GROSS-MOTOR OUTCOMES

5.5.1 Hammersmith Infant Neurological Examination subcategory (HINE) scores to predict gross motor outcomes on the Alberta Infant Motor Scale (AIMS)

Literature exploring the predictive ability of HINE subcategory scores and single items to predict gross motor and neurodevelopmental outcome is scarce. According to our results, individual HINE subcategory scores were more predictive of gross motor outcome than single HINE score items for all infants assessed at 11-16 weeks corrected age. The reflexes subcategory of the HINE was found to be most predictive of gross motor outcome with AUC=0.875. Interestingly, the reflexes subcategory score was found to be even more predictive than HINE total score to predict gross motor delay on the AIMS. The movement HINE subcategory was found to be the least predictive. This contrasts to findings in other studies where the authors found the movement subcategory of the HINE to be the most predictive of locomotor function and CP diagnosis at 1-2 years of age (Pizzardi *et al*., 2008; Romeo *et al*., 2009). Romeo *et al*., (2009) did however find single items of the reflex subcategory including ventral suspension and lateral tilting to be of the most predictive items of later locomotor function at 2 years corrected age. The difference in the findings between our two studies may be again explained by the fact that the study by Romeo *et al.* (2009) included a larger number of more severe cases with a higher incidence of abnormal motor outcomes in their infants compared to our study, and this may have influenced the results achieved.

5.5.2 Hammersmith Infant Neurological Examination (HINE) single items to predict gross motor outcome on the Alberta Infant Motor Scale (AIMS)

Our study findings suggest that HINE subcategory total scores were more sensitive and specific to predict later gross motor delay on the AIMS compared to any single subcategory item. Further analysis of reflexes and reactions subcategory of the HINE

found lateral tilting to be most predictive of gross motor outcome on the AIMS with AUC=0.802. All the single items under the reflexes and reactions subcategory had an AUC ranging from 0.706 to 0.780, thus indicating that they were all good indicators of later gross motor delay on the AIMS. Results from our study differ from findings in other studies (Pizzardi *et al*., 2008; Romeo *et al*., 2009) where quality and quantity of movement (assessed at 3 months corrected age) were found to be the single items most predictive of neurodevelopmental impairment. Both Pizzardi *et al*. (2008) and Romeo *et al.* (2009) only found single items from the reflexes and reactions subcategory such as tendon reflexes and arm protection to be indicative of later CP diagnosis and motor functioning when assessed at 12 months corrected age. In our study, the tone subcategory of the HINE was also shown to be predictive of gross motor delay on the AIMS with ventral suspension being the only single item under the assessment of tone subcategory that showed a good correlation to later gross motor development (AUC=0.700). Pizzardi *et al.* (2008) also found ventral suspension to be predictive of later CP diagnosis in their study with AUC=0.91, and concluded that single items from the tone subcategory, especially those assessing the upper limb and axis, were very predictive of later neurodevelopmental impairment (especially when assessed in the first term of age). Differences in results compared to our study can be explained by the large discrepancy in sample size between that of our study (n=100) and Pizzardi *et al.* (2008) (n=658). Although both studies included both preterm and term born infants with a large variety of gestational ages and birthweights, it is worth noting that other studies have only studied the ability of HINE single items to predict CP, and not gross motor delay and minor neurological impairment, as was the case in our study. It is this fact, that makes it difficult to compare results found in our study to other published research. More studies investigating the predictive validity of single items to predict gross motor outcome alone are warranted before any valid conclusion can be made.

5.5.3 Predictive ability of Prechtl's General Movement Assessment (GMA) with Motor Optimality Score (MOS) subcategories to predict gross motor outcomes on the Alberta Infant Motor Scale (AIMS)

It is well reported in the literature that fidgety movements are very predictive of severe neurological outcomes in infants at both 12 up until 24 months corrected age (Burger

& Louw, 2009). Our study found fidgety movements observed at early as 11-16 weeks corrected age to be predictive (AUC=0.700) of later gross motor outcome on the AIMS at 12-15 months corrected age. Song *et al.* (2016) investigated the predictive validity of Prechtl's GMA to predict later gross motor function on the AIMS at 12 months corrected age in a sample of 44 preterm infants. The authors found fidgety movements at 3 months corrected age to be a good predictor of later gross motor function on the AIMS with absent fidgety movements having a sensitivity and specificity of 75% and 83.3% respectively to predict gross motor delay (Song, Chang, Shin, Park *et al*., 2016). Like our study, the authors also utilised the 5th percentile on the AIMS as a cut-off to determine gross motor delay.

Fewer studies however report on the predictive ability of MOS subcategory items to predict later neurodevelopmental delay, as most studies only report on the presence of absence of fidgety movements and not the subsequent quality and quantity of the motor repertoire. We also found the observed postural patterns subcategory to have good predictive ability of later gross motor function in our sample of high-risk infants (AUC=0.708). Results from our study failed to show a significant correlation between age-adequate motor repertoire on the MOS and later gross motor outcome (AUC=0.608). These findings differ to that of Bruggink *et al*. (2009) where the authors found a low score on the age adequate subcategory to be associated with poorer motor outcomes (Bruggink, Butcher, Stremmelaar, Prechtl *et al*. 2009). Literature also reports a good correlation between the movement patterns subcategory on the MOS and later gross motor function (Einspieler *et al*., 2019), but this was not substantiated in our study findings. A possible explanation can be provided given that all Einspieler *et al*. (2019) only included infants in CP in their study, and our study included all high-risk infants that fit our inclusion criteria, regardless of CP diagnosis or not. Only one of the infants in our study had a cramped-synchronized movement pattern. Infants evaluated in the studies by Ferrari *et al*. (2002), Bruggink *et al.* (2009) and others all included many infants with a cramped synchronised movement pattern, therefore resulting in a poorer subcategory score and subsequently poorer later motor outcome, thus providing an explanation for the discrepancy in results reported in their studies compared to ours. It is also well reported in the literature that cramped-synchronized movements are highly predictive of severe CP (Einspieler *et al*., 2019; Novak *et al*., 2017).

Örtqvist, Einspieler & Ådén (2021) also found infants with poorer scores on the age-adequacy subcategory of the MOS evaluated at 3 months corrected age to be at higher risk for later developmental delay. They did not find any differences between their infants with normal or adverse outcomes with regards to observed movement and postural patterns or movement character. Our study included significantly more infants (n=100) than that of Örtqvist, Einspieler & Ådén (n=42), and while our study also included preterm born infants, Örtqvist and co-authors exclusively included extremely preterm infants (born <28 weeks gestation) and evaluated neurodevelopmental outcome at a much later stage (12 years of age) than was the case in our study (infants evaluated at 12-15 months corrected age).

5.5.4 Single items on Prechtl's General Movement Assessment (GMA) with Motor Optimality Score (MOS) to predict gross motor outcomes on the Alberta Infant Motor Scale (AIMS)

Of the infants that were classified as having a severe or atypical gross motor delay according to the AIMS at 12-15 months corrected age, 73.3% did not have hand-to-hand contact or hand-to-mouth contact observed at 11-16 weeks corrected age. Forty-six point seven percent (46.7%) of infants that scored <5th percentile on the AIMS did not have foot-to-foot contact observed at 11-16 weeks corrected age. Chi-square test, however failed to show a significant correlation between the absence of these movements at 11-16 weeks corrected age and later gross motor outcome. P-values for hand-to-mouth contact, hand-to-hand contact, and foot-to-foot contact were p=0.28, p=1.79, p=0.24 respectively. A leg lift was not observed in 40% of infants that scored less than the 5th percentile on the AIMS, and it was also not significant with regards to prediction of later gross motor delay. Body symmetry was abnormal in 93.3% of the infants that had a gross motor delay at 12-15 months corrected age on the AIMS, but also not statistically significant. A monotonous movement character was the only single item on the MOS found to be significant to predict gross motor delay on the AIMS with p=0.02. Einspieler *et al.* (2019) also reported that 82.3% of the infants in their study later diagnosed with CP had a monotonous movement character observed at 3-5 months corrected age.

In the study performed by Einspieler *et al*. (2019) the authors also found a high percentage of infants later diagnosed with neurodevelopmental delay and CP to not

have observed foot-to-foot contact (74.6%), hand-to-mouth contact (81.8%) or hand-to-hand contact (90.4%) at 3-5 months corrected age. Einspieler *et al*. (2019) noted that movements such as hand-to-hand contact to require either whole body or visuomotor coordination, and this may explain why these movements are often atypical or absent in infants with neurodevelopmental delay or a later CP diagnosis. The authors also found body symmetry to be significant to detect later neurodevelopmental impairment result ($p<0.01$). Similar to the results in our study, the authors found a large percentage of infants (88%) with significant motor impairments such as a dyskinesia to have abnormal body symmetry at 3-5 months corrected age. Other studies have found arching, atypical head movements (inability of infants to maintain the head in midline), and atypical or non-variable finger postures to be associated with the later diagnosis of CP and GMFCS levels III-V (Einspieler & Prechtl, 2005; Einspieler *et al*., 2019; Jones, Morgan, Shelton and Thorogood, 2007). This was not the case in our study and can be contributed to the low number of infants (n=7) diagnosed with CP and severe motor impairment in our study as a comparison. It is also worth noting that large studies such as that done by Einspieler *et al*. (2019) only included infants diagnosed with CP, and our study included all high-risk infants fitting our inclusion criteria, regardless of CP diagnosis.

5.6 INFANTS WITH CEREBRAL PALSY: NEURODEVELOPMENTAL OUTCOME AND GROSS MOTOR FUNCTION CLASSIFICATION

Seven percent (7%) of the infants in our sample had a provisional CP diagnosis at 12-15 months corrected age. Five of the seven infants (71.43%) had spastic quadriplegic CP, one infant was classified as having suspected evolving diplegic CP, and one infant was classified with right-sided hemiplegia. Our study findings from TCH coincide with study findings of Mahlaba, Nakwa and Rodda (2020) who conducted a descriptive study on children diagnosed with CP at Chris Hani Baragwanath hospital in Gauteng, South Africa. Seventy to 75% of the infants in their study were diagnosed with spastic quadriplegic CP, like our study findings of 71.43%. In both studies, there was a strong association between the type of CP and the GMFCS classification. All the infants suspected with CP in our study were classified as being level either level III or V on the GMFCS, whereas in the study by Mahlaba, Nakwa and Rodda (2020), 27% of the

infants were at level IV, and 12.5% level V on the GMFCS. In both studies, all the infants that scored between level IV and V on the GMFCS had no means of independent movement and were diagnosed with quadriplegia. The discrepancy in the outcome of infants with CP on the GMFCS when comparing the two studies can simply be explained by the sample of Mahlaba, Nakwa and Rodda (2020) containing significantly more infants with CP (n=145) than in our study (n=7). A wider variety of CP classification and motor severity is to be expected in a bigger sample.

It is worth noting that some literature reports a discrepancy between GMFCS classification in young infants versus older children (Gorter, Ketelaar, Rosenbaum, Helders *et al*., 2008; Park, 2020). In a study investigating the stability of the GMFCS in 77 participants over time, it was found that 42% of the overall percentage of children's GMFCS levels changed with one or two levels from infancy to early childhood (Gorter *et al*., 2008). The authors concluded that that GMFCS classification, when used to assess young infants, is less precise than when it is used to classify older children. It has been recommended in the literature that there may be a need for reclassification according to the GMFCS at age 2 years old or older as it may change as time progresses and more clinical information becomes available (Gorter *et al*., 2008; Park, 2020). There is a large variation in gross motor development in both infants with atypical and typical gross motor development, and at such a young age there is limited clinical information available for assessors to utilise to make an accurate classification utilising the GMFCS, and this may provide a possible explanation for this change in classification over time (Gorter *et al*., 2008). The infants with CP in our study were classified according to the GMFCS in early infancy (12-15 months corrected age), and thus it is likely that their classification may change over time.

A study conducted by van Toorn *et al.* (2007) investigating the aetiology of children with CP at Tygerberg hospital further supports our study findings (Toorn, Laughton, van Zyl, Doets *et al*., 2007). Spastic quadriplegia is the predominant type of CP at TCH, as was the case in our study. The increased prevalence of spastic quadriplegia in developing countries, such as South Africa, may be due to increased rates of severe birth asphyxia and acquired central nervous system infections. This possible explanation was also reported by van Toorn *et al.* (2007) in their study, as their study findings showed a high rate of severe perinatal birth asphyxia (45% of perinatal CP

cases) and central nervous system infections (82% of acquired CP cases) in the infants diagnosed with CP at TCH.

Fidgety movements were absent in six out of the seven (85.71%) infants diagnosed with CP in our study. Our study findings therefore again support the findings that absent fidgety movements are highly predictive of the development of later CP (Burger, Louw & Frieg, 2011; Einspieler *et al*., 2019). All the infants diagnosed with CP had a HINE total score <40. Only one infant with CP had normal fidgety movements and a MOS score of ≥25 at 11-16 weeks corrected age, while all the other infants with CP had absent fidgety movements and a total MOS score of ≤14. These study findings coincide with that of Einspieler *et al*. (2019) were the authors concluded that a MOS of ≤14 and absent fidgety movements are highly predictive of infants at risk for neurodevelopmental and functional abnormalities, and that these infants warrant early referral for intervention.

In the study performed by Einspieler *et al*. (2019) the authors suggested that MOS scores of >14 were associated with GMFCS levels I-II, and a MOS score of <8 was strongly associated with GMFCS levels IV-V. In contrast, infants from our study sample with a MOS of 14-25 and a diagnosis of CP were all classified as GMFCS level III or V. The COVID-19 pandemic in South Africa also placed further strain on an already struggling healthcare system, with the result that many clinics and outpatient departments were closed for long periods on end, resulting in many infants being unable to attend their physiotherapy or occupational therapy sessions. This could have limited motor development and functional ability at 12-15 months corrected age.

5.7 STUDY LIMITATIONS AND STRENGTHS

A limitation of this study is that high-risk infants were only assessed on a singular occasion at 12-15 months corrected age, and that subsequent evaluations were not performed to establish a trajectory of gross motor development. Literature reports that transient neurological abnormalities in infants can occur in 40-80% of cases and may disappear by the second year of life year. Children classified as having a gross motor delay at 12-15 months corrected age may therefore present with normal gross motor development at a later follow-up evaluation (Fuentefria, Silveira & Procianoy, 2017).

During gross motor evaluations using the AIMS it was noted that a subset of study participants utilised an infant walking ring (baby walker) at some stage during early infancy. The use of infant walking rings often stems from the belief of caregivers that it will assist to accelerate gait acquisition and help to strengthen their infants' legs (Chagasa, Fonseca, Santos, Souza *et al.*, 2020). Some literature suggests a correlation between walking ring use in infancy, and poorer gross motor outcomes, with some studies also reporting gait deviations with infant walking ring use (Chagasa *et al*., 2020). Infant caregivers were however inconsistent at reporting infant walking ring use and were also often unable to recall at what age infants started using the device, and for how long. The impact that infant walking ring use could have had on gross motor outcomes in the infants in our study could therefore not be statistically analysed and reported.

COVID-19 had a definite impact on the follow-up attendance of mothers and infants at the neonatal high-risk of TCH. We can only speculate that poorer attendance was rooted in parental fear that infants would contract the disease in a high-risk setting such as a hospital. Due to COVID-19 protocols implemented at TCH the research consultant was prohibited to send SMSs to infant caregivers to remind them to attend their follow-up appointments at the high-risk clinic during the harsher lockdown periods. The ongoing taxi-violence in South Africa at the time of data collection, almost definitely resulted in poorer follow up at the high-risk clinic, as a large proportion of the South African population utilises this form of public transport. Furthermore, caregivers expressed being hesitant to expose their infants to potential illness by utilising public transport, especially since the majority of the population in South Africa had not been immunised against COVID-19 at the time of study data collection. A larger study sample with a wider variety of presentations and neonatal risk factors could have possibly led to a different study result.

The study did however have several strengths. The principal investigator (PI) was the only person that evaluated the gross motor outcomes of infants with the AIMS. The PI was also properly trained in the application of, and evaluation of infants with the AIMS. Both the HINE and Prechtl's GMA with the MOS were scored independently by three qualified individuals in the absence of the PI. The PI therefore only had access to both the HINE and MOS scores of infants (done at 11-16 weeks corrected age) after evaluation and completion of the gross motor assessment using the AIMS at 12-15

months corrected age, thus eliminating the risk of observer-expectancy bias. The PI was also blinded to infant's medical history and HINE and Prechtl's GMA with MOS scores prior to gross motor evaluation using the AIMS.

CHAPTER 6

CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

South Africa has an over-burdened and resource scarce healthcare system. The neonatal intensive care and high care units at Tygerberg Children's Hospital (TCH) provide care to a vast majority of high-risk infants each year. Advances in neonatal and maternal care have led to an increase in the survival rate of these infants, but although mortality rates have declined, morbidity rates are on the rise as a result (Pascal *et al*., 2018).

The results of this study indicated that both the Hammersmith Infant Neurological Examination (HINE) and Prechtl's General Movement Assessment (GMA) with the Motor Optimality Score (MOS) had good predictive validity with the aim to predict later gross motor outcomes of high-risk infants on the Alberta Infant Motor Scale (AIMS). Our results mirror that of other studies, where both HINE and Prechtl's GMA with MOS scores (performed as early as 3 months corrected age) are predictive of later gross motor and neurodevelopmental outcome. Both neurological assessments were able to distinguish between those infants who would require possible future intervention and regular follow-up, and those for whom this is not needed. The HINE had higher sensitivity to predict later gross motor delay than the MOS. The HINE had lower positive predictive value (PPV) to predict gross motor delay compared to the MOS, but negative predictive values (NPV) for both assessments were very similar and very high. Both HINE and MOS total scores were more predictive of later gross motor outcomes than subcategory or single item scores. The presence or absence of fidgety movements as early as 11-16 weeks corrected age is highly predictive of later neurodevelopmental outcome, especially cerebral palsy (CP). The reflexes and reactions subcategory of the HINE was found to be predictive of later gross motor outcome, but this differs from opinions in other published studies.

Both the HINE and Prechtl's GMA with the MOS had very high PPV and NPV to predict infants with provisional CP diagnosis. The MOS had a higher sensitivity to predict CP than the HINE, but sensitivity values for both assessments were low. This is most likely

resultant of the low number of infants provisionally diagnosed with CP in our study. Both the HINE and Prechtl's GMA with the later addition of the MOS were specifically developed to screen for the possibility of later CP diagnosis, and thus it was not developed with the intent of predicting gross motor outcomes. The application of both the HINE and the MOS to diagnose other neurodevelopmental outcomes other than CP is gaining interest among researchers. The results of our study support that there may be value in interpreting both HINE and MOS total scores with the aim to predict gross motor outcome. This topic however warrants further research, and it is suggested that further research be done on a larger sample of infants, specifically infants with abnormal motor outcome. Both the HINE and Prechtl's GMA with the MOS measure different, but complementary constructs. The HINE includes evaluation of tone and reflexes, thus measuring neurological function as well as deviations in posture while the GMA with the MOS has the unique ability to detect later movement disorders by further analysis of the quality of movement. The results of our study do not indicate a preference of utilising the HINE or Prechtl's GMA with the MOS above the other, and we thus advocate for the use of both neurological assessments in conjunction of one another to provide a comprehensive picture of an infant's possible neurodevelopmental outcome.

In this study we were able to provide a specific cut-off score on both the HINE, as well as the MOS, based on the best predictive value for determining gross motor delay at 12-15 months corrected age in our specific cohort of infants. We are however at present unable to establish whether these proposed values can be reliably applied to other high-risk populations at risk of gross motor delay. We thus recommend that further longitudinal studies on large cohorts of low risk as well as high-risk infants would be needed, but can suggest that cut-off scores be determined, and individualised in each research study sample.

6.2 RECOMMENDATIONS

This study found both the HINE and Prechtl's GMA with the MOS to be highly predictive of later CP diagnosis, and a good predictor of later gross motor outcome in a sample of high-risk infants.

6.2.1 Clinical implications of applying Prechtl's General Movement Assessment (GMA) with Motor Optimality Score (MOS) in a clinical setting

There is to the best of our knowledge, currently only approximately 30 health care professionals trained and qualified to evaluate infants according to Prechtl's method in South Africa. Prechtl's method has been widely praised in the literature to have a high predictive validity of severe developmental impairment. Literature investigating the validity of Prechtl's GMA with the MOS to predict later minor developmental impairments (such as was the case in our study) is also increasing. A trained individual can perform the evaluation easily, and in a timely manner. The evaluation has the added benefit of being a hands-off assessment, which makes it especially beneficial in the current COVID-19 pandemic, where it is encouraged to limit person-person contact as best possible. Furthermore, the evaluation method is inexpensive, as video recordings can now be made utilising the camera application on any smart phone. Training in this method is extremely expensive however, as most training courses are held overseas, and course attendance costs a considerable amount of money, even in the instances where the trainers present the course in South Africa.

Prechtl's GMA with the MOS can identify infants at an early age (as early as 3 months corrected age) who are at great risk for adverse developmental outcome and warrant further screening and regular follow-up. Utilising Prechtl's method is therefore advantageous in a country such as South Africa especially in a setting like TCH where resources are limited, and staff are already overwhelmed with the number of infants in need for follow-up and screening. Prechtl's method can identify those infants who would really warrant follow-up, and those who would not, and could therefore lessen this burden in the clinical setting.

It would therefore be very beneficial to have more clinical staff trained in Prechtl's method. Clinicians from other countries receive funding to attend these courses, and it can therefore be argued that it would be beneficial to provide interested South African clinicians with bursaries or funding to attend these courses.

6.2.2 Clinical implications of applying the Hammersmith Infant Neurological Examination (HINE) in the clinical setting

Our study proved the HINE performed as early as 11-16 weeks corrected age to be predictive of both later gross motor function, as well as CP diagnosis in high-risk infants. The HINE is a simple assessment tool that is easy to perform in a timely manner in as little as 10-15 minutes (Maitre *et al*., 2016; Romeo *et al*., 2016). Clinicians do not need any formal training to perform the HINE, thus no funding is needed to educate clinicians on how to perform the evaluation. The HINE proforma is available for free online and can be downloaded and printed to utilise in the clinical setting. Currently, to the best of the knowledge of the principal investigator (PI), the clinical use of the HINE is not advocated at undergraduate level in both the undergraduate courses of BSc Physiotherapy and MBChB at Stellenbosch University. As the results of our study and others prove, the HINE is very predictive of the later detection of both minor and major neurodevelopmental delays, and we therefore advocate for the inclusion of the HINE as part of infant evaluation tests and outcome measures to be included in undergraduate curricula.

6.2.3 Suggestions for future research

The results of our study support that there may be value in interpreting both HINE and MOS total scores with the aim to predict gross motor outcome, and the researcher suggests that this topic warrants further research. Further research done should ideally include a larger sample of infants, specifically infants with atypical motor outcome. We suggest that further longitudinal studies that include large cohorts of low risk as well as high-risk infants be done.

Follow-up studies, or studies that re-evaluate infants over an extended period of time (for example at 12-15 months corrected age, and then again at 2 and 4 years corrected age) is also warranted and could provide further insight as to how gross motor development trajectories may change over time.

Furthermore, we suggest that subsequent studies investigating the HINE and Prechtl's GMA with the MOS should determine and individualise cut-off scores for assessing infants to their specific research study sample, for example a large cohort of full-term infants with HIE.

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ADDENDA

ADDENDUM A

HEALTH RESEARCH ETHICS COMMITTEE APPROVAL LETTER

UNIVERSITEIT
STELLENBOSCH
UNIVERSITY

Approval Notice

New Application

10/11/2020

Project ID: 16807

HREC Reference No: S20/07/163

Project Title: The predictive validity of Hammersmith Infant Neurological Examination versus Prechtl's General Movement Assessment with Motor Optimality Score on gross motor outcomes in high-risk infants

Dear Miss Emma Jansen van Rensburg

The **Response to Stipulations** received on 10/11/2020 09:34 was reviewed by members of **Health Research Ethics Committee** via **expedited** review procedures on 10/11/2020.

Thank you for attending to the specified stipulations, your research protocol is now finally approved.

Please note the following information about your approved research protocol:

Protocol Approval Date: 15 October 2020

Protocol Expiry Date: 14 October 2021

Please remember to use your Project ID 16807 and Ethics Reference Number S20/07/163 on any documents or correspondence with the HREC concerning your research protocol.

Please note that the HREC has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.

After Ethical Review

Translation of the informed consent document(s) to the language(s) applicable to your study participants should now be submitted to the HREC.

Please note you can submit your progress report through the online ethics application process, available at: Links Application Form Direct Link and the application should be submitted to the HREC before the year has expired. Please see *Forms and Instructions* on our HREC website (www.sun.ac.za/healthresearchethics) for guidance on how to submit a progress report.

The HREC will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly for an external audit.

Please note that for studies involving the use of questionnaires, the final copy should be uploaded on Infonetica.

Provincial and City of Cape Town Approval

Please note that for research at a primary or secondary healthcare facility, permission must still be obtained from the relevant authorities (Western Cape Departement of Health and/or City Health) to conduct the research as stated in the protocol. Please consult the Western Cape Government website for access to the online Health Research Approval Process, see: https://www.westerncape.gov.za/general-publication/health-research-approval-process. Research that will be conducted at any tertiary academic institution requires approval from the relevant hospital manager. Ethics approval is required BEFORE approval can be obtained from these health authorities.

We wish you the best as you conduct your research.

For standard HREC forms and instructions, please visit: Forms and Instructions on our HREC website https://applyethics.sun.ac.za/ProjectView/Index/16807

If you have any questions or need further assistance, please contact the HREC office at 021 938 9677.

Yours sincerely,

Mrs. Brightness Nxumalo
HREC 2 Coordinator

National Health Research Ethics Council (NHREC) Registration Number:

ADDENDUM B

Western Cape Department of Health Approval Letters:

Tygerberg Hospital

Western Cape Government
Health

TYGERBERG HOSPITAL
REFERENCE:
Research Projects
ENQUIRIES: **Dr GG Marinus**
TELEPHONE:**021 938 5752**

Project ID: 16807

Ethics Reference: S20/07/163

TITLE: **The predictive validity of Hammersmith Infant Neurological Examination versus Prechtl's General Movement Assessment with Motor Optimality Score on gross motor outcomes in high-risk infants**

Dear Miss Emma Jansen van Rensburg

PERMISSION TO CONDUCT YOUR RESEARCH AT TYGERBERG HOSPITAL.

1. In accordance with the Provincial Research Policy and Tygerberg Hospital Notice No 40/2009, permission is hereby granted for you to conduct the above-mentioned research here at Tygerberg Hospital.

2. Researchers, in accessing Provincial health facilities, are expressing consent to provide the Department with an electronic copy of the final feedback within six months of completion of research. This can be submitted to the Provincial Research Co-Ordinator (Health.Research@westerncape.gov.za).

DR GG MARINUS
MANAGER: MEDICAL SERVICES

Date: 15/01/2021

Administration Building, Francie van Zijl Avenue, Parow, 7500 Private Bag X3, Tygerberg, 7505
tel: +27 21 938-6267 fax: +27 21 938-4890 www.capegateway.go.v.za

Project ID: 16807

Ethics Reference: S20/07/163

TITLE: **The predictive validity of Hammersmith Infant Neurological Examination versus Prechtl's General Movement Assessment with Motor Optimality Score on gross motor outcomes in high-risk infants**

NAME GRANVILLE MARINUS

TITLE MANAGER: MEDICAL SERVICES - RESEARCH

DATE 15/01/2021

BY [SIGNATURE]

An authorized representative of Tygerberg Hospital

Western Cape Government
Health

Prof Johan Smith
Head of Neonatology
Department of Paediatrics & Child Health
Tygerberg Children's Hospital
Tel: 021 938 6480
jjs7@sun.ac.za

17 December 2020

To whom it may concern

RE:

Research study of Emma Anita Jansen van Rensburg
The predictive validity of Hammersmith Infant Neurological Examination versus Prechtl's Motor Optimality Score on functional outcomes in high-risk infants at 12-15 months corrected age.

This study will take place during 2021 at the High Risk Clinic at C3A Specialist Outpatients under the supervision of Dr JI van Zyl who runs the clinic. I am aware of the nature of this study and Ms Jansen van Rensburg has my permission to proceed.

Regards

Prof. J Smith

Secretary:
Room 49, Gold Avenue
Francie van Zyl Avenue/Private Bag X3
Tygerberg, 7505
Tel: 021 938-4538
Fax: 021 938-4858

ADDENDUM C

PARTICIPATION INFORMATION LEAFLET AND CONSENT FORM

English, Afrikaans and isiXhosa

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:
The predictive validity of Hammersmith Infant Neurological Examination versus Prechtl's General Movement Assessment with Motor Optimality Score on gross motor outcomes in high-risk infants at 12-15 months corrected age: a descriptive study

REFERENCE NUMBER: S20/07/163

PRINCIPAL INVESTIGATOR (PI): Emma Anita Jansen van Rensburg

ADDRESS: Division of Physiotherapy, Medical School
Stellenbosch University
Francie Van Zijl Drive, Tygerberg, 7505
Cape Town, South Africa

CONTACT NUMBER: 0718733535

You are being invited to participate in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask questions if there is anything regarding this study that you do not understand. It is important that you are satisfied that you clearly understand what this research entails and how you could be involved. Your participation is voluntary, and participation may be declined. If you say no, this will not affect you negatively in any way. You are also free to withdraw from the study at any point, even if you agree to participate initially. This study has been approved by the Health Research Ethics Committee at Stellenbosch University and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study about?
The study will take place at Tygerberg Children's Hospital (TCH), Bellville, Cape Town at the neonatal high-risk clinic. This is the clinic where you bring your baby for their follow up assessments with their doctor. The aim of the project is to determine which of the two neurological assessments performed on your child at 12-16 weeks corrected age after birth most accurately predicted how functional your child would be at 12-15 months corrected age, therefore if they are behind in their gross motor development or not.

How will my baby be evaluated?
The researcher will place your child on a clean, disinfected, and safe surface and observe how your child moves. Your child will be observed from a distance, and only prompted into positions when needed. The evaluation performed will not be longer that 10-15 minutes in duration. During the evaluation, your child will be fully, but lightly dressed. You may be present during the assessment but may be asked not to interact with your baby unless required. During the study, all gathered information will be coded so that the information regarding your child will only be known to the researcher.

Why have you been invited to participate?
Your child fits the criteria of infants we would like to assess in the study:

- Your child was born preterm (before 33 weeks' gestation) and admitted to TCH.
- Your child weighed less than 1500g at birth.
- Your child is classified as "high risk" for neurodevelopmental delay due to existing pathology.

What will your responsibilities be?
You will be responsible for bringing your child for their follow up evaluation at the neonatal high-risk clinic when they are at 12-15 months corrected age. You will be required to console your child if needed.

Will you benefit from taking part in this research?
You will be notified of any abnormalities regarding your child's motor development if detected during the assessments, and thus will be referred to appropriate healthcare practitioners. Future high-risk babies may benefit from the study as this will lead to a better understanding of their early development and earlier identification of babies that may require therapeutic intervention.

Are there any risks involved in taking part in this research?
Your child's participation in the study does not present any risks to him/her.

If you do not agree to take part, what alternatives do you have?
If you do not wish for your child to take part in this study or feel the need to withdraw him/her at any stage, there will be no negative consequences. Participation is completely voluntary.

Who will have access to your medical records?
The information collected will be coded and treated as confidential. If it is used in a publication or thesis, the identity of your child will remain anonymous. Only the researcher, assessors and the healthcare staff who already have access to your child's medical records, will have access to this information.

What will happen in the unlikely event of injury occurring as a direct result of your participation in this research study?
In the unlikely event of an injury, participants will be treated by the nursing staff or Doctors at TCH.

Will you be paid to take part in this study and are there any costs involved?
No, you will not be paid to participate in the study. You and your child will, however, receive a healthy snack to enjoy when you bring your child for follow up assessment at the neonatal high-risk clinic, Paediatric Outpatients C3A, TCH. There will be no costs involved if you do participate.

Is there anything else that you should know or do?
You can contact the Health Research Ethics Committee at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by your study investigator. A copy of this information and consent form for your own records will be provided.

Declaration by participant
By signing below, I ……..…….. agree to take part in a research study entitled: **The predictive validity of Hammersmith Infant Neurological Examination versus Prechtl's General Movement Assessment with Motor Optimality Score on gross motor outcomes in high-risk infants at 12-15 months corrected age: a descriptive study**.
I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is voluntary and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.
- I understand that by agreeing that my child may participate in this study, I allow the PI to access my child's medical and clinic records and assessments, and that all information will be treated confidentially.

Signed at (place) .....…….. on (date) ……..…….. 202_

Signature of parent/legal
guardian……

Please separately sign for the following statement: I hereby consent that the data and information collected in this study may be used for future research in the field of neuro/motor development in high-risk infants. I understand that my child's information will be treated confidentially, and that to protect my child's privacy, their name will be replaced with a unique code or study number. Please tick YES/NO box and sign next to your choice.

YES	NO

Signature:…….

Declaration by investigator

I (name) ……..…… declare that:

- I explained the information in this document to
……..
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above.

Signed at (place) .....….....…….. on (date) ……...……..202_

Signature of investigator

……

STUDIE DEELNEMER INLIGTINGSBLAD EN TOESTEMMINGS VORM

TITEL VAN DIE NAVORSINGS STUDIE:
Die voorspellende geldigheid van die Hammersmith baba neurologiese evaluasie (Hammersmith Infant Neurological Examination) in vergelyking met Prechtl se algemene bewegings assessering met motoriese optimaliteits telling (General Movement Assessment with Motor Optimality Score) vir die voorspelling van grof motoriese uitkomste in hoë-risiko babas by 12-15 maande gekorrigeerde ouderdom: 'n beskrywende studie.

VERWYSINGS NOMMER: S20/07/163

HOOF ONDERSOEKER: Emma Anita Jansen van Rensburg

ADRES: Departement van Fisioterapie, Mediese Skool
Universiteit van Stellenbosch
Francie van Zijl Weg, Tygerberg, 7505
Kaapstad, Suid-Afrika

KONTAK NOMMER: 0718733535

U word genooi om deel te neem aan 'n navorsings projek. Die besonderhede van die projek word in onderstaande dokument weergegee. Neem asseblief 'n paar minute om die inligting wat hier uiteen gesit is deeglik na te gaan. Dit is belangrik dat u presies verstaan wat die navorsings studie behels, en hoe u daarby betrokke kan wees. U deelname is vrywillig, en u mag deelname weier. U baba sal nie negatief beïnvloed word, sou u deelname aan die studie van die hand wys nie. U kan ook enige tyd van die studie onttrek, al het u aanvanklik ingestem tot deelname aan die studie. Hierdie studie is goedgekeur deur die Gesondheidsnavorsing Etiese Kommitee van die Universiteit van Stellenbosch (GNEK) en sal uitgevoer word volgens etiese riglyne en beginsels soos uiteengesit deur die internasionale verklaring van Helsinki, Suid-Afrikaanse riglyne vir goeie kliniese praktyk, en die Mediese Navorsingsraad (MNR) etiese riglyne vir navorsing.

Waaroor gaan die studie?
Die studie sal geskied in die neonatale hoë-risiko kliniek by Tygerberg Kinderhospitaal, Bellville, Kaapstad. Dit is die kliniek waarnatoe u baba gebring word vir opvolg ondersoeke/afsprake met hul Dokter. Die doel van die projek is om vas te stel watter een van die twee neurologiese ondersoeke, gedoen op u baba toe hy/sy 12-16 weke gekorrigeerde ouderdom was, mees voorspellend is van hoe funksioneel u kind is by 12-15 maande gekkorigeerde ouderdom. Dus, of u kind agter is met hulle grof motoriese ontwikkeling of nie.

Hoe sal my baba ge-evalueer word?
Die navorser sal u kind op 'n skoon en veilige oppervlak plaas en observeer hoe hulle beweeg. U kind sal vanaf 'n afstand geobserveer word, en slegs in posisies in gehelp word as nodig. Die evaluasie sal nie langer as 10-15 minute duur nie. U mag teenwoordig wees tydens die evaluasie, maar mag gevra word om asseblief nie met u baba interaksie te hê nie, tensy dit so benodig word. Al die inligting wat ingesamel word tydens die verloop van die studie sal gekodeer word, sodat geen persoonlike inligting van u kind tot die navorsers bekend sal wees nie.

Hoekom is ek genooi om deel te neem aan die studie?
U kind voldoen aan die kriteria vir babas wat ons graag in die studie sal wil insluit:

- U kind is vroeg gebore (voor 33 weke van swangerskap) en opgeneem by Tygerberg Hospitaal.
- U kind het minder as 1500g geweeg by geboorte.
- U kind is geklassifiseer as "hoë-risiko" vir moontlike neuro-ontwikellingsvertraging as gevolg van 'n bestaande patologie.

Wat sal jou verantwoordelikhede behels?
U sal daarvoor verantwoordelik wees om u kind te bring vir hul opvolg evaluasie by die neonatale hoë-risiko kliniek wanneer hulle 12-15 maande gekorrigeerde ouderdom is. U sal gevra word om u kind te troos tydens die evaluasie, sou dit nodig wees.

Sal U daarby baatvind om deel te neem aan die navorsing?

U sal ingelig word van enige abnormaliteite ten opsigte van jou kind se motoriese ontwikkeling, sou dit so opgelet word gedurende die evaluasies. Indien nodig, sal u kind verwys word na die toepaslike gesondheids praktisyne vir die nodige intervensie. Ander toekomstige hoë-risiko babas sal baatvind by die resultate van die studie, omdat dit sal lei tot ‘n beter verstaan van die vroeë ontwikkeling van hierdie babas, asook vroeë identifisering van babas wat moontlik terapeutiese intervesie sal benodig in die toekoms.

Is daar enige risikos verbonde aan deelname aan die navorsings studie?
Daar is geen risikos verbonde aan u kind se deelname aan die studie nie. Die studie word as lae-risiko beskou.

As U nie instem vir deelname aan die studie nie, watter ander opsies is daar?
Sou u nie instem tot deelname van u kind in die studie nie, of later voel dat u eerder u kind uit die studie wil onttrek, sal daar geen negatiewe gevolge wees nie. Deelname aan die studie is volkome vrywillig.

Wie sal toegang tot die mediese rekords hê?
Die inligting wat versamel word sal gekodeer word, en as vertroulik hanteer word. Sou enige inligting gebruik word in ‘n publikasie of tesis, sal u kind se identiteit verbloem word en anoniem wees. Slegs die navorser, assesseerders en gesondheids personeel wat alreeds toegang tot u kind se mediese rekords het, sal toegang tot enige vertroulike inligting hê.

Wat sal gebeur in die onwaarskynlike geval van besering as gevolg van direkte betrokkenheid van u kind in die studie?
In die onwaarskynlike geval van ‘n besering, sal die betrokke partye behandel word deur die Dokters en verplegings personeel op die perseel by Tygerberg Hospitaal.

Sal u betaal word om deel te neem aan die studie, en is daar enige ander kostes betrokke?
Nee, u sal nie geldelik vergoed word vir u deelname aan die studie nie. Beide uself en u kind sal egter ‘n gesonde peuselhappie ontvang om te geniet wanneer u kind gebring word vir hulle opvolg ondersoek by die neonatale hoë-risiko kliniek, Pediatriese Buite pasiënte C3A, Tygerberg Kinderhospitaal. Daar sal geen kostes vir u wees, sou u besluit om deel te neem aan die studie nie.

Is daar enige iets anders wat u moet doen of weet?
U kan die Gesondheidsnavorsings Etiese Kommitee (GNEK) kontak by 021-938-9207 as daar enige verdere navrae, besware of klagtes is wat nie voldoende aangespreek kan word deur die hoof navorser nie. ‘n Kopie van hierdie inligting en toestemmingsbrief sal ook aan ‘n verskaf word, vir u eie liaseëring.

Verklaring deur deelnemer:
Deur die onderstaande te teken stem ek …….. in om deel te neem aan die navorsings studie getiteld: **Die voorspellende geldigheid van die Hammersmith baba neurologiese evaluasie (Hammersmith Infant Neurological Examination) in vergelyking met Prechtl se algemene bewegings assessering met motoriese optimaliteits telling (General Movement Assessment with Motor Optimality Score) vir die voorspelling van grof motoriese uitkomste in hoë-risiko babas by 12-15 maande gekorrigeerde ouderdom: ‘n beskrywende studie.**
Ek verklaar dat:

- Ek self die bogenoemde inligting gelees het, of dat ‘n ander party die inligting aan my voorgelees het, en dat die toestemmingsbrief geskryf is in ‘n taal waarin ek vlot en gemaklik is.
- Ek tyd gehad het om vrae te vra en dat al my vrae voldoende beantwoord is.
- Ek verstaan dat my deelname aan die studie vrywillig is, en dat ek nie gedwing is om deel te neem nie.
- Ek enige tyd die studie mag verlaat en dat ek nie daarvoor gepenaliseer sal word nie.
- Ek gevra kan word om die studie te verlaat voordat dit voltooi is, sou die studie Dokter of navorser voel dat dit in my beste belange is, of as ek nie die studie plan volg soos ooreengekom nie.
- Ek verstaan dat deur in te stem tot my kind se deelname in die studie, ek die hoof navorser toelaat om my kind se mediese en kliniek rekords na te gaan, en dat alle inligting as vertroulik hanteer sal word.

Onderteken by (plek) …… op (datum) ……..202_

Handtekening van ouer/wetlike voog……

Teken asseblief afsonderlik vir die volgende stelling: Ek gee Hiermee toestemming dat die data en inligting wat ingesamel is tydens die studie wel gebruik mag word vir verdere navorsing in die veld van neuro-ontwikkeling in hoë-risiko babas. Ek verstaan dat my kind se inligting vertroulik hanteer sal word, en dat my kind se naam met ‘n unieke kode, of studie nommer vervang sal word om hulle privaatheid te beskerm. Dui asseblief JA/NEE aan deur ‘n merkie te maak in die gepaste boksie.

JA	NEE

Handeteking:……..

Verklaring deur navorser
Ek (naam)…… verklaar dat:
Ek die inligting in hierdie document verduidelik het aan……
Ek hom/haar aangemoedig het om vrae te vra, en voldoende tyd geneem het om die vrae te beantwoord.
Ek tevrede is da thy/sy alle aspekte van wat die navorsing behels, voldoende verstaan, soos hier bo bespreek.

Onderteken by (plek) …… op (datum)
……202_

Handtekening van navorser
……..

INCWADI YOKWAZISA UMNTU OVUMAYO UKUSEBENZISANA NESIFUNDO SOPHANDO ESI

IMEKO YESIFUNDO SENZULU-LWAZI:

Isifundo sithelekisha imbono kaHammersmidt malunga nokuqwalasela imithambo-luvo losana (Infant Neurological Examination) kunendlela uPrechti avavanya ngayo indlela yokuziphapha kweentsana ezisengozini ethile xa zineenyanga esi-12-15. Sisifundo senkcazo.

INOMBOLO YESIFUNDO: S20/07/163

UMPHATHI WESIFUNDO: Emma Anita Janse van Rensburg

IADRESI: Division of Physiotherapy, Medical School
Stellenbosch University
Francie van Zijl Drive, Tygerberg, 7505
Cape Town, South Africa

INOMBOLO-FONI 071 873 3535

Uyamenywa ukusebenzisana nesifundo esi. Inkqubo yaso iyacaciswa kule ncwadi. Khawuthathe ixesha lokufunda nzulu le ncwadi. Kubalulekile ukuba uqonde kakuhle inkqubo yesifundo nendlela wosebenzisana naso.

Ukusebenzisana kuxhomekeka kokuvuma kwakho. Unelungelo lokwala. Ukuba akufuni ukusebenzisana nesifundo, usana lwakho aludingleki. Unelungelo lokuyeka phakathi ukuba akusafuni ukusebenzisana nesifonfo esi.

Isifundo sivunyelwe yikomiti ephetheyo iinkqubo ezisekweni zemphilo(Health Research Ethics Committee) yaseUniversiti saseStellenbosch. Inkqubo yesifundo ivumelana iinkqubo ezisekweni zelizwe lonke saseHelsinki (International Declaration of Helsinki), kwanenkqubo yokuphatha impilo saseSouth Africa kwanenkokelo yeMedical Research Council (yi-MRC) yaseSouth Africa.

ISIFUNDO ESI SIQWALASELA NTONI?

Isifundo esi siqhutywa yikliniki yeentsana ezisand-ukuzalwa zinengxaki emphilweni, zizalelwe esiBhedlele yabantwana eseTygerberg (TCH) iseBellville. Yikliniki apho uzisa usana lwakho ukuvavanywa ngugqirha.

Usana lwakho luqala ukuvavanywa ngeendlela ezimbini kuqwalaselwa imithambo-luvo yalo injani xa luneeveki ezi-12-16 emva kokuzalwa. Oku kuthelekishwa nendlela luziphatha ngayo xa luphinde luvavanywe xa luneenyanga ezi-12-15. Ngale ndlela woqondwa nokuba yiyiphi indlela lwaqala ukuvavanywa ngoyo kunceda ncono ukuqonda nokuba umntwana wokhula ngokufanelekileyo nokuba hayi.

USANA LWAKHO LUYAKUVAVANYWA NJANI NA?

Umphenguli wobeka usana lwakho etafileni ehlambulukileyo engenangozi. Woqwalasela indlela usana lushukuma ngayo.Umphenguli woluqwalasela eme ecaleni losana lwakho, angaluchukumisi ngaphandle kokuba abone ukuba lufuna ukujikwa. Lo msebenzi uthatha malunga nemizuzu e-10-15. Xa usana luyavavanywa luzakungxitywa ngehempe eyodwa. Lonke ixesha unina wokuba nalo usana, kodwa akafaneli ukuluchukumisa usana ngaphandle kokuxelwa ngumphenguli. Konke okuqondwa ngosana ngumphenguli wobhalwa ngendlela eyodwa enokuqondwa ngumphenguli yedwa.

KUTHENI NA UKUBA UCELIWE UKUSEBENZISANA NALO MSEBENZI?

Uceliwe ngokuba usana lwakho lubonakalisa iimpawo ezifanele uvavanyo olu:

- Usana lwakho lwazalwa iiveki ezi-33 wena ukhulelwe zingekapheli, usana lwalalisiwa e-TCH.
- Usana lwakhol wabangaphantsi kwe-1.5 killogram ekuzalweni kwalo.
- Usana lwakho lwabanengozi yokuba imithambo-luvo yalo ingakhuli ngokufanelekileyo ngengxa yesizathu ezi.

ZITHINI IIMFANELO ZAKHO?

Ufanele ukuzisa umtwana wakho eklinikini yokuvavanya imithambo-luvo ukuba aqwalaselwe xa aneenyanga ezi-12-15. Ufanele ukuthuthuzela umtwana xa kufuneka.

WOZUZA NTONI NGALO VAVANYO?

Wozuza ngokwaziswa ukuba kubonakala ukuba umtwana akhule ngokungafanelekanga. Oku kuyakumnceda ngokudityaniswa nabanyangi abanamava ngalemeko. Kuyakunceda njalo ukuba iqondwe nzulu indlela imithambo-luvo yeentsana ihluma ngayo ukuze zincedwe kwangoku xa kufuneka. Ngalendlela wonceda nabanye abazelwe benengxaki le.

ITHINI INGOZI EMTWANINI NGALO VAVANYO?

Ayikho ngosi emtwanini wakho tu.

KUTHENI UKUBA AKUVUMI UKUSEBENZISANA NALO MSEBENZI?

Ayikho ingxaki ukuba akuvumi ukuthabathela inxaxheba kulo msebenzi. Futhi unelungelo lokuyeka phakathi. Ayikho nyanzelo ukusebenzisana nawo.

NGOOBANI ABANELUNGELO LOKUBONA IINCWADI ZENGXELO YALO VAVANYO?

Konke okwaziwa ngomntwana wakho kubhalwe ngendlela eyodwa kugcinwe ngasese. Ukuba oku okwaziwa ngaye kuyasetyenziswa encwadi yengxelo yesifundo, igama lomtwana wakho alibizwa. Ngabasebenzi bemphilo bodwa abanelungelo lokubona iincwadi zemphilo.

KUTHENI UKUBA UMTWANA WENZAKALISWA YINTO EYENZIWA XA EPHANTSI KWALO VAVANYO?

Ukuba umtwana wenzakaliswa ngokuzenzekelayo, wonyangwa ngoogqirha noomongikazi beTygerberg Hospital.

WOVUZWA NA XA UVUMAYO UKUSEBENZISANA NALO MSEBENZI OKHANYE WOHLAWULA MALINI?.

Hayi, akuvuzwa futhi akuhlawuli mali. Xhesha umtwana wakho woziswa ukuvavanywa xa eneenyanga esi-12-15 ufanele ukumzisa kwi-out patients ko C3A yesibedlele sabantwana yeseTygerberg. Apho nonikwa into yokutya. Akubatali into ngayo.

IKHONA NA ENYE INTO UFANELE UKUYAZI OKANYE UKUYENZA?

Ukuba ikhona into okrokrisayo okanye into ofuna ukukhalaza ngayo malunga nalo msebenzi ingekacaciselwe ngumphahdi wesifundo, unelungelo lokuthetha nabaphathi beKomiti ephetheyo iinkqubo ezisekweni zemphilo (Health Research Ethics Committee) ko-021 938 9207. Wonikwa ikokpi yale ncwadi yesivumo enencaciso esiginiwe nguwe ukuze uyigcine.

ISIVUMO SONINA

Ngokusigina ezantsi, mna ……. ndiyavuma ukusebenzisana nesifunso sophando esibiswa

Isifundo sokuthelekisha imbono kaHammersmidt malunga nokqwalasela imithambo-luvo losana (Infant Neurological Examination) kunendlela uPrechti avavanya ngayo indlela yokuziphapha kweentsana ezisengozini ezithile xa zineenyanga esi-12-15. Sisifundo senkcazo.

Ndiyavuma ukuba

- Ndiyifundile okanye ifundelwe kum le ncwadi ecacisa wonke lo msebenzi kwanale ncwadi yesivumo, ithi ibhaliwe ngolwimi endiliqondayo kanye.
- Ndanikwa ithuba lokubuza oku endifuna ukucaciselwa ngayo, kwacaciselwa ngokufanelekileyo.
- Ndisebenzisana nalomsebenzi ngokwesigqibo sam, ndinganyanzelwanga.
- Ndinelungelo lokuyeka phakathi. Ukuba ndenza njalo andinatyala.
- Ndingacelwa ukuzahlula nesifundo esi singekagqitywa ukuba ugqira noba umphandi abona ukuba kuyakundilungela okanye ukuba andisebenzisani ngendlela endavumeleyo.
- Ngokuvuma ukuba umtwana wam wavavanywa ngenqhubo yesifundo esi, umphathi wesifundo unelungelo lokubona iincwadi zemphilo nezovavanyo zakhe, azigcine ngasese.

Isiginiwe e- …….. (indawo)

ngomhla we ……. ka- ……. 202…..

Isandla somzali nokuba umgcini …….

Khawusigine nendawo esezantsi:

Ndiyavuma ilungelo lokuba konke okwaziwa ngesifundo esi kusetyenziswe kophando lwenzulu-lwazi malunga neengxaki zemithambo-luvo nokuziphatha kweentsana. Ndiqonda ukuba igama lomtwana wam neencwadi zemphilo zakhe ziyafihlwa. Endaweni yokusebeniza igama lakhe wobhalwa inombolo ethile.

Lathisa indawo oyivumayo usigine: EWE HAYI ……..

Isiqinisekiso somphandi

Mna (igama) …… ndivumau kuba

Ndiyicacisile le ncwadi ko-
……

Ndamnika ithuba lokubuza imibuzo ndize ndizicacisele ngokubanzi.

Ndiqinisekile ukuba yena uyaqonda kakuhle konke okucaciselweyo kule ncwadi.

Isiginiwe e- …….. (indawo)

ngomhla we …… ka- …….. 202…..

Isandla somphandi ……

ADDENDUM D

STUDY ASSESSMENT TOOLS

Hammersmith Infant Neurological Examination, Prechtl's General Movement Assessment with Motor Optimality Score, and the Alberta Infant Motor Scale

HAMMERSMITH INFANT NEUROLOGICAL EXAMINATION (v 07.07.17)

Name **Date of birth**

Gestational age **Date of examination**

Chronological age / Corrected age **Head circumference**

SUMMARY OF EXAMINATION
Global score (max 78)
Number of asymmetries
Behavioural score (not part of the optimality score)

Cranial nerve function	**score**	**(max 15)**
Posture	**score**	**(max 18)**
Movements	**score**	**(max 6)**
Tone	**score**	**(max 24)**
Reflexes and reactions	**score**	**(max 15)**

COMMENTS

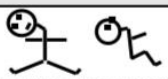
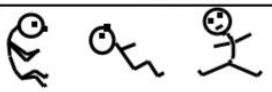
(Throughout the exam, if a response is not optimal but not poor enough to score 1, give a score of 2)

NEUROLOGICAL EXAMINATION

ASSESSMENT OF CRANIAL NERVE FUNCTION

	score 3	2	score 1	score 0	score	Asymmetry / Comments
Facial appearance (at rest and when crying or stimulated)	Smiles or reacts to stimuli by closing eyes and grimacing		Closes eyes but not tightly, poor facial expression	Expressionless, does not react to stimuli		
Eye movements	Normal conjugate eye movements		**Intermittent** Deviation of eyes or abnormal movements	**Continuous** Deviation of eyes or abnormal movements		
Visual response Test ability to follow a black/white target	Follows the target in a complete arc		Follows target in an incomplete or asymmetrical arc	Does not follow the target		
Auditory response Test the response to a rattle	Reacts to stimuli from both sides		Doubtful reaction to stimuli or asymmetry of response	No response		
Sucking/swallowing Watch infant suck on breast or bottle. If older, ask about feeding, assoc. cough, excessive dribbling	Good suck and swallowing		Poor suck and/or swallow	No sucking reflex, no swallowing		

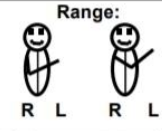
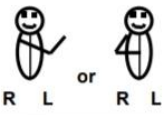
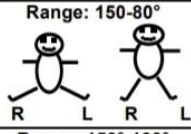
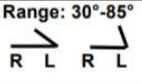
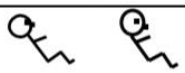
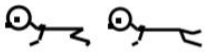
ASSESSMENT OF POSTURE (note any asymmetries)

	score 3	score 2	score 1	score 0	sc	Asymmetry / comments
Head in sitting	 Straight; in midline		 Slightly to side *or* backward *or* forward	 Markedly to side *or* backward *or* forward		
Trunk in sitting	 Straight		 Slightly curved or bent to side	 Very rounded rocketing back bent sideway		
Arms at rest	In a neutral position, central straight or slightly bent		**Slight** internal rotation *or* external rotation **Intermittent** dystonic posture	**Marked** internal rotation *or* external rotation or dystonic posture hemiplegic posture		
Hands	Hands open		**Intermittent** adducted thumb *or* fisting	**Persistent** adducted thumb *or* fisting		
Legs in sitting in supine and in standing	Able to sit with a straight back and legs straight or slightly bent (long sitting)  Legs in neutral position straight *or* slightly bent	**Slight** internal rotation or external rotation	Sit with straight back but knees bent at 15-20 °  Internal rotation *or* external rotation at the hips	Unable to sit straight unless knees markedly bent (no long sitting)  **Marked** internal rotation *or* external rotation *or* fixed extension or flexion or contractures at hips and knees		
Feet in supine and in standing	Central in neutral position Toes straight midway between flexion and extension		**Slight** internal rotation *or* external rotation **Intermittent** Tendency to stand on tiptoes or toes up or curling under	**Marked** internal rotation *or* external rotation at the ankle **Persistent** Tendency to stand on tiptoes *or* toes up or curling under		

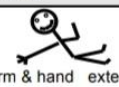
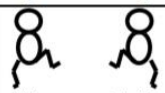
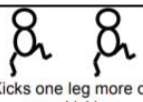
ASSESSMENT OF MOVEMENTS

	Score 3	Score 2	Score 1	Score 0	score	Asymmetry / comments
Quantity Watch infant lying in supine	Normal		Excessive or sluggish	Minimal or none		
Quality Observe infant's spontaneous voluntary motor activity during the course of the assessment	Free, alternating, and smooth		Jerky Slight tremor	• Cramped & synchronous • Extensor spasms • Athetoid • Ataxic • Very tremulous • Myoclonic spasm • Dystonic movement		

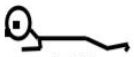
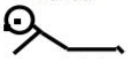
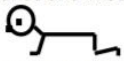
ASSESSMENT OF TONE

	Score 3	Score 2	Score 1	Score 0	sc	Asym/Co
Scarf sign Take the infant's hand and pull the arm across the chest until there is resistance. Note the position of the elbow in relation to the midline.	**Range:** 					
Passive shoulder elevation Lift arm up alongside infant's head. Note resistance at shoulder and elbow.	Resistance overcomeable 	Resistance difficult to overcome	No resistance 	Resistance, not overcomeable 		
Pronation/supination Steady the upper arm while pronating and supinating forearm, note resistance	Full pronation and supination, no resistance		Resistance to full pronation / supination overcomeable	Full pronation and supination not possible, marked resistance		
Hip adductors With both the infant's legs extended, abduct them as far as possible. The angle formed by the legs is noted.	**Range: 150-80°** 	**150-160°** 	**>170°** 	**<80°** 		
Popliteal angle Keeping the infant's bottom on the bed, flex both hips onto the abdomen, then extend the knees until there is resistance. Note the angle between upper and lower leg.	**Range: 150°-100°** 	**150-160°** 	**~90° or > 170°** 	**<80°** 		
Ankle dorsiflexion With knee extended, dorsiflex the ankle. Note the angle between foot and leg.	**Range: 30°-85°** 	**20-30°** 	**<20°or 90°** 	**> 90°** 		
Pull to sit Pull infant to sit by the wrists. (support head if necessary)						
Ventral suspension Hold infant horizontally around trunk in ventral suspension; note position of back, limbs and head.						

REFLEXES AND REACTIONS

	Score 3	Score 2	Score 1	Score 0	sc	Asym / Co
Arm protection Pull the infant by one arm from the supine position (steady the contralateral hip) and note the reaction of arm on opposite side.	 Arm & hand extend R L		 Arm semi-flexed R L	 Arm fully flexed R L		
Vertical suspension hold infant under axilla making sure legs do not touch any surface – you may "tickle" feet to stimulate kicking.	 Kicks symmetrically		 Kicks one leg more or poor kicking	 No kicking even if stimulated or scissoring		
Lateral tilting (describe side up). Hold infant up vertically near to hips and tilt sideways towards the horizontal. Note response of trunk, spine, limbs and head.						
Forward parachute Hold infant up vertically and quickly tilt forwards. Note reaction /symmetry of arm responses,	 (after 6 months)		 (after 6 months)			
Tendon Reflexes Have child relaxed, sitting or lying – use small hammer	Easily elicitable biceps knee ankle	Mildly brisk bicep knee ankle	Brisk biceps knee ankle	Clonus or absent biceps knee ankle		

SECTION 2 MOTOR MILESTONES (not scored; note asymmetries)

Head control	Unable to maintain head upright normal to 3m	Wobbles normal up to 4m	Maintained upright all the time normal from 5m			**Please note age at which maximum skill is achieved**
Sitting	Cannot sit	With support at hips  normal at 4m	Props  normal at 6m	Stable sit  normal at 7-8m	Pivots (rotates)  normal at 9m	Observed: Reported (age):
Voluntary grasp – note side	No grasp	Uses whole hand	Index finger and thumb but immature grasp	Pincer grasp		Observed: Reported (age):
Ability to kick in supine	No kicking	Kicks horizontally but legs do not lift	Upward (vertically)  normal at 3m	Touches leg  normal at 4-5m	Touches toes  normal at 5-6m	Observed: Reported (age):
Rolling - note through which side(s)	No rolling	Rolling to side normal at 4m	Prone to supine normal at 6 m	Supine to prone normal at 6 m		Observed: Reported (age):
Crawling - note if bottom shuffling	Does not lift head	On elbows  normal at 3m	On outstretched hands  normal at 4m	Crawling flat on abdomen  normal at 8m	Crawling on hands and knees  normal at 10m	Observed: Reported (age):
Standing	Does not support weight	Supports weight normal at 4m	Stands with support normal at 7m	Stands unaided normal at 12m		Observed: Reported (age):
Walking		Bouncing normal at 6m	Cruising (walks holding on) normal at 12m	Walking independently normal by 15m		Observed: Reported (age):

SECTION 3 BEHAVIOUR (not scored)

	1	2	3	4	5	6	Comment
Conscious state	Unrousable	Drowsy	Sleep but wakes easily	Awake but no interest	Loses interest	Maintains interest	
Emotional state	Irritable, not consolable	Irritable, carer can console	Irritable when approached	Neither happy or unhappy	Happy and smiling		
Social orientation	Avoiding, withdrawn	Hesitant	Accepts approach	Friendly			

For enquiries about the Hammersmith Infant Neurological examination, please contact either Prof Frances Cowan f.cowan@imperial.ac.uk, Prof Leena Haataja leena.haataja@hus.fi or Prof Eugenio Mercuri eumercuri@gmail.com

The Motor Optimality Score for 3- to 5-Month-Old Infants – Revised

Christa Einspieler and Arie Bos for the GM Trust 2000, 2019

Einspieler et al., submitted to J Clin Med 2019

Name: .....

Date of Birth: Gestational Age at Birth: Birth Weight:

Recording Date: Postmenstrual / Postterm Age:

Fidgety Movements (N, normal; A, atypical):

N Fidgety Movements A Abnormal Exaggerated A Absent
N A Sporadic (age-specific)

Observed Movement Patterns (N, normal; A, atypical): normal atypical

N A Swipes	N A Hand-to-Mouth Contact	N A Arching
N A Wiggling-Oscillating	N A Hand-to-Hand Contact	N A Rolling to Side
N A Kicking	N A Fiddling	N A Visual Exploration
N A Excitement Bursts	N Reaching	N Hand Regard
N A Smiles	N A Foot-to-Foot Contact	N A Head Anteflexion
N A Mouth Movements	N A Legs Lift	A Circular Arm Movements
A Tongue Movements	N Hand-to-Toe Contact	A Almost No Leg Movements
N A Side-to-Side Movements of the Head	A Segmental Movements of Fingers and Wrists	A
		add

Observed Postural Patterns (N, normal; A, atypical): normal atypical

N A Head Centered	N A Variability of Finger Postures	A Hyperextension of Neck
N A Body Symmetry	A Predominant Fisting	A Hyperextension of Trunk
N A Asymmetric Tonic Neck (ATN) Posture	A Synchronized Opening and Closing of Fingers	A Extended Arms
A Flat Posture	A Finger Spreading	A Extended Legs
	A Asymmetry of Finger Post.	A
		add

Movement Character:

N Smooth and Fluent	A Stiff	A Predominantly Slow
A Monotonous	A Tremulous	A Predominantly Fast
A Jerky	A Cramped-Synchronized	A
		add

Motor Optimality List:

i.	Fidgety Movements	+ ++, * **	normal	❑ 12
			abnormal exaggerated	❑ 4
		±	absent / sporadic	❑ 1
ii.	Observed Movement Patterns		N > A	❑ 4
			N = A	❑ 2
			N < A	❑ 1
iii.	Age-Adequate Movement Repertoire (do not consider fidgety movements)		present	❑ 4
			reduced	❑ 2
			absent	❑ 1
iv.	Observed Postural Patterns		N > A	❑ 4
			N = A	❑ 2
			N < A	❑ 1
v.	Movement Character		smooth and fluent	❑ 4
			abnormal but not CS	❑ 2
			cramped-synchronized (CS)	❑ 1

Motor Optimality Score (MOS): from 28 to 5

ALBERTA INFANT MOTOR SCALE

Record Booklet

Name _____ Date of Assessment Year / Month / Day

Identification Number _____ Date of Birth / /

Examiner _____ Chronological Age / /

Place of Assessment _____ Corrected Age / /

	Previous Items Credited	Items Credited in Window	Subscale Score
Prone			
Supine			
Sit			
Stand			

Total Score ☐ Percentile ☐

Comments/Recommendations

(1)

Alberta Infant Motor Scale

STUDY #

PRONE

Prone Lying (1)

Physiological flexion
Turns head to clear nose from surface

Prone Lying (2)

Lifts head symmetrically to 45°
Cannot maintain head in midline

Prone Prop

Elbows behind shoulders
Unsustained head raising to 45°

Forearm Support (1)

Lifts and maintains head past 45°
Elbows in line with shoulders
Chest centered

Prone Mobility

Head to 90°
Uncontrolled weight shifts

Forearm Support (2)

Elbows in front of shoulders
Active chin tuck with neck elongation

SUPINE

Supine Lying (1)

Physiological flexion
Head rotation: mouth to hand
Random arm and leg movements

Supine Lying (3)

Head in midline
Moves arms but unable to bring hands to midline

Supine Lying (2)

Head rotation toward midline
Nonobligatory ATNR

Supine Lying (4)

Neck flexors active—chin tuck
Brings hands to midline

Hands to Knees

Chin tuck
Reaches hands to knees
Abdominals active

SITTING

Sitting With Support

Lifts and maintains head in midline briefly

Sitting With Propped Arms

Maintains head in midline
Supports weight on arms briefly

Pull to Sit

Chin tuck: head in line or in front of body

STANDING

Supported Standing (1)

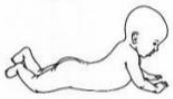
May have intermittent hip and knee flexion

Supported Standing (2)

Head in line with body
Hips behind shoulders
Variable movement of legs

(2)

Extended Arm Support



Arms extended
Chin tuck and chest elevated
Lateral weight shift

Rolling Prone to Supine Without Rotation

Movement initiated by head
Trunk moves as one unit

Swimming

Active extensor pattern

Reaching from Forearm Support

Active weight shift from one side
Controlled reach with free arm

Pivoting

Pivots
Movement in arms and legs
Lateral trunk flexion

Four-Point Kneeling (1)

Legs flexed, abducted, and externally rotated
Lumbar lordosis
Maintains position

Rolling Prone to Supine with Rotation

Trunk rotation

Hands to Feet

Can maintain legs in mid-range
Pelvic mobility present

Active Extension

Pushes into extension with legs

Rolling Supine to Prone Without Rotation

Lateral head righting
Trunk moves as one unit

Rolling Supine to Prone with Rotation

Trunk rotation

Unsustained Sitting

Scapular adduction and humeral extension
Cannot maintain position

Sitting With Arm Support

Thoracic spine extended
Head movements free from trunk: propped on extended arms

Unsustained Sitting Without Arm Support

Cannot be left alone in sitting indefinitely

Weight Shift in Unsustained Sitting

Weight shift forward, backward, or sideways
Cannot be left alone in sitting

Sitting Without Arm Support (1)

Arms move away from body
Can play with a toy
Can be left alone in sitting

Reach With Rotation in Sitting

Sits independently
Reaches for toy with trunk rotation

Supported Standing (3)

Hips in line with shoulders
Active control of trunk
Variable movements of legs

3

Propped Sidelying

Dissociation of legs
Shoulder stability
Rotation within body axis

Reciprocal Crawling

Reciprocal arm and leg movements with trunk rotation

Four-Point Kneeling to Sitting or Half-Sitting

Plays in and out of position
May get to sitting

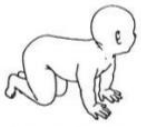
Reciprocal Creeping (1)

Legs abducted, and externally rotated
Lumbar lordosis: weight shift side to side with lateral trunk flexion

Reaching from Extended Arm Support

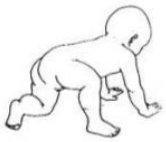
Reaches with extended arm
Trunk rotation

Four-Point Kneeling (2)



Hips aligned under pelvis
Flattening of lumbar spine

Modified Four-Point Kneeling

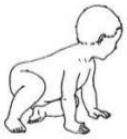


Plays in position
May move forward

Sitting to Prone

Moves out of sitting to achieve prone lying
Pulls with arms; legs inactive

Sitting to Four-Point Kneeling



Actively lifts pelvis, buttocks, and unweighted leg to assume four-point kneeling

Sitting Without Arm Support (2)

Position of legs varies
Infant moves in and out of positions easily

Pulls to Stand With Support

Pushes down with arms and extends knees

Pulls to Stand/Stands

Pulls to stand; shifts weight from side to side

Supported Standing With Rotation

Rotation of trunk and pelvis

Cruising Without Rotation

Cruises sideways without rotation

Half-Kneeling

May assume standing or play in position

Controlled Lowering Through Standing

Controlled lowering from standing

(4)

Reciprocal Creeping (2)

Lumbar spine flat
Moves with trunk rotation

Cruising With Rotation

Cruises with rotation

Stands Alone

Stands alone momentarily
Balance reactions in feet

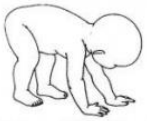
Early Stepping

Walks independently; moves quickly with short steps

Standing from Modified Squat

Moves from squat to standing with controlled flexion and extension of hips and knees

Standing from Quadruped Position



Pushes quickly with hands to get to standing

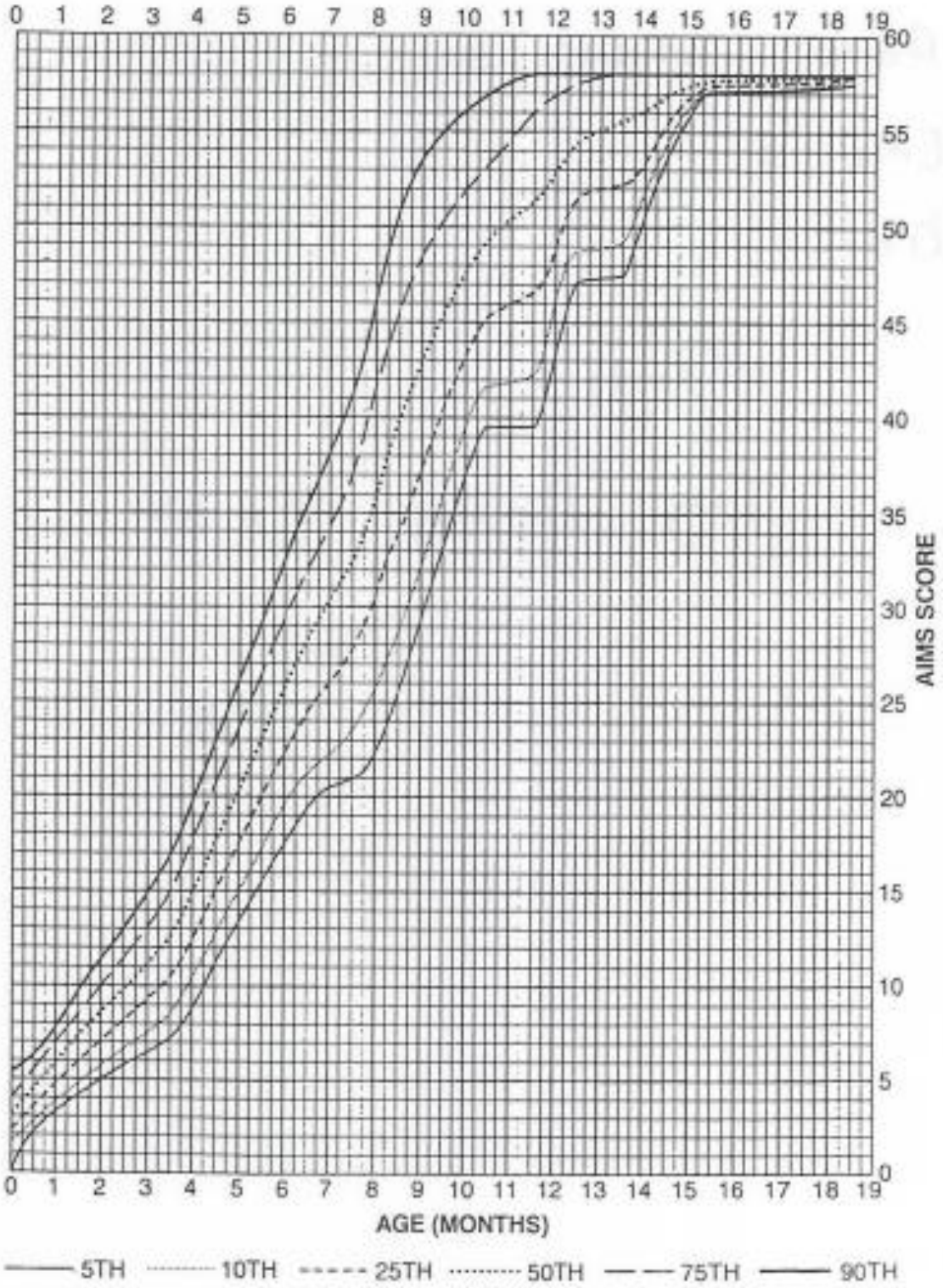
Walks Alone

Walks independently

Squat

Maintains position by balance reactions in feet and position of trunk

Percentile Ranks



(6)