UNIVERSITY OF RWANDA
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ASSESSMENT OF PREVENTABLE CAUSES AND PREDICTORS OF INDEPENDENT AMBUILATION FOR CHILDREN WITH CEREBRAL PALSY IN RWANDA

A dissertation submitted in partial fulfilment of the requirements for the degree of Master of Medicine in Orthopaedic Surgery in the School of Medicine and Pharmacy, College of Medicine and Health Sciences.

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DECLARATION

I declare that this dissertation entitled "**Assessment of preventable causes and predictors of independent ambulation for children with Cerebral Palsy in Rwanda**" is my own work and it has not been submitted for any degree at the University of Rwanda or any other institution.

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DEDICATIONS

To my wife, Dr Mwiseneza for your love, patience and hard work,

To my children, Ntwali Kanyemera and Isaro Kanyemera for your love and motivation,

To my parents, Mukansoro and late Kanyemera for your love,

To my sister and brother for your love and presence,

To all lecturers, teachers, and fellows who shaped me,

I dedicate this dissertation.

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LIST OF SYMBOLS AND ACRONYMS

ADL: Activities of Daily Life

ANC: Antenatal Care

BCPR: Bangladesh Cerebral Palsy Register

CCO: Centre de ChirurgieOrthopedique

CCPR: Canadian Cerebral Palsy Register

CNS: Centre Nervous System

CP: Cerebral Palsy

FDA: Food Drug Administration

GA: Gestational Age

GABA: Gamma-Aminobutyric Acid

GMA: General Movement Assessment

GMFCS: Growth Motor Function Classification System

GMFCS-E&R: Growth Motor Function Classification System – Revised &Expanded

HICs: High Income Countries

HINE: Hammersmith Infant Neurological Examination

ICF: International Classification of Functioning, Disability and Health

IUGR: Intra Uterine Growth Restriction

LMICs: Low-Middle Income Countries

NCD: Non-Communicable Diseases

NICU: Neonatal Intensive Care Unit

NCPD: National Council of Person with Disabilities

PVL: Periventricula Leukomalacia

SCPE: Surveillance of Cerebral Palsy in Europe

SSA: Sub Saharan Africa

TORCH: Toxoplasmosis, Rubella, Cytomegalovirus and Herpes simplex

UTI: Urinary Tract Infection

WHO: World Health Organization

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ABSTRACT

Background: Cerebral palsy (CP) is commonly source of motor dysfunction in paediatric population worldwide. Its burden to families and country is highly remarkable. Although in developed countries there is increasing information on clinical features of paediatric patients with cerebral palsy, in developing Countries experience significant paucity of clinical data on cerebral palsy. This study has objectives to determine preventable causes and predictors of independent ambulation of CP in our country.

Methodology: A retrospective study was carried out in specialized hospital, Centre de ChirurgieOrthopedique (CCO) de Rilima since January 2016 to June 2020. We selected all children diagnosed clinically with cerebral palsy; age limit was 2 years to 18 years. Univariate analysis was performed to determine preventable causes of cerebral palsy and their modes of treatment then we used Chi square and logistic regression to establish the risk factors of independent ambulation in CP patients.

Results: Three hundred and ninety-five (395) patients were enrolled in our study of which 53% (n=213) were male and 46% (n=182) were female with median age of 4years. The most common motor type is spastic 71%. Regarding topographic distribution, quadriplegia was the most common 65.6%. The most common motor severity was GMFCS V 48.1%. Significant risk factors found are fetal distress 27.6%, low birth weight 20.5% and congenital malformation 13.67%. A couple of factors were found to be significantly predicting independent ambulation such as ability to sit before 2years ($p=0.004$), motor severity and topographic distribution ($p<0.001$), absence of both intellectual disability, visual impairment and epilepsy ($p<0.001$). The commonest cerebral palsy treatment mode was gait training (55.7%) while tenotomy (4.5%) and tendon lengthening (8.6%) were not frequently used.

Conclusion: The most of patients (91.1%) with CP found in this study are term babies same as what found by other authors in LMICs and many risk factors identified are preventable, so establishment of preventive and management strategies in developing countries are highly needed.

Key words: cerebral palsy, independent ambulation, preventable causes.

CHAPTER ONE: INTRODUCTION

1.1. Background

Cerebral palsy (CP) defined as a term referring to static disease of the growing brain where the injury to immature brain happens during antenatal, neonatal or infant period and affects the evolution of motion and posture, resulting into activity restriction.[1,2] Frequently, the motor conditions are linked with epilepsy, disruption in hearing, vision sensory, behaviour, discernment, cognitive state and communication skils.[3] The CP is a burden to family and country, its severity is raised by the fact that among the affected population around 40% are unable to walk independently, around to one third suffer from epilepsy, up to one third have verbal disabilities and about another one third live with cognitive impairment.[4] The prevention of CP is possible based on that preventable risk factors before, during and after conception are highly connected to possibility of having cerebral palsy.[4]

Although up to 50% of the causes of CP are unknown but some authors described a set of congenital brain birth defects, inherited disorders, inborn metabolic diseases and congenital or acquired bacterial and viral diseases as causes.[5] CP is commonly known as the main root of physical dysfunction during infancy period, considering its scarcity occurrence, heterogeneity in aetiologies and sometimes absence of known causative agent make CP a complex condition to study.[6,7]

Cerebral palsy is classified physiologically in five types: spastic, dyskinetic, ataxic, hypotonic and mixed and topographically in four types: monoplegia which is rare, hemiplegia, diplegia and quadriplegia. It can also be classified according to the ability of motor function based on Gross Motor Function Classification System (GMFCS) in five levels which gives details regarding the seriousness of functional restriction by considering the child's need or not of the mobility devices.[5,6]

Despite that the CP is complex condition to study and predict the outcome, there are some factors that influencing its prognosis.[6]

The knowledge about predictors of outcome for any disease is of great importance in all corners; on treating personnel, patients and family, this will help; in selecting confidently appropriate approach, in communication between treating clinicians and their clients, and also will increase the adherence and compliance to any intervention given to the patient.[8] Therefore many studies highlighted CP outcome measurements tools[9] with some specific clinical and imaging features of CP which are used to predict the outcome.[8,9]

The description of outcome predictors involves the highlighting the determinants which are independent variables that contribute positively or negatively to the CP prognosis.[8] These variables are related to the patient's disease including clinical features of CP (like gravity and anatomical location of spastic symptoms, extent of cognitive disability) and environment related such as family care, socioeconomic category of the parents or family and school environment.[8,10]

Worldwide, the approximated prevalence is 2-2.5 per one thousand live births, this incidence is directly related to gestational age because studies showed that it occurs in 1 out 20 preterm babies who survived. Interestingly the most affected population by CP is full term infants despite those premature babies are at high risk of getting CP. In fact, the proportion of babies born at term is always higher than the proportion of living preterm infants babies.[11]

Many studies done in industrialized countries reported the same prevalence on cerebral palsy, it is ranging from 2 to 2.5 per 1000 children. Additionally, authors showed that the affected children proportion remains stable or increased[12]. This reflects to the improvement of prenatal, perinatal and post-natal care, equipped neonatology unity so that the rate of survivorship of preterm and very preterm neonates is increasing consistently.[12]

The incidence of CP in Lower and Middle-Income nations (LMICs) is roughly similar when considered to one from HICs. It is paradoxically, difficulty to understand such prevalence similarity when considering the differences between LMICs and HICs in terms of perinatal and infants mortality rate[13]. Nevertheless, the reasonable difference is seen in clinical presentation of the disease between developed and developing countries,

additionally perinatal asphyxia and hyperbilirubinemia are most common causes of cerebral palsy in LMICs.[13]

Despite limited data in LMICs, study done in Moldova, author described a prevalence around 3.4 per 1000 children and other studies estimate 3.4 to 4.5 per one thousand live children in developing nations.[13]

As reported in world report on disability 2011by WHO, approximately 5% of all paediatric population are affected with moderate or severe deformities and mental disorders, among them around 80% are coming from poor countries.[14]

In African countries especially those located in the south of Sahara there is limited information on CP knowledge but there is a reason to be confident that there is obvious difference between black African countries and other parts in the world regarding the living style, parental health, limited access to health facility, infections, traditional delivery support and etc.[15–17] Interestingly there is no single published study done in Rwanda about cerebral palsy specifically, and this is the opportunity for this study.

1.2. Problem description and Research Justification

CP is a burden to orthopaedic practice worldwide especially in LMICs including Rwanda. The role of orthopaedic surgery is to optimise function and prevent further deformities, It is not a curable condition[18], In study directed by Rehbein, I et al proclaimed that around 41% of patients in the age group of 8 to 15years with grade I according to GMFCS, 54% with grade II and around 62% of grade III, IV or V have been underwent orthopaedic procedure in their life.[19] While it can be possible to prevent CP, on one hand it is difficult to treat and to bear its impact on patient's family and the country, on another hand, the parents spend the whole time looking after their dependents children. There is lack of knowledge about this condition in terms of prognosis, role of intervention, which is impairing family contribution regarding the management given to paediatric patients with cerebral palsy (relationship centered-care).

As of today, no single research in Rwanda has been conducted on the analytical review of causes and prognosis of CP. The epidemiological data on these causes would clarify those preventable versus unpreventable. This is the object of this study which shall

review 4 years analysis of causes of CP in Rwanda. It will therefore yield recommendations that shall help to decrease the burden of CP on families in particular and the health system in general and it will help to raise awareness about the CP in society.

1.3. Research question

What are the preventable causes or risk factors and prognostic predictors of independent ambulation of CP patients followed at Centre de Chirurgic Orthopedique (CCO) Rilima?

1.4. Research Goals

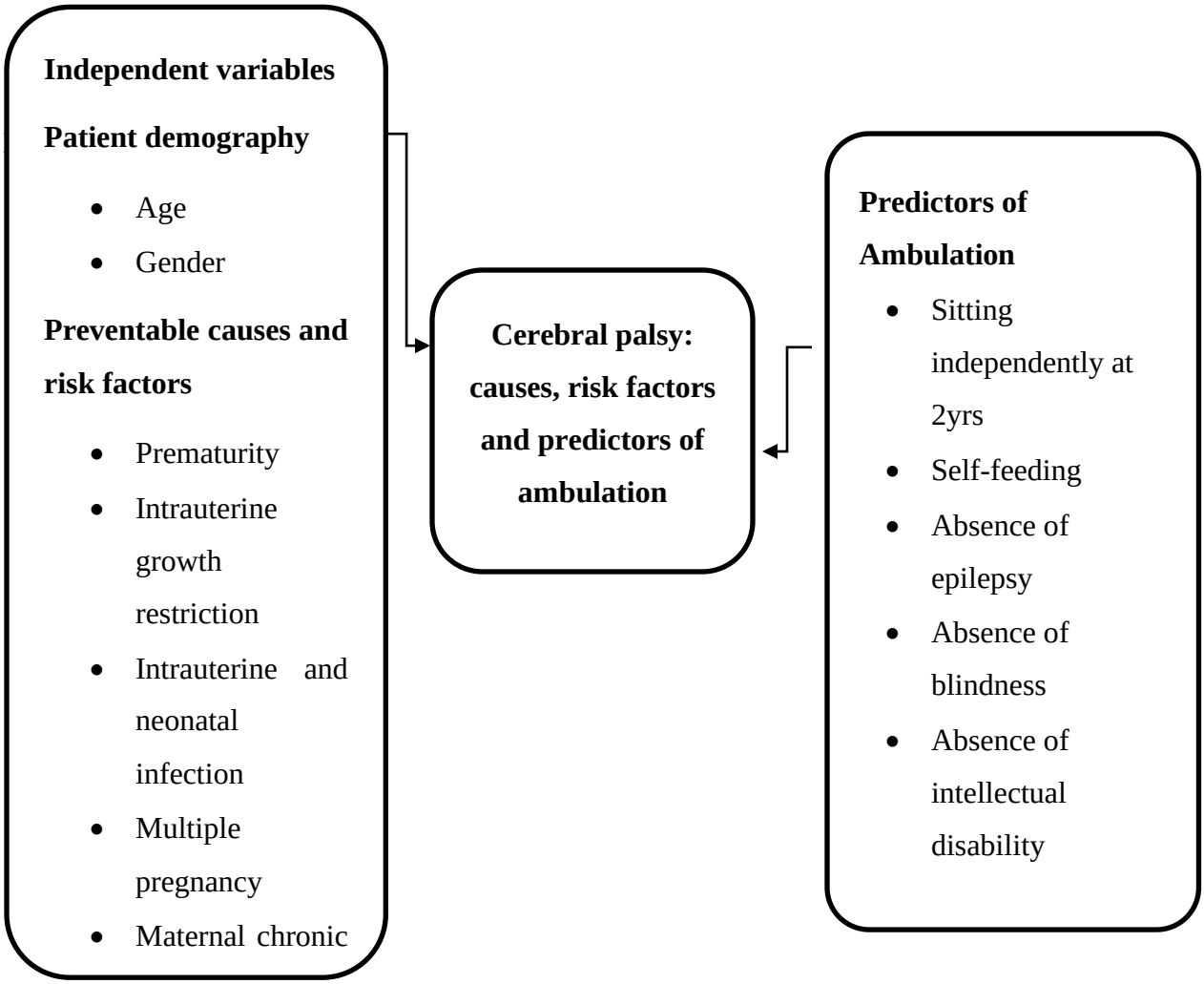
1.4.1. General Goals

- To assess etiological factors and predictors of ambulation in Cerebral Palsy patients followed at CCO Rilima

1.4.2. Specific Goals

- To identify different preventable causes and risk factors of CP in cases followed at CCO Rilima.
- To determine modes of treatment offered to children with CP in CCO Rilima
- To identify factors predicting the independent ambulation in CP patients followed at CCO Rilima.

1.5. Conceptual Framework



CHAPTER TWO: LITERATURE REVIEW

2.1. Introduction

This chapter emphasises on the explanation, epidemiology and classification of the cerebral palsy, we detail on risk and etiological factors of Cerebral Palsy by clarifying those can be preventable, the factors influencing the outcome of cerebral palsy patients and role of orthopaedic in management of CP will be also discussed in this chapter.

2.2. Definition of cerebral palsy

Cerebral palsy is a familiar condition starting in growing brain and leading to catastrophic motor dysfunction, it was reported firstly by an orthopaedic surgeon, William Little in 1840 as cerebral paresis.[20] In the beginning, He concentrated his attention to joint stiffness and malformation caused by spasticity and paralysis. He related the spasticity and paralysis to the damage of developing fetal or infant brain by prematurity or perinatal asphyxia.[20,21] Cerebral Palsy is first and foremost a disease of body motion and position balance. Cerebral palsy is elucidated as a category of enduring motor impairments syndrome leading to activity restrictions that are assigned to static distraction happened in growing human fetus or early childhood brain.[21]

CP is a blanket term comprising of a complexity set of distinct aetiologies and risk factors contributing to motor functional disability in addition with a diversity concomitant diseases including seizures, cognitive difficulties, sensory impairment, and abnormal behaviour.[22] It may be described as static encephalopathy considering that primary lesion or injury to immature brain are static however the clinical manifestation are prone to progress with time secondary to growth and evolution of brain plasticity and differentiation of the central nervous system cells.[23]

2.3. Epidemiology

Cerebral palsy is known as the major global origin of physical abnormality in paediatric population worldwide.[24] With the support of the statistics from HICs, the occurrence of cerebral palsy has been proclaimed globally around 2/1000 live children.[25] From the beginning, the epidemiology of CP concentrated to its frequency, who is affected by the condition and highlighting the causes and risk factors specifically those which can be preventable. Its frequency in western industrialised countries is calculated by the rate per a thousand children and is approximately varying between 2 to 2.5 per 1000 children with male roughly more affected than female (ratio of 1,33:1).[26]

Although, in the past the poor standard of obstetrical and perinatal supervision were taken as the preventable causes of CP and advances technique were elaborated to decrease the incidence of the disease, by introducing obstetrical monitoring machines, increase in obstetrical interventions (i.e forceps and caesarean sections), unfortunately there was no reduction in cases rate has been reported, reasonable explanation is that currently due to advance in medicine there is decline in neonatal death and rise in survivorship of very low birth weight newborns.[26]

In LMICs, considering the health facilities capacity, limited access to health care and population's economic status, there is a justifiable reason to think that the prevalence of CP is high when compared to one from HICs.[27] Unfortunately, it is difficulty to confirm that assumption because there is fewest evidence based on large sample size studies like general population-based study in order to get suitable data.[28]Khandaker G. et al conducted a study in general population of Bangladesh and it was considered as the first study of this type in LMICs, it revealed an occurrence of 3.4/1000 children which is more than to what reported in HICs.[28] Another study conducted on Ugandans general population has reported a prevalence of 2.7/1000 live births.[16]

The post neonatal acquired CP has been reported to be high in LMICs compared to HICs and in majority of cases is associated with avoidable causes like different types of infective encephalitis (vaccine-preventable infectious encephalopathy).[27]

A study conducted in rural Indonesia using a community-based key informant method survey has reported 46.9% of post neonatal acquired CP which is very elevated when compared to 6% reported in HICs and it is even very high compared to other LMICs.[27] In Bangladesh perinatal and prenatal risk factors are approximated to 61.6% of children affected with CP[28], in Egypt it is very high and is estimated to 90.4%,[29] those factors are intrapartum respiratory disease of the newborns, neonatal hypoxic ischemic encephalopathy and systemic or brain infections.[27,28] The proportion of 6.1% of acquired factors in post neonatal period were reported and are associated with pneumonia, sepsis, drowning and trauma.[28]

In our region East Africa, the prevalence of CP is roughly the same as what found in other LMICs, only one study based on general population was conducted in Uganda has published prevalence of 2.7/1000 live children.[16] But the big challenge is the paucity of reliable and unbiased data in the region due to lack of population registers, it is assumed that significant amount of paediatric patients with CP are hidden in family, never consult the hospital, the reason is that, there are no laws or policies elaborated to protect their specific needs, their right, fight against stigma and marginalization.[30,31]

In our country Rwanda, like elsewhere in resource-poor setting there is lack of epidemiological data on cerebral palsy, some reports and survey focus in general on childhood disability including physical disability, mental deficiencies and developmental retardation.[32] The WHO in one report estimated that around 10% of children globally live with disability and it is also estimated that 80% of disabled people (children and adults) live in LMICs.[32]

In survey conducted in Rwanda on different centres in charge of disabled children revealed a significant number of 2,192 children with disabilities cared in 43 centres in the study visit conducted by National Council of Person with Disabilities (NCPD).[33] In another study conducted in Rwanda reported that around 4.8% of population (Ministry of Health 2002) live with severe or moderate disability. Additionally, the records from Gatagara centre 2003 on the disabilities related to conditions affecting the central nervous system revealed Cerebral Palsy as predominant condition.[34]

2.4. Classification of cerebral palsy

The CP is heterogeneous disease when etiological factors, motor type and severity of impairments are concerned, hence its classification into clinical groups remains a challenge.[21,35] Although CP is very challenged to define and make a reliable and validity single classification, the categorization into clinical groups is very important. Therefore different classification for CP are available.[35] Normally the classification of CP is used for describing the severity and nature of disability, revealing which type of appropriate management, highlighting the possible predictors of outcome and providing data to researchers by helping in scientifically comparison of cases series of CP.[36]

Three types of CP classification are popular and they will be described in details in this study, those different groupings are based on motor category, geography and motor gravity.[21] The classification of CP is highly dependent to some factors like age of the child, the source of medical information (parents, caretaker or clinical notes,…) and the capacity of hospital setting in terms of neuroimaging.[36] Therefore the same patient can be classified differently on different occasion, basing on the age, the clinical manifestations will change with age, and of course the medical history given by a biological parent will be definitely different to what given by a caretaker or extracted from the patient's file, in this context the child's condition will be classified differently in two different hospitals due to the affordability to neuroimaging.[35,36]

2.4.1. Physiological Classification

The physiological classification provides an information about the site involved in immature brain based on the motor type and abnormal movement resulted.[11,35] Hence, the CP is classified at least into five types according to pathophysiological classification: **spastic** when the corticospinal (pyramidal) tracts are effected, **dyskinetic** which is characterised by dystonia and choreoathetosis when the basal ganglia(extrapyramidal) is affected, classified as **hypotonic** and **ataxic** when it is the cerebellum (extrapyramidal) involved,[11,37] the fifth type is **mixed** when the patient presented with features of spasticity and choreoathetosis.[11]

Actually the clinical manifestation in spastic CP patients are persistent while the extrapyramidal neuromotor findings vary with the age,[35] and the movement disorder usually presents at the second year of life, most of the time associated with speech impairment.[11] In this classification, the spastic type is more common ranging between 75% to 85%,[11,21,37] the dyskinetic and ataxic occur in 7% and 4% of patients respectively.[21] The predominant hypotonic motor type CP occurs rarely, approximately in 3% of children affected.[11,21]

2.4.2. Anatomical Classification

The anatomical classification also known as topographic or geographical classification,[35,37] it classifies the spastic type CP based on extremities (limbs) distribution of neuromotor disorders into unilateral (hemiplegia, monoplegia) and bilateral (quadriplegia, diplegia) spastic CP.[21,37]

Unilateral spastic CP includes **hemiplegia** (40%-60%)[21] which affects lower and upper limb of the same side (left or right sided)[35] with symptoms dominance located either on lower or upper extremities[38] but most of time upper extremities involved more than lower extremities,[37] and **monoplegia** which is very rare, it is affecting one limb[35] usually lower.[37]

Bilateral spastic CP consists of **diplegia** (10%-36%)[39] with the involvement of both limbs but the lower limbs affected by the spasticity and weakness more than upper extremities and **tetraplegia** with both extremities and trunk equally involved in 24%-31% approximately.[21,35,37,38]

This type of CP classification has an advantage in assessing possible aetiologies of CP because these geographical subtypes can be related to specific causes.[35] For example, a patient diagnosed with tetraplegic spastic CP suggests a serious birth asphyxia, infectious diseases in neonatal period and metabolic or inherited conditions; a patient with diplegia brings attention to brain tissue death (periventricular leukomalacia) which occurs before, during or after birth mostly affecting premature babies or birth underweight while hemiplegia suggests intrauterine or neonatal stroke and periventricular haemorrhagic infarction.[35,40]

2.4.3. Gross Motor Function Classification System (GMFCS)

The GMFCS is the familiar categorization type used among the other many existing functional classifications of cerebral palsy. These classifications are constructed based on the ability of manual activities, communication, eating and drinking function. They are at standard level, recognised internationally, trustable and harmonised each other.[35,41] The GMFCS predicts the severity of CP in children over two years of age,[21] it is a functional scale that classifies a CP patient in five levels according to the capacity of walking independently (Level I), needs of mobility devices and complete lack of muscle power (Level V) when the gravity force is concerned (bed-ridden patient).[21,35,41]

It was described firstly by Palisano et al. in 1997, intended to evaluate gross motor skills abilities and restrictions in paediatric population under 12years.[42] The first version has its limitations, the age group of lesser than 12years, therefore Palisano et al. in 2007 developed a revised & expanded GMFCS by respecting the difference in motor development regarding the age groups including children between 12-18years.[35,43] The 12-18years age group has been created considering that the performance of ambulation and mobility is highly linked to physical, social, environmental aspects and individual features including interests, forechoice and inspiration.[43,44] In this revised motor classification, functional grading were developed on the basis of age bands with first group for children younger than 2years, second group with 2-4years, third group with 4-6years, fourth group with 6-12years and fifth group including 12-18years but the abilities of performance are the same in 6-12years and 12-18years.[35,41]

In general, the current GMFCS is designed according to the guidelines published by World Health Organization in its department working on disability.[35]

It is simple, understandable and easy to use in terms of quick communication between medical practitioners and families,[41,43] the GMFCS is helpful in setting goals, elaborating appropriate management and predicting long term mobility.[21,43] This functional classification system was developed also for use in clinical research and its reliability and stability were assessed and showed promising results.[43,45,46]

The highest mobility, a child can expect to have is well described in age band 6-12years.[35,41] Hence, The revised and expanded motor classification between 6 years and 12years categorise paediatric patients in five levels: Leve I as child who walks independently with near normal motor skills, the child is able to jump and run, the only limitation is speed and balance,[35,41] it affects around 35%.[37] Individuals in Level II can ambulate independently, walking upstairs with a railing but difficulty on rough ground and they experience limitation to jump or run (approximately affects 16%).[37,41] Patients in GMFCS Grade III ambulate using walking frame device and wheelchair for long distance, it occurs in 14% approximately.[37,43] Patients in Level IV are severely limited in walking, they use mobility devices that need external support for movement or electronic controlled mobility devices (16%).[37,41] Lastly, patients in Grade V are nonambulators, completely dependent in all aspects of care, they are carried in wheelchair in all daily activities (18%).[35,37,41]

2.5. Etiological and Risk factors of cerebral palsy

The assessment of etiological and risk factors related to CP consists of evaluating when the brain insult occurred, either during pregnancy or after birth. Therefore, etiological factors are classified as postnatal/post-neonatal if the child was doing well until day 28 of life and something went wrong between day 28 to 2years of age otherwise the timing is classified as prenatal or perinatal.[12,47] The isolation of single cause of CP is very challenging, some patients present with combination or sequence of events resulting in cerebral palsy.[12] In fact the aetiology of cerebral palsy is multifactorial and heterogeneous making harder to study, Frequently many studies describe causes and risk factors concomitantly.[47,48]

Prenatal/Perinatal: The perinatal refers to period between 22nd week of gestational age and around 4 weeks of life after birth.[47] Risk factors during the antenatal periods are enormous, are consist of parental age, lack of regular antenatal consultations, use of teratogenic drug or alcohol, maternal diabetes mellitus, any febrile disease during pregnancy and multiple gestations are associated with developing CP.[12,47]

The most familiar leading causes in antenatal and perinatal period are prematurity which contributes for around 35% of all cases,[49] preterm labour is elucidated as delivery of a baby with gestational age (GA) below 37 weeks,[47] the risk of getting cerebral palsy is increasing proportionally to the lowest number of GA, for instance the risk rate is 30 times elevated in premature children with GA below 33 weeks when compared with term babies, approximately 70 per 1000 live births.[49] The other described causes and risk factors of CP are congenital brain malformation, instruments assisted delivery, any condition that resulting in difficult breathing or gasping to neonate in first five minutes of life (birth asphyxia), neonatal jaundice, congenital infection (vertically transmitted infections), antepartum hemorrhage and cerebral vascular conditions mainly diagnosed on brain imaging.[12,47,48]

Post neonatal acquired CP: This is the period between 28days of life and two years, in this period the most common causes of CP are dominated by infections and physical injuries. During the assessment of CP patients, the history of convulsion, systemic infection and admission in neonatal unit are relevant in extracting the causes.[47] Some causes highlighted in literature included malaria, meningitis and seizures (most common in developing countries), congenital HIV and hemiglobinopathies like sickle cell disease are likely to cause brain injury and cerebrovascular accidents respectively in post neonatal periods. The physical injuries consist of motor vehicle accidents, home falls and drowning.[12,47] The contribution of genetic predisposition to CP is not negligible, recent studies described approximately 1-2% of CP had been related to gene mutations.[49]Erez, O. et al. showed genetic involvement in CP to 48% in term babies and 24% in preterm idiopathic CP patients.[50] Despite effort used in describing and studying on aetiologies of CP, we are still having high proportion of CP without known causes, approximately 30% of all affected cases.[51]

2.5.1. Preventable etiological and risk factors of Cerebral palsy

The occurrence of cerebral palsy in HICs is obviously declining, currently it is estimated to 1.4 per 1000 children, this has been described in many recent studies and without doubt, it is a result of advanced intervention modalities to prevent CP elaborated in developed countries.[52]

Hence, the understanding on CP as unpreventable or untreatable condition is changing progressively as result of advanced knowledge about the disease, elaboration of national registries, many studies on basic science, strengthening in perinatal care, and advancement in early diagnosis and intervention.[52,53]

Actually, studies showed that the developing brain injury occurs mostly in perinatal period (in utero and during the first 28 days of life) with rate estimated to 80% for intrauterine brain damage, 10% at the time of birth (natal period) and the remaining 10% occurs in early childhood (post neonatal acquired CP).[53,54] So the intervention measures to prevent cerebral palsy should focus in perinatal period.

Prematurity

The prematurity is a term refers to neonate born before 37 weeks of gestational age, it is classified according to WHO as extremely premature babies (< 28 weeks of GA), very premature babies (28 weeks - 32 weeks of GA) and moderate to late preterm babies (32 weeks - 37weeks of GA).[48] Premature delivery is the main risk contributor for CP, it presents in around 35% to 45% of children diagnosed with CP[49,52,54] and the risk is multiplying as the weeks of gestation age are decreasing, for instance the prevalence of CP is 70/1000 children born at <33 weeks and it is highest in premature babies of less than 28weeks at the rate of 111.8/1000 live births.[49] For this reason any intervention used to prolong gestation age (GA) or minimising risk of preterm delivery willy dramatically decrease the occurrence of CP.[55]

Fetal growth restriction

Fetal growth restriction refers to a baby born with low weight (small size) compared to the expected birthweight for specific gestational age. Its contribution on the occurrence of cerebral palsy is well remarkable. The prevalence of CP is approximated to 59.2/1000 children born with birth weight of <1500g while it is around 1.33/1000 live births in babies weighing > 2500g at birth.[50] In fact, disorders which cause difficulties in foetal growth, affect also neuronal development which leads to CP.[50] In large epidemiological study done in Australia declared Intrauterine Growth Restriction (IUGR) as potential factor for developing CP and specifically severe cerebral palsy increase proportionally with the gravity of fetal small size compared to its gestational age.[49] Many risk factors to IUGR are known and some of them are preventable, they are related to placenta factors (eg, poor implantation), maternal factors like smoking which is responsible to one third of IUGR, fetal factors and genetic factors.[49,56]

Intrauterine infection and neonatal infection

In many different type of studies, white matter brain lesion also referred to cystic periventricular leukomalacia (PVL) detected by neonatal brain ultrasound, It is described as the potential source for developing cerebral palsy.[57] Some of the causes of white matter brain lesion are maternal infection and neonatal sepsis due to acquired infection or congenital infection (vertical transmission).[49,57] A strong statistical analysis of studies assessing the relationship between the chorioamnionitis and cystic periventricular leukomalacia found that the cystic PVL is strongly associated to chorioamnionitis clinically and histologically.[50,57] Occasionally maternal viral or bacterial infections can be asymptomatic, therefore during child assessment, maternal report of fever and urinary tract infection during pregnancy are significantly related to high risk of having cerebral palsy.[49]

Birth asphyxia

In the beginning birth hypoxia was considered to be the main reason of nearly all cases of cerebral palsy by W.J Little (the man who discovered cerebral palsy in 1840)[53] but recent evidence showed that the birth asphyxia is actually rare cause of cerebral palsy.[54] Currently, the term birth asphyxia is outdated, the updated term is neonatal

encephalopathy which can be caused by acute or chronic hypoxia confirmed by metabolic acidosis measured from the umbilical arterial blood gases, it can also be caused by infection and placental or umbilical vessels thrombosis.[49,54] Different authors demonstrated that approximately 13% of children born at term who suffered with neonatal hypoxic encephalopathy manifest cerebral palsy clinical features in coming months or years.[49]

Congenital malformations

The high frequency of congenital malformation in cerebral palsy patients is remarkable when compared to general population[49] and the chance of acquiring cerebral palsy is increasing exponentially if these malformations are associated with intrauterine growth restriction.[50]

The cerebral malformation like microcephaly and hydrocephaly are the most common congenital disorders associated with CP but non cerebral malformation are also represented such as heart related (12%), kidneys and urinary tract (5.4%) and locomotor system (5.4%).[49,50]

Multiple pregnancy

Multiple pregnancy is correlated with increased probability of developing CP than single pregnancy. It is revealed that among twins, if one developed cerebral palsy, probability of the remaining child to develop the same condition is multiplied by 15.[50,58] A study conducted in Australia in 1980 showed that the occurrence of cerebral palsy in single pregnancy, twins pregnancy and triplets pregnancy is 1.6, 7.3 and 28 per 1000 children respectively.[59] Furthermore, if there is a fetal demise in twin pregnancy, the risk of developing CP in surviving fetus is markedly increased by factor 8, from 12/1000 to 96/1000 live briths.[59] Hence, It is highly recommended to proceed with single embryo in vitro fertilization program.[49]

Maternal chronic conditions

Maternal chronic diseases such as diabetes mellitus type 1 and 2, rheumatoid arthritis, systematic lupus erythematosus, chronic hypertension, hyper or hypothyroidism condition, heart diseases, chronic kidney diseases and etc., are highly linked to offspring cerebral palsy. Many of them are direct causes of chronic inflammation, altered thrombotic state, placenta abnormalities which will lead to preterm delivery, congenital malformation and intrauterine growth restriction.[60] Overall mothers with chronic diseases present a risk of around 30% of having children with cerebral palsy and maternal autoimmune diseases are linked with a particular high probability of getting offspring with CP when other chronic conditions are considered.[60–62]

2.6. Factors influencing outcome of cerebral palsy

It is of paramount importance to assess predictors of outcome in CP, to understand the type and gravity of disease, to help in planning appropriate intervention and make simple the communication between treating personnel and the caretaker of the patient. Unfortunately, it is very challenging to measure the outcome because of the nature of CP condition, Cerebral palsy syndrome is not an acute condition, it is a chronic disease, incurable disease despite any effort to interventions a child with CP will remain with it.[9,63] But there are treatment modalities elaborated to decrease the burden of the disease to patient him/herself and to the family by helping the child to achieve motor function ability at the level of full independency in activities of daily life (ADL) so the capacity to predict the prognosis has a great role in guiding interventions, preventing or reducing the poor outcome (hip dislocations, malnutrition, pain and decrease of community participation,…).[64]

The best outcome parents can expect is the independency in daily activities performance of their children, most of the time this ability is directly related to the ambulation capability.

Orawan K. et al. described the prognostic predictors for ambulation, those factors including the cerebral palsy type, timing of developmental motor milestones, persistency of primitive reflexes and postural reaction, epilepsy and seizure, vision and hearing sensory impairments, intellectual disability, sitting at 2 years of life without support and eating without help all are important factors to predict future walking ability.[65,66]

Sitting without support at 2 years of life

The ability of sitting at the age of 2 years is the main factor for predicting the future independent ambulation among cerebral palsy patients.[65,66] In the meta-analysis published by Keeratisiroj, O et al. They found that children able to sit before the age of 2years are 5-folds predicted to have independent ambulation than children who start sitting after 2 years of age.[65] Sitting is the best early motor skills for predicting walking without support, it is clear that sitting is related to postural control which is the potentiality to keep stability against the ground gravity, this milestone development is the key fundamental in predicting the upright position development and it allows good and safe performance of daily activities.[65–67]

Eating independently

The self-feeding, meaning the ability of using hands with intact oromotor function is the powerful determinant for independent walking in paediatric patients with cerebral palsy.[66] The paediatric patients generally suffer from poor growth due to malnutrition, apart from the low economic status of the families another reason is poor feeding capacity of the patient, hence the ability of self-eating affects significantly the ability of independent walking.[66] The study done on non-ambulatory CP patients by Kulaka et al showed that more than a half of nonambulatory children need an external assistance for feeding.[68]

Type of Cerebral palsy

The category of cerebral palsy, which correlates directly to the brain part affected is strongly linked to the ability of walking without support.[66,69] In fact, spastic quadriplegic (or tetraplegic) type is significant poor prognostic predictor of independent ambulation when compared to other CP types. In one study done by Montgomery (Maryland/USA),

described that walking independently is significantly associated with spastic hemiplegia, walking with assistive devices is linked to spastic diplegia, and the Author concluded that spastic quadriplegic is the poorest prognostic factor for ambulation.[70] In other studies found that ataxic and hypotonic cerebral palsy represent the best prognosis for walking independently than dyskinetic and spastic cerebral palsy patients.[66,71]

Visual impairment

The absence of visual impairment is another significant predictor of future ambulation as the good vision is strongly related to the ability of maintaining balance especially in upright position. In statistical analysis done by Keeratisiroj et al. revealed that paediatric patients with CP wich is not linked with visual disturbance are expected to have unassisted ambulation 2 to 3-folds compared to children with blindeness.[65] Yvonne W. et al conducted a study based on large general population in United State of America and the author highghlited that the lack of visual impairment is directly related to ambualtion without support at the age of 6 years.[71]

Epilepsy and seizures

The epilepsy is a disorder of uncontrolled brain cells activity leading to seizures, when occurred in developing brain leads to abnormal brain development which affect negatively gross motor development.[65] Actually, the absence of seizures in cerebral palsy children is vigorously related to future independent walking. Many studies combined, come up with a conclusion that the chance of future unaided ambulation in cerebral palsy patient is 1 to 2-folds higher than the paediatric patients with cerebral palsy associated with epilepsy.[65,66,71]

Intellectual disability

Cerebral palsy Children with intellectual disability or cognitive impairments are prone to learning disabilities, hence it is difficult to teach them about how to ambulate independently.[65,66] It is also observed that in CP patients with intellectual disability, the motor milestone development is delayed and sensorimotor function is affected negatively.[65] In addition, the absence of intellectual disturbance in children with CP is a strong predictor of ambulating independently, in one meta-analysis revealed that children

without intellectual disability represent a high chance of walking without support better than children with cognition problems by 2-folds.[65,66,69,71]

2.7. Role of orthopaedics in management of cerebral palsy

Normally, the CP is a non-progressive encephalopathy but associated musculoskeletal condition is progressive, changing along the time as the child grows.[18] Therefore, the CP involves in abnormal growth of bones and muscles resulting in different musculoskeletal impairments such as joints contractures and dislocations, bone deformities, persistent pain which leads to difficulties in ambulation and management of CP patients.[18,19]

The management of CP involves multidisciplinary approach, thus the orthopaedic surgery contributes explicitly in treatment of CP patients, the role of orthopaedic surgery is mandatory in increasing or maintain the motor function ability level, improving pain and prevent deformities.[6,18]

2.7.1. Non operative management

The non-operative management of cerebral palsy consists of physical therapy and occupational therapy directed to motor disorders in CP children, it's a long-term process targeting to enhance the best possible quality of life to children and their caretakers.[38,72] Conservative management of CP comprises the following treatment modalities: pharmacological support, nutrition support and physical rehabilitation. The latter is built on neuroplasticity, this is the capacity brain tissues to change in response to internal or external stimuli. This ability of brain cells gives space to acquisition of learning, memorizing, adaptation and compensations changes to affected functions.[38,72–74] The significant modification secondary to intrinsic or extrinsic stimuli occurs in early stage of life, Hence the early diagnosis and intervention is highly recommended and is directly related to better outcome.[74]

The main target for CP management is spasticity, the well-known symptom defined as increased muscle spasm which affecting passive and active movement leading to joints contractures, joints deformities, finally causing non ambulatory state associated with thrombosis risk, pressure sores and infections.[38] Approach to spasticity involves general rehabilitation, sometimes in accordance with pharmacological products. The main

pharmacological agents used in treating spasticity are Baclofen, its mechanism of action is not fully understood[75] yet It acts on spinal cord by inhibiting both monosynaptic and polysynaptic reflexes, can be used as oral medication or continuous intrathecal pump. [38,75] and Diazepam, an anxiolytic benzodiazepine which is approved by FDA for treatment of musculoskeletal spasm in paediatric population above 6months and adults. It acts by binding to GABA a receptor chloride ions channels and reduces neurons excitability.[75] The third known medication used for treating spasticity is Botulinum toxin A which is a neurotoxin made by a clostridium botulinum bacteria, It acts by inhibiting acetylcholine secretion to neuromuscular junction resulting in muscle weakness, reduced spasticity, the botulinum toxin A is also approved by FDA in children aged 2years and adults.[38,72,75,76] Some published papers support the utilization of botulinum toxin drug in treatment of pain post orthopaedic interventions due spastic cerebral palsy.[77,78]

The conservative management of cerebral palsy involves also management of many comorbidities associated with CP, such as intellectual disability, visual impairments, epilepsy and malnutrition. The medical and neurological disorders related to cerebral palsy are influencing directly the outcome of CP thus multidisciplinary approach is mandatory in order to ameliorate the standard of living of the patient.[79] Currently, cerebral palsy is the well-known origin of motor dysfunction but It is considerably linked to other medical and neurological diseases presented predominantly when compared with general population, Surveillance of cerebral palsy in Europe published that around 31% of cerebral palsy patients have intellectual disability, 21% have epilepsy and 11% have severe vision impairment.[80]

2.7.2. Operative Management

Although there are many options of nonoperative management of cerebral palsy conditions, orthopaedic procedures on bony and soft tissues remain irreplaceable.[81] The target of operative care in cerebral palsy patients is to improve function status, prevent pain and further deformities.[18]To plan for better outcome from surgery, there are couple of requirements that should be considered such as experienced paediatric orthopaedic surgeon, good patient selection, and good timing for orthopaedic surgery otherwise the outcome should be worse than previous function status.[18,81–83] The selection of suitable

time for surgery is directed by CNS maturation status, failure of conservative management (i.e oral baclofen, Botulinum Toxin A), ability of ambulation, the progress status of joints contractures and bony deformities development and lack of significant functional improvement in the last six months. Thus the operative management should not be the last option instead must be planned and included in durable management of patients with CP.[18,82,83]

The operative management is related to the degree of functional capability of the patient, most of the time the motor function ability is evaluated by the standard known tool, which is GMFCS. The objectives of orthopaedic surgery for ambulatory population (GMFCS level I-III) are classified in two entities by Sharan, D et al (1) to improve gait quality by correcting biomechanics in order to enhance endurance (walk long distance, running, recreational activity and pain free) and (2) to improve gait appearance by decreasing dependency to walking aids, reducing orthotics usage and correcting feet and knees deformities. For nonambulatory (GMFCS level IV-V) patients, the objective of surgery is to reduce or prevent pain, to make ease performance of daily needs function like dressing, toileting, body hygiene, sitting/lying down and to improve quality of life.[18] The widespread orthopaedic interventions consists of tenotomy and tendon lengthening, soft tissues transfers, selective dorsal rhizotomy and corrective osteotomies of bony deformities.[18,84]

CHAPTER THREE: METHODOLOGY

3.1. Introduction

This chapter describes the methods utilised in this work, it is composed of the following sections: study settings, study design, inclusion and exclusion criteria, methods of data collection, data management and analysis and ethical considerations. The methodology is specific to the objectives of the study.

3.2. Study setting

The research work was carried out in a specialised hospital, Centre de ChirurgieOrthopeediquePediatrique de Rilima(CCO Rilima), this is a health organisation possessed by the catholic church, Kigali Archdiocese in Rwanda. The hospital is located in sector of Rilima, Bugesera district, Eastern Province of Rwanda at 50km from Kigali (Capital city of Rwanda). The hospital covers paediatric patients in particular and recently started to receive adults patients with orthopaedic pathologies from all regions of the country with capacity of 98 beds including private rooms.

3.3. Study design

A retrospective study was caried out on the paediatric patients followed at CCO Rilima for cerebral palsy since January 2016 to June 2020 assessing documented causes or risk factors, predictors of ambulation and mode of treatment given to cerebral palsy patients.

3.4. Inclusion criteria

We selected all patients with cerebral palsy, diagnosis confirmed clinically, the age is ranging between 2 years and 18 years at first day of consultation and patients were given an appointment to be followed at CCO Rilima.

3.5. Exclusion criteria

We excluded all patients consulted once and patients with age not included in this interval of 2 to 18 years.

3.6. Sample size

Sample size determination is the technique to define an appropriate estimated amount of participants people to represent a such population. This is done to prevent too small size to avoid invalid results in population being studied.

In our study we used sample size calculation according to Andrew Fisher' formula. We considered 95% as confidence level, Standard deviation of 0.5 and confidence interval of ± 0.05.

Then we calculated sample size as follows:

Sample size $= \frac{Z^2\ Std\ Dev(1-Std\ Dev)}{d^2}$

Where,

Z: standard normal variation or Z-score which is equal to 1.96 for confidence level of 95%.

Std Dev: standard deviation of 0.5

d: absolute error fixed to 0.05

Sample size = 385 patients

3.7. Data collection Methods

3.7.1. Data collection instruments

A specific designed form sheet was used to extract information from patients file including demographic data. It was designed based on variables specific to the current study's objectives.

3.7.2. Administration of data collection instruments

The data were collected from the patients' file followed for CP at CCO Rilima, the questionnaire was filled by the investigator.

3.8. Data management and Analysis

Collected data was recorded on questionnaire sheets till we reached the estimated sample size number of patients with CP who were followed at CCO Rilima since January 2016 to June 2020. Microsoft Excel 2018 was used for data entry and SPSS 24.0 was used for data analysis. After collection, data were introduced in computerized format, encrypted, and justified for omission and errors.

Afterwards, data were transferred into SPSS version 24 and was again justified for omissions and errors, at this level analysis was done. Univariate, Bivariate and Multivariate analysis were performed. Ambulation was encoded as dichotomous variable (walker and non-walker) and the walker was encoded by 1 while non-walker was encoded by 0. At first round, univariate analysis was performed to determine preventable causes of cerebral palsy and their modes of treatments.

Chi-square test was utilized to establish the relationship between ambulation (dependent variables) and predictors (independent variables). The p-value <0.05 was utilized to confirm significant variables and those confirmed were filtrated and proceeded into multivariate analysis. Logistic regression was carried out to calibrate for possible confounders and decide adjusted odd ratio for variables which were statistically significant at multivariate level. Predictors with a p-value less than 0.05 at the level of multivariate stage was confirmed as ambulation predictors. Frequency and percentage in tables and figures were used to present data.

3.9. Ethical consideration

Data collection started after getting the authorisation from CCO Rilima research and ethical departments. Patients' data was used only for the research purpose. Confidential storage of patients' information was considered, only principal investigator knows which patient is having a certain condition or related complication.

The approval of this study was given by Institutional Review Board (IRB) at the University of Rwanda, College of Medicine and Health Sciences.

CHAPTER FOUR: RESULTS

4.1. Introduction

This chapter details the results of the study using descriptive statistics with figures, tables and inferential statistics on preventable causes and predictors of independent ambulation in cerebral palsy patients.

4.2. Demographic description of study population

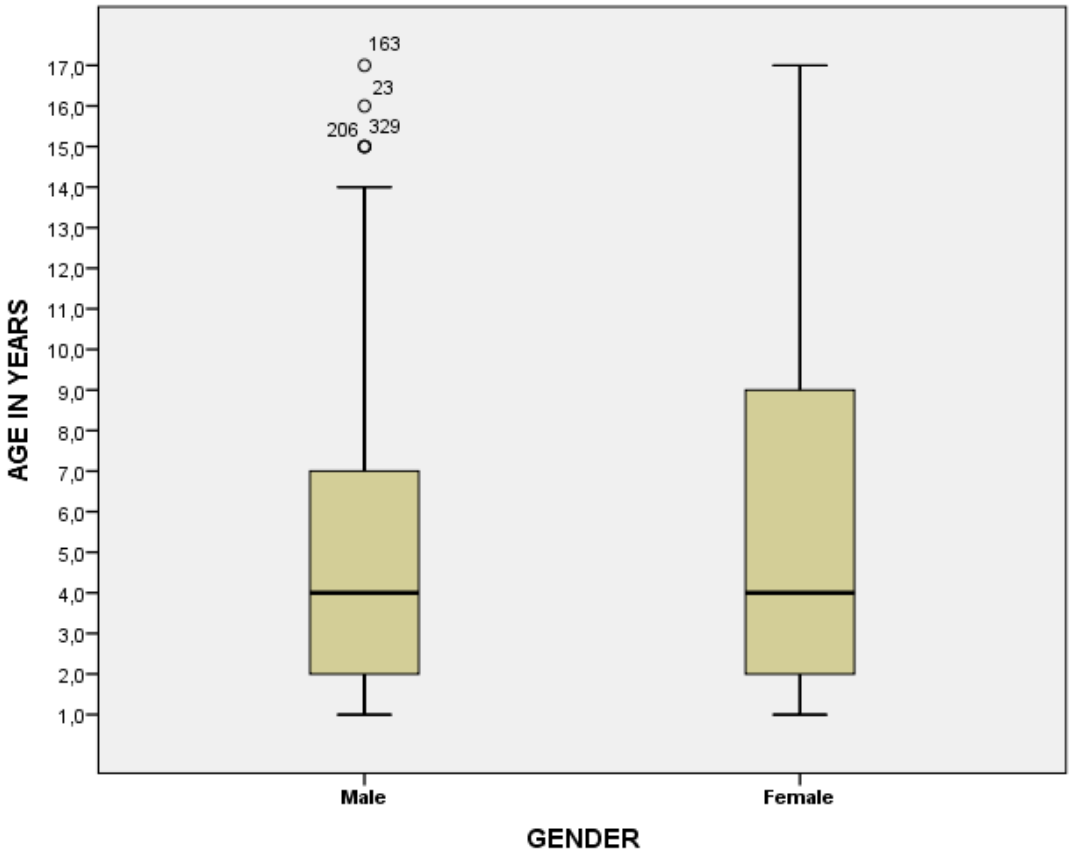


Figure 4. 1.Demographic features of study population

In males, their first quartiles and third quartiles are two (2) and seven (7) years old respectively while for females, first quartiles and third quartiles are two (2) and nine (9) years old. For both males and females, median age is 4 years old. Ages positioned at 23rd (16years old), 163rd (17years old), 206th (15years old) and 329th (15 years old) are outliers of normal male's age distribution.

4.3. Preventable causes and risk factors for CP

Table 4. 1.Presented maternal illness during pregnancy

Variables	Frequency	Percent
None	355	89,9
Oligohydramnios	2	,6
Fever	3	,8
Bleeding	3	,8
Chronic disease	1	,3
Trauma	2	,5
Preeclampsia	3	,8
Diabetes Mellitus	1	,3
Eclampsia	5	1,3
Maternal death	2	,5
Multiple Abortions	1	,3
PPH	1	,3
PROM	3	,8
Uterine rupture	2	,5

Majority of mothers of children with CP did not report any preventable illness during their pregnancy (89.9%).

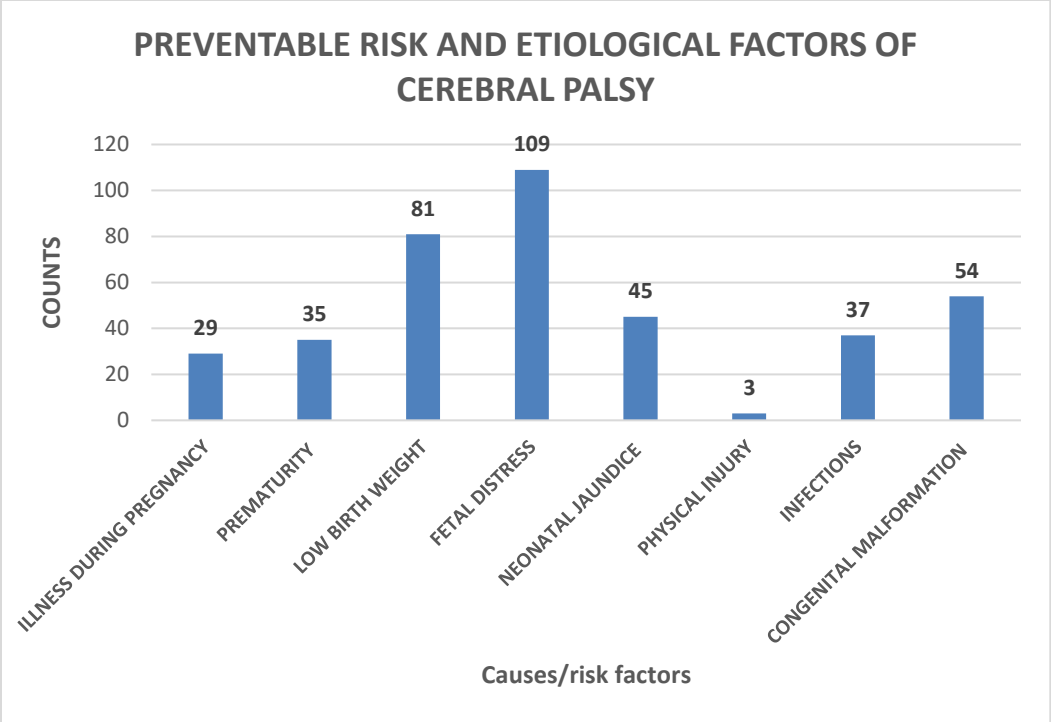


Figure 4. 2.Preventable risk and etiological factors of CP

Figures of 4.2 shows that foetal distress (27.6%), low birth weight (20.5%) and congenital malformations (13.67%) are commonest identified risk and etiological factors of CP among patients who consulted at CCO RILIMA. They make a total of 61.7% combined.

Distribution of congenital malformation among children with cerebral malformation

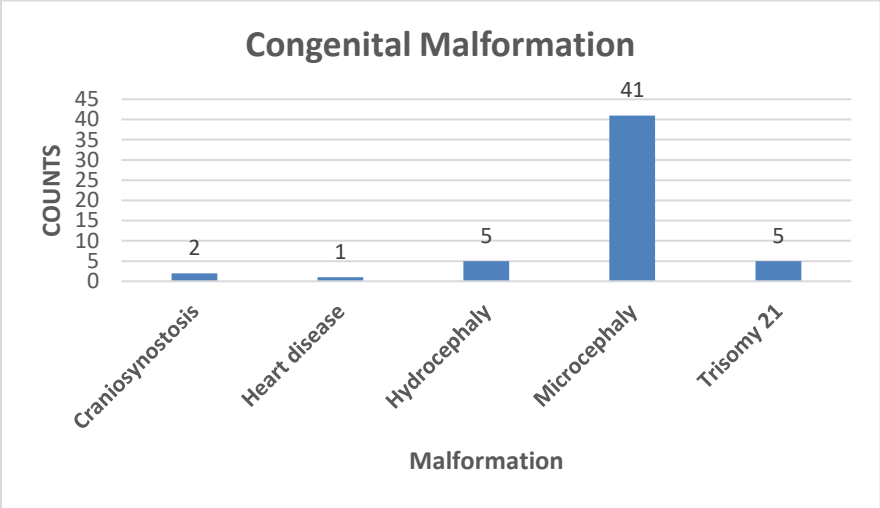


Figure 4. 3.Encountered congenital malformation among children with cerebral palsy

Figure 4.3 reveals that the total number of paediatric patients with cerebral palsy associated with congenital malformation is 54, among of them; microcephaly (75.9%), hydrocephaly (9.2%) and trisomy 21 (9.2%) are most frequent.

4.4. Modes of treatment for cerebral palsy at Centre de ChirurgieOrthopeedique (CCO) RILIMA

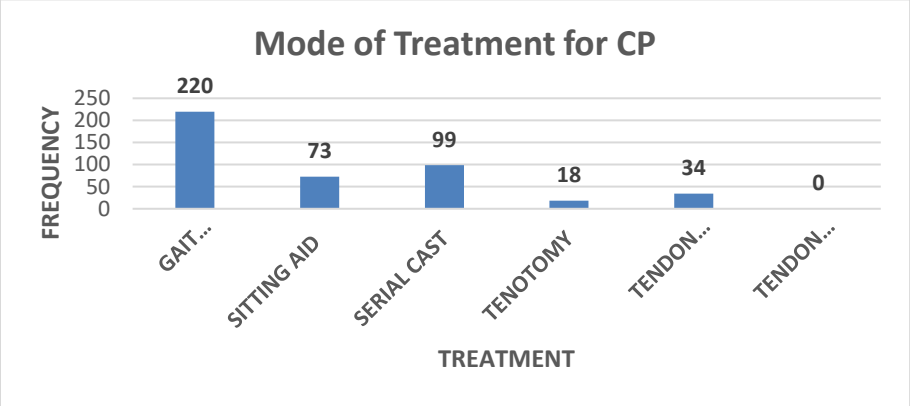


Figure 4. 4. Cerebral palsy treatment mode at CCO RILIMA

Figure 4.4. shows that the commonest cerebral palsy treatment was gait training (55.7%) while tenotomy (4.5%) and tendon lengthening (8.6%) were not frequently used as treatment modes for cerebral palsy at RILIMA.

4.5. Determinants of ambulation among patients with cerebral palsy at CCO RILIMA

Table 4. 2.Ambulation risk factors

Variables	p-value
Age	**0.048**
Gender	0.271
Pregnancy status	0.697
Illness during pregnancy	0.410
Place of birth	0.678
Birth weight	0.307
Gestational age	0.606
Fetal distress	0.294
Neonatal jaundice	0.320
Neonatal admission	**0.026**
Congenital malformation	**0.044**
Physical injury	0.858
Infections	0.634

Table 4.2. shows that determinants for ambulation among children with cerebral palsy are age (early they consult, better is the outcome), neonatal admission (neonates treated for jaundice are associated with good outcome) and congenital malformation (babies born with congenital malformation present poor outcome).

Table 4. 3.Predictors of ambulation in children with CP at CCO RILIMA

Predictor	**p-value**
Ability to sit	**0.004**
Absence of visual dysfunction	**<0.001**
Absence of intelligence disability	**<0.001**
Absence of epilepsy	**<0.001**
Self-feeding	**<0.001**
Head control	**<0.001**
Ability to stand up	**<0.001**
Ability to crawl	**<0.001**
Incomprehensive words	**<0.001**
Comprehensive words	**<0.001**
First sentence	**<0.001**
Motor type	0.043
Topographic distribution	**<0.001**
Motor severity	**<0.001**

Table 4.3. shows that predictors of ambulation among paediatric patients with cerebral palsy are absence of visual dysfunction, epilepsy and intelligence disability. Other predictors are ability to self-eat, control head, sit, stand up, crawl, produce words either comprehensible or incomprehensible and formulate sentence, motor type, topographic distribution and motor severity of cerebral palsy**.**

CHAPTER FIVE: DISCUSSION

The study showed that among three hundred ninety-five (395) patients enrolled, male age distribution is 2years and 7 years for first quartile and third quartile respectively, while for female, first quartile and third quartile are 2 years and 9 years respectively. For both sexes, median age at first consultation is 4 years old. In this study, finding revealed that significant number of children delay to consult for both sexes where a large number (50%) consulted at 4 years of life. Those results are comparable to other studies conducted in LMICs.[85–87] Despite the fact that the diagnosis of cerebral palsy remains clinical (following clinical and neurological signs of the patient)[21,74], in LMICs early diagnosis is still challenge and this affects directly to functional outcome as the early intervention improves neuroplasticity.[74,88] Our findings on the age of first consultation are the same as many other studies conducted in developing countries. For instance, in Bangladesh the diagnosis of cerebral palsy is made at 4 years 1 month, in Indonesia at 6 years 5 months, in Nepal at 4 years 5 months and at 2 years 6 months in Ghana.[86] Differently, in industrialized countries, the diagnosis of cerebral palsy is made at 12 to 24 months and is still considered as late. Interestingly in Australia, 21% of children have diagnosis of CP before 6 months[21] in another study done in Sidney showed that high risk of CP children can have diagnosis at 4.4 months where neuroplasticity is high and the author concluded that clinicians should be confident to make diagnosis of CP at the age below 12 months.[89] The 3 tools with accuracy predictive validity and capable to detect cerebral palsy in 6 months corrected age are elaborated: (1) Neonate neuroimaging MRI (sensitivity 86-89%), (2) General Movement Assessment (GMA) with sensitivity of 98% and (3) Hammersmith Infant Neurological Examination (HINE) with 90% of sensitivity.[21,74,89]

In this study, the majority of mothers around 89.9% did not report any preventable disease during pregnancy, although several studies showed that maternal comorbidities were linked to high risk of CP in offspring with special risk in case of autoimmune condition.[60,61,90,91] Among the reason for this insignificant findings are: (1) the investigator didn't follow the antenatal care (ANC) of mothers, for emphasizing on the full assessment of maternal condition during pregnancy, this is one of the disadvantages

of retrospective study. (2) Some conditions are underreported by health facilities during antenatal care like asymptomatic urinary tract infections (UTI) which can leads to chorioamnionitis and studies reported that UTI presented in first two trimesters of pregnancy can increase the risk of CP at 50% secondary to brain damage by inflammatory cytokines or leading to preterm birth.[91] (3) Patients' files where information was extracted were filled without intention of this study. (4) Possible poor communication between patients and health personnel, where patients are not well explained about their conditions. Ineffective communication between treating doctor and patient occurs frequently and is the leading causes of poor healthcare outcome and lack of patient satisfaction, the main reason identified are time related (doctors' work overload), patient's privacy and unrealistic expectation of the patient.[92,93] The miscommunication between doctor and patient is the source of ignorance about the risk and etiological factors of CP.[94]

In one study conducted in Ghana reported that primary caregivers (parents or family) of cerebral palsy children perceive that CP is a condition caused by witchcraft in 40% of respondents, 12% thought that it is the punishment of God or Gods, 10% believes that are cursed and 54% know nothing about the risk factor of CP.[95]

The risk and etiological factors of CP have been recognised in the following categories: before pregnancy (pre-conceptional maternal health status or living style), perinatal, neonatal and post neonatal periods. Fortunately, many of them are preventable.[38] In this study, fetal distress or birth asphyxia, low birth weight and congenital malformation found to be the commonest causes or risk factors associated with cerebral palsy in patients consulted Centre de Chirurgieorthopedique (CCO) Rilima, both combined represent 61.7%. Other significant risk factors or causes of cerebral palsy in this study are; neonatal jaundice (11.4%), infections (9.4%), prematurity (8.9%) and illness during pregnancy contribute to 7.3%. These finding are very compatible with what other authors described, mainly those carried out in LMICs, as reported by Duke, R et al in study conducted in Nigeria that birth asphyxia found in one third of cerebral palsy children.[47]

Komomo I. et al reported also birth asphyxia as predominant risk factor for cerebral palsy, he described in his study that severe birth asphyxia presented in 55.7%, meningitis 20%, viral encephalitis 12.9% neonatal jaundice 8.6% and 2.9% of paediatric patients with CP were born preterm.[96]

The birth asphyxia significantly found as the main contributor of cerebral palsy in our setting which is similar to other studies from developing countries, is due to lack of appropriate obstetric care at delivery time, home deliveries[96] and poor antenatal care screening as many studies highlight that causal pathway of respiratory failure at the last minute of delivery is complex and it is not caused only by poor intrapartum monitoring instead it is related also to maternal conditions like intrauterine infections, placental abnormalities which clarify that the problem of the neonate is congenital, instead of being acquired at the last minute of delivery.[47,97–99] Prematurity is least represented in our study 8.9% (n=35) which is similar to study conducted in Nigeria[96] (2.9%), Raushan I. et al reported 13.2-24.3% of preterm babies of cerebral palsy in LMIC[100], in Egypt reported 25.8% of preterm infants with CP,[48] this is totally different to what reported in high income countries, for instance in South Korea, prematurity represents 59.51% among children with CP.[100] In general in High Income Countries (HIC), preterm babies account around 40% of cerebral palsy patients.[101] This difference is explained by the lack of equipped neonatal intensive care unit (NICU), lack of enough trained neonatologist that result to early death of many premature babies secondary to neonatal infections, and respiratory problems.

Congenital malformations are strong predictors of cerebral palsy. In this study, congenital anomalies represented 13.67% (n=54) of all children with cerebral palsy followed at CCO Rilima, the most common, are cerebral conditions with microcephaly predominately represented with 75.9% (n=41) and hydrocephaly found in 9% (n=5) of all congenital anomalies associated with cerebral palsy. Non-cerebral congenital anomalies are least found in our study with chromosomal related anomaly 9% (n=5), craniosynostosis found in 3.7% (n=2) and one (1.85%) child born with heart disease of all congenital anomalies found in this study. These finding are consistent with other studies from developing countries as well as from HICs.

In the study conducted in Egypt and Vietnam , the author reported cerebral malformation in 6.5%[48] and birth defect in 14.8%[102] respectively. The similar findings were also reported based on the study carried out in Bangladesh where 11% of congenital anomalies presented 86% were neurological conditions.[103] This study showed 13.67% of congenital malformations, similar with what reported by authors in some high income countries, in Europe, Garne, E. et al reported 11.9% of cerebral and non-cerebral congenital malformations in paediatric patients with cerebral palsy[104], Rankin J. et al conducted a population based study in three European countries and found that 15% of CP patients had congenital malformations.[105] Our findings are low when compared to what found in Canadian Cerebral Palsy Register (CCPR) 23%[106] but are in range of 12-32% reported in a study done by Goldsmith, S. et al.[107]

Cerebral palsy is the well-known origin of motor disability in paediatric population worldwide[65,108] and parents who consult health facility mainly ask if their child will attain the capacity of walking, it is understandable that inability to ambulate for these children will limit their participation in physical activities, recreation and social events which will end up by suffering loneliness.[67,71,108] As independent walking is the main goal for patients and parents, medical knowledge should emphasize on potential determinants of ambulation for cerebral palsy children and any intervention have to be conducted to ameliorate the ability of walking.[67] In this study, we found that early milestones development are the strong predictors of independent ambulation, such as ability to self-eating, head control, crawl, stand up with both present with a p value of <0.001. Ability to sit (p= 0.004) before 2 years old is also found to be significant for predicting independent walking capacity. The other strong predictors of ambulation found in this study are presence of intact intellectual capacity (p<0.001), no epilepsy or seizures (p<0.001) intact vision sensory (p<0.001), Motor severity (p<0.001) which is defined by Gross Motor Function Classification System and topographic distribution (p<0.001) of cerebral palsy. These results are similar with what other authors published.[65–67,71,108] Independent walking in paediatric patients living with this motor disability secondary to brain injury is the cornerstone for improving the individual quality of life. Therefore, all therapeutic decisions and restoration objectives must be planned in considering these prognostic factors of ambulation.[65,69]

The management of cerebral palsy is complex and involves multidisciplinary approach (physical therapist, occupational therapist, orthopaedic surgeons, neurologist,…) usually depending on the affected systems.[109] The main goals of CP management should be focused on: (i) improving capacity of interacting with friends, (ii) ability to perform daily activities and needs, (iii) achieving certain degree of ambulation, (iv) improve joints mobility in order to decrease pain and preserve optimal function.[110–112] Worldwide, numerous therapeutic intervention are available using different techniques including traditional physiotherapy, occupational therapy, neurodevelopment treatment, speech/language therapy, recently developed also electrical stimulation technique[113–115] but studies showed that physiotherapy and occupational therapy remain the cornerstone in rehabilitation of CP children associated with good outcome.[114]

In our study, we found that a significant number of patients assigned to gait training 55.7% (n=220), around 25% (n=99) has received serial casting and sitting training has offered to 18.5% (n=73) as conservative management, this combine physiotherapy and occupational therapy.

These results are compatible with what published by Faraz, S. et al[116]. Additionally, surgical management is not frequently done at CCO Rilima. For instance, tenotomy or tendon release was done in 4.5% (n=18) of children with CP and tendon lengthening in 8.6% (n=34). In this study we found limited number of surgical procedures performed in our setting when compared to other studies, like one study conducted in Lahore, Pakistan the author reported that surgical interventions done were tendon transfer, tendon release, tendon and muscle lengthening, neurectomy, capsulotomies, osteotomies and arthrodesis.[116] Some major surgical procedures such as spine deformities (scoliosis and kyphosis) correction, proximal femur and pelvic osteotomies were described and performed in some settings.[117,118] The disparities revealed by our study can be explained by lack of proper equipment, patients' ability to pay and limited number of trained paediatric orthopedic surgeons.

CHAPTER SIX: CONCLUSION AND RECOMMENDATION

6.1. Conclusion

Cerebral palsy is generally known source of long-lasting motor disabilities in paediatric population globally, leading to limited participation in daily activities, it is associated with different disabling comorbidities such as impaired cognition, hearing and visual problems, epilepsy which interfere with management and good outcome.

The results of our study revealed that risk and etiological factors of CP are complex, such as birth asphyxia, intrauterine growth restriction, congenital malformation, infections, neonatal jaundice, prematurity, …and they are very remarkable in term babies more than preterm (8.9%) which is the same finding as reported in the other many studies conducted in developing countries, these results reflect that preventive measures are feasible and should be focused on infants born at term. Advanced knowledge in aetiology and pathophysiology of cerebral palsy is keystone for researchers in elaborating prevention and treatment guidelines for cerebral palsy patients. Different preventive strategies are described include improved perinatal care, measures to prolong pregnancies like use of magnesium sulphate, antenatal steroids for mothers at high chance of having premature delivery and induced hypothermia to neonates confirmed to have hypoxic ischemic encephalopathy.

Early diagnosis and intervention are mandatory for optimizing the neuroplasticity for expecting to have acceptable outcome and minimise further complication. Currently there is no effective treatment method to cure CP. Conservative and surgical management for CP have good impact on muscle power and improve activities of daily living (ADL) but no change has been shown to motor type, topographic distribution and motor severity of cerebral palsy.

6.2. Recommendations

6.2.1. To different hospitals in Rwanda

- To all primary care providers include general practitioner, paediatrician, gynaecologist to focus in assessment and treatment of maternal non communicable disease (NCDs) as they contribute significantly in cerebral palsy risk factors.
- To address the preventable causes of cerebral palsy in order to reduce its burden to family and to the country in general.
- To adopt international guideline tool for making early appropriate diagnosis of CP in endangered neonates and infants published in 2017 which are General Movement Assessment (GMA), Neonate MRI and Hammersmith Infant Neurological examination (HINE).

6.2.2. To the Ministry of Health

- To underline the burden of cerebral palsy in Rwandan society and plan how to facilitate access to medical care by building enough specialised centres and training of staff.
- To make advocacy in international organization for support of cerebral palsy children's management, education and social life.
- To initialise the national cerebral palsy register for facilitating to understand trends in cerebral palsy disease with related risk factors and ease availability of data for future research.

6.2.3. To future researchers

- To conduct a nationwide study based on large general population to record the prevalence of cerebral palsy in Rwanda and its related risk factors.

REFERENCES

1. Almasri, N. A. & Palisano, R. J. **Predictors of needs for families of children with cerebral palsy.***Disabil. Rehabil.***36**, 210–219 (2014).
2. Al-mayahi, A. A. & Al-mayahi, A. A. **Early Markers for Cerebral Palsy**. *Intechopen* 3–18 (2018) doi:10.5772/intechopen.79466.
3. Patel, D. R., Neelakantan, M., Pandher, K. & Merrick, J. **Cerebral palsy in children: A clinical overview**. *Transl. Pediatr.***9**, S125–S135 (2020).
4. Korzeniewski, S. J., Slaughter, J., Lenski, M. & Haak, P. **The complex aetiology of cerebral palsy**. *Nat. Rev. Neurol.***14**, (2018).
5. Belonwu R O, Gwarzo G D, A. S. I. **Cerebral Palsy in Kano , Nigeria - A Review**. *Niger. J. Med.***18**, 186–189 (2009).
6. Agency for Clinical Innovation. **Management Of Cerebral Palsy In Children : A Guide For Allied Health Professionals**. (NSW MINISTRY OF HEALTH, 2018).
7. Arnaud, C., Hollung, S. J. & Himmelmann, K. S**urveillance of Cerebral Palsy in Europe (SCPE) Scientific report 1998 - 2018**. *https://eu-rd-platform.jrc.ec.europa.eu/sites/default/files/SCPE%20Scientific%20report%201998-2018.pdf*.
8. Annette Majnemer, B. M. **New Directions in the Outcome Evaluation of Children With Cerebral Palsy**. *Semin. Pediatr. Neurol.***11**, 11–17 (2004).
9. Jilda Vargus Adams, M. Ms. **Understanding function and other outcomes in cerebral palsy**. *Phys Med Rehabil Clin N Am***20**, 567–575 (2010).
10. Liu, H. *et al.***Treatment response prediction of rehabilitation program in children with cerebral palsy using radiomics strategy : protocol for a multicenter prospective cohort study in west China**. *Quant Imaging Med surg***9**, 1402–1412 (2019).
11. Jan, M. M. S. **Cerebral Palsy: Comprehensive Review and Update**. *Ann Saudi Med***26**, 123–132 (2006).
12. Reddihough, D. S. & Collins, K. J. **The epidemiology and causes of cerebral palsy**.

*Aust. J. Physiother.***49**, 7–12 (2003).

13. Gincota Bufteac, E., Andersen, G. L., Torstein, V. & Jahnsen, R. C**erebral palsy in Moldova: subtypes, severity and associated impairments**. *BMC Pediatr.***18**, 1–9 (2018).

14. World Health Organization. **Summary World Report On Disability**. *World Health* 1–24 (2011).

15. Kakooza-mwesige, A., Forssberg, H., Eliasson, A. & Tumwine, J. K. **Cerebral palsy in children in Kampala , Uganda : clinical subtypes , motor function and co-morbidities**. *BMC Res. Notes* 1–10 (2015) doi:10.1186/s13104-015-1125-9.

16. Kakooza-mwesige, A. *et al.***Articles Prevalence of cerebral palsy in Uganda : a population-based study**. *Lancet* 1–8 (2017) doi:10.1016/S2214-109X(17)30374-1.

17. Mlinda, S. J. **The effect of a practical nutrition education programme on feeding skills of caregivers of children with cerebral palsy at Muhimbili National Hospital , in Tanzania**. 1–10 (2018) doi:10.1111/cch.12553.

18. Sharan, D. **Orthopedic surgery in cerebral palsy: Instructional course lecture**. *Indian J. orthpedics***51(3)**, 240–255 (2017).

19. Rehbein, I. *et al.***Analysis of orthopedic surgical procedures in children with cerebral palsy**. *World J Orthop 2020 April 18; 11(4) 222-231***11**, 222–231 (2020).

20. Kurt, E. E. **Definition , Epidemiology , and Etiological Factors of Cerebral Palsy**. *IntechOpen* 3–20 (2016) doi:http://dx.doi.org/10.5772/64768 5.

21. Velde, A., Morgan, C., Novak, I., Tantsis, E. & Badawi, N. E**arly Diagnosis and Classification of Cerebral Palsy : An Historical Perspective and Barriers to an Early Diagnosis.***Clin. Med. (Northfield. Il).* 1–13 (2019).

22. Donald, K. A. *et al.***Pediatric Cerebral Palsy in Africa : A Systematic Review**. *Semin. Pediatr. Neurol.***21**, 30–35 (2014).

23. Sankar, C. & Mundkur, N. **Cerebral palsy-definition, classification, etiology and early diagnosis.***Indian J. Pediatr.***72**, 865–868 (2005).

24. Donald, K. A. *et al.***Pediatric Cerebral Palsy in Africa : Where Are We ?** (2015) doi:10.1177/0883073814549245.

25. Khandaker, G. *et al.***Protocol for hospital based-surveillance of cerebral palsy (CP) in Hanoi using the Paediatric Active Enhanced Disease Surveillance mechanism (PAEDS- Vietnam): a study towards developing hospital-based disease surveillance in Vietnam**. *BMJ Open***912**, 1–5 (2017).

26. Shevell, M. & Dagenais, L. **The Epidemiology of Cerebral Palsy : New Perspectives From a Canadian Registry**. *Semin. Pediatr. Neurol.***20**, 60–64 (2013).

27. Jahan, I. *et al.***Epidemiology of cerebral palsy in Sumba Island, Indonesia.***Dev. Med. Child Neurol.***62**, 1414–1422 (2020).

28. Khandaker, G. & Smithers-sheedy, H. **Epidemiology of cerebral palsy in Bangladesh : a population-based surveillance study**. *Dev. Med. Child Neurol.* 1–9 (2018) doi:10.1111/dmcn.14013.

29. El-tallawy, H. N. *et al.***Epidemiology of cerebral palsy in El-Kharga District-New**. *Brain Dev.***33**, 406–411 (2011).

30. Namaganda, L. H. *et al.***Excessive premature mortality among children with cerebral palsy in rural Uganda: A longitudinal, population-based study**. *PLoS One***15**, 1–14 (2020).

31. Patel P, Baier J, Baranov E, Khurana E, Gambrah-Sampaney C, Johnson A, et al. **Health beliefs regarding pediatric cerebral palsy among caregivers in Botswana : A qualitative study**. *Child Care Heal. Dev.* 1–8 (2017) doi:https://doi.org/10.1111/cch.12490.

32. Gladstone, M. **A review of the incidence and prevalence , types and aetiology of childhood cerebral palsy in resource-poor settings**. 181–196 (2010) doi:10.1179/146532810X12786388978481.

33. National Council of Persons with Disabilities (NCPD), N. C. for C. (NCC). **Report on National Assessment of Centres caring for Children with Disabilities in Rwanda**. (2016).

34. Thomas, P. & Officer, D. P. **Rwanda Country Report Rwandan National Association of the Deaf Rwandan Union of the Blind**. (2005).

35. Chukwukere, C. **Clinical Classification of of Cerebral Palsy**. *Intechopen* (2018) doi:10.5772/intechopen.79246.

36. Bax, M. *et al.***Review Proposed definition and classification of cerebral palsy**. *Exec. Comm. Defin. Cereb. Palsy* 571–576 (2005).

37. Agarwal, A. & Verma, I. **Review article Cerebral palsy in children : An overview**. *J. Clin. Orthop. Trauma***3**, 77–81 (2012).

38. Sadowska1, M., 2, B. S.-H. & 3, I. K. **Cerebral Palsy : Current Opinions on Definition , Epidemiology , Risk Factors , Classification and Treatment Options**. *Neuropsychiatr. Dis. Treat.***16**, 1505–1518 (2020).

39. Badawi, N. & AM, N. B. **Australian Cerebral Palsy Register Report. (2018)**. (2019).

40. Pfeifer, L. I., Silva, D. B. R., Funayama, C. A. R. & Santos, J. L. **Classification of cerebral palsy: Association between gender, age, motor type, topography and gross motor function**. *Arq. Neuropsiquiatr.***67**, 1057–1061 (2009).

41. Paulson, A. & Vargus-Adams, J. **Overview of four functional classification systems commonly used in cerebral palsy**. *Children***4**, (2017).

42. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, G. B. **Development and function in children to classiffy gross motor reliability of a system, with cerebral palsy**. *Dev. Med. Child Neurol.* 39:214-223. (1997).

43. Palisano, R. **Gross Motor Function Classification System for Cerebral Palsy**. *Dev. Med. Child Neurol.* (2008) doi:10.1111/j.1469-8749.1997.tb07414.x.

44. Tieman, B. L. *et al.***Changes in Mobility of Children with Cerebral Palsy Over Time and Across Environmental Settings**. *Phys. Occup. Ther. Pediatr.* (2004) doi:10.1300/J006v24n01.

45. Wood, E.; Rosenbaum, P. **The Gross Motor Function Classification System for Cerebral Palsy : a study of reliability and stability over time**. *Dev. Med. Child. Neurol.* 42:292-296 (2000).

46. Morris, C., Orth, S. R. & Perinatal, N. **Reliability of family report for the Gross Motor Function Classification System**. *Dev. Med. Child. Neurol.* 46:455-460 (2004).

47. Duke, R. *et al.***Clinical features and aetiology of cerebral palsy in children from Cross River State , Nigeria**. *Arch Dis Child* 1–6 (2020) doi:10.1136/archdischild-2019-317932.

48. Salama, D., Elmagid, A. & Magdy, H. **Evaluation of risk factors for cerebral palsy**. *Egypt. J. Neurol. Psychiatry Neurosurg.* 1–9 (2021).

49. Alastair H. MacLennan, MD, FRANZCOG, Suzanna C. Thompson, MB.BS, FRACP, Jozef Gecz, P. & PII: **Cerebral Palsy – Causes, pathways, and the role of genetic variants Alastair**. *Am. J. Obstet. Gynecol.* 1–21 of 67 (2015) doi:10.1016/j.ajog.2015.05.034.

50. Moshe Stavsky1, Omer Mor1, Salvatore Andrea Mastrolia2, S. G. & Nandor Gabor Than4, 5, 6 and Offer Erez7*. **Cerebral Palsy — Trends in epidemiology and Recent Development in Prenatal Mechanisms of Disease , Treatment , and Prevention**. *Front. Pediatr.***5**, 1–10 (2017).

51. christine cans Javier de-la-cruz marie-ange merme. **Epidemiology of cerebral palsy. *Paediatr***. *Child Health (Oxford).* 1–6 (2008).

52. Badawi, N., Mcintyre, S. & Hunt, R. O. D. W. **Perinatal care with a view to preventing cerebral palsy**. *Dev. Med. Child Neurol.* (2020) doi:10.1111/dmcn.14754.

53. Gowda, V. K. **Recent advances in cerebral palsy**. *Karnataka Pediatr. J.***35**, 4–18 (2020).

54. Shepherd, E. *et al.***Neonatal interventions for preventing cerebral palsy: An overview of Cochrane Systematic Reviews**. *Cochrane Database Syst. Rev.***2018**, (2018).

55. T. Michael O'Shea, MD, M. D**iagnosis, Treatment, and Prevention of Cerebral Palsy in Near-Term/Term Infants**. *Clin Obs. Gynecol.***51**, 816–828 (2011).

56. Sharma, D., Shastri, S. & Sharma, P. I**ntrauterine Growth Restriction : Antenatal and Postnatal Aspects**. *Clin. Med. insights Pediatr.* 67–83 (2016) doi:10.4137/CMPed.S40070.TYPE.

57. Yoon, B. H., Park, C. W. & Chaiworapongsa, T. **Intrauterine infection and the development of cerebral palsy**. *BJOG An Int. J. Obstet. Gynaecol.***110**, 124–127 (2003).

58. Nelson, K. B., Blair, E. & Ph, D. **Prenatal Factors in Singletons with Cerebral Palsy Born at or near Term**. *N Engl J Med* 373:946–53 (2015) doi:10.1056/NEJMra1505261.

59. Petterson, B., Nelson, K. B., Watson, L. & Stanley, F. **Twins , triplets , and cerebral palsy in births in Western Australia in the 1980s**. *bmj***307**, 1239–43 (1993).

60. Strøm, M. S., Tollånes, M. C., Wilcox, A. J., Lie, T. & Forthun, I. **Maternal Chronic Conditions and Risk of Cerebral Palsy in Offspring : A National Cohort Study**. *Pediatrics***147**, (2021).

61. Petersen, T. G. *et al.***Maternal thyroid disorder in pregnancy and risk of cerebral palsy in the child : a population-based cohort study**. *BMC Pediatr.* 1–11 (2018).

62. Forthun, I., Econ, M., Wilcox, A. J., Strandberg-larsen, K. & Moster, D. **Maternal Prepregnancy BMI and Risk of Cerebral Palsy in Offspring**. *Pediatrics***138**, (2016).

63. Vargus-Adams, J. N. **Outcome Assessment and Function in Cerebral Palsy**. *Phys. Med. Rehabil. Clin. N. Am.***31**, 131–141 (2020).

64. Boyd, R. N. *et al.***PREDICT-CP: Study protocol of implementation of comprehensive surveillance to predict outcomes for school-aged children with cerebral palsy**. *BMJ Open***7**, 1–20 (2017).

65. Keeratisiroj, O., Thawinchai, N., Siritaratiwat, W. & Pratoomsoot, C. **Prognostic predictors for ambulation in children with cerebral palsy : a systematic review and meta- analysis of observational studies**. *Disabil. Rehabil.***0**, 000 (2016).

66. Keeratisiroj, O. & Thawinchai, N. P**rognostic Predictors for Ambulation in Thai Children With Cerebral Palsy Aged 2 to 18 Years**. *J. Child Neurol.* (2015) doi:10.1177/0883073815582267.

67. Denise M. Begnoche, Lisa A. Chiarello, Robert J. Palisano, Edward J. Gracely, Sarah Westcott McCoy, M. N. O. **Predictors of Independent Walking in Young Children With Cerebral Palsy**. *Am. Phys. Ther. Assoc.***96**, (2015).

68. Wojciech Kułaka,∗, Bo˙zena Okurowska-Zawadaa, Dorota Sienkiewicza, G. P.-P. and E.

G. **The clinical signs and risk factors of non-ambulatory children with cerebral palsy**. *J. Pediatr. Neurol.***9**, 447–454 (2012).

69. Kułak, W., Sendrowski, K., Okurowska-zawada, B. & Sienkiewicz, D. **Prognostic factors of the independent walking in children with cerebral palsy**. *J Pediatr Neurol***20**, 29–34 (2011).

70. Montgomery, P. C. **Predicting potential for ambulation in children with cerebral palsy**. *Pediatric Physical Therapy* vol. 10 148–155 (1998).

71. Wu, Y. W., Day, S. M., Strauss, D. J. & Shavelle, R. M. **Prognosis for Ambulation in Cerebral Palsy : A Population-Based Study**. *Pediatrics***114**, (2004).

72. Peck, J. *et al.***Interventional Approaches to Pain and Spasticity Related to Cerebral Palsy**. *Psychopharmacol. Bull.***50**, 108–120 (2020).

73. Shaffer, J. **Neuroplasticity and Clinical Practice : Building Brain Power for Health**. *Front. Psychol.***7**, 1–12 (2016).

74. Novak I, Morgan C, A. L. **Early, Accurate Diagnosis and Early Intervention in Cerebral Palsy Advances in Diagnosis and Treatment**. *JAMA Pediatr***2086**, 1–11 (2017).

75. Reilly, M., Liuzzo, K. & Blackmer, A. B. **Pharmacological Management of Spasticity in Children With Cerebral Palsy**. *J. Pediatr. Heal. Care***34**, 495–509 (2021).

76. Blumetti, F. C., Belloti, J. C., Tamaoki, M. J. S. & Pinto, J. A. **Botulinum toxin type A in the treatment of lower limb spasticity in children with cerebral palsy**. *Cochrane Database Syst. Rev.***2019**, (2019).

77. Löwing, K., Thews, K., Haglund-Åkerlind, Y. & Gutierrez-Farewik, E. M. **Effects of Botulinum Toxin-A and Goal-Directed Physiotherapy in Children with Cerebral Palsy GMFCS Levels I & II**. *Phys. Occup. Ther. Pediatr.***37**, 268–282 (2017).

78. Balaban, B., Tok, F., Tan, A. K. & Matthews, D. J. **Botulinum toxin a treatment in children with cerebral palsy its effects on walking and energy expenditure**. *Am. J. Phys. Med. Rehabil.***91**, 53–64 (2012).

79. Hollung, S. J. *et al.***Comorbidities in cerebral palsy: a patient registry study**. *Dev.*

*Med. Child Neurol.***62**, 97–103 (2020).

80. Pruitt, D. W. & Tsai, T. **Common Medical Comorbidities Associated with Cerebral Palsy**. *Phys. Med. Rehabil. Clin. N. Am.***20**, 453–467 (2009).

81. Karol, L. A. **Surgical management of the lower extremity in ambulatory children with cerebral palsy**. *J. Am. Acad. Orthop. Surg.***12**, 196–203 (2004).

82. Švehlík, M. *et al.***The influence of age at single-event multilevel surgery on outcome in children with cerebral palsy who walk with flexed knee gait.***Dev. Med. Child Neurol.***53**, 730–735 (2011).

83. Skoutelis, V. C., Kanellopoulos, A. D., Kontogeorgakos, V. A., Dinopoulos, A. & Papagelopoulos, P. J. **The orthopaedic aspect of spastic cerebral palsy**. *J. Orthop.***22**, 553–558 (2020).

84. Sung, K. H. *et al.***Factors influencing outcomes after medial hamstring lengthening with semitendinosus transfer in patients with cerebral palsy**. *J. Neuroeng. Rehabil.***14**, 1–13 (2017).

85. Mahlaba, N., Nakwa, F. L. & Rodda, J. R. **A descriptive study of children with cerebral palsy at chris hani baragwanath academic hospital**. *SAJCH South African J. Child Heal.***14**, 4–9 (2020).

86. Jahan, I. *et al.***Epidemiology of cerebral palsy in low- and middle-income countries: preliminary findings from an international multi-centre cerebral palsy register**. *Dev. Med. Child Neurol.***63**, 1327–1336 (2021).

87. Kakooza-mwesige, A. *et al.***Articles Prevalence of cerebral palsy in Uganda : a population-based study**. *Lancet Glob. Heal.***5**, e1275–e1282 (2015).

88. Hadders-algra, M. **Early diagnosis and early intervention in cerebral palsy**. *Front. Neurol.***5**, 1–14 (2014).

89. Velde, A. *et al.***Age of Diagnosis , Fidelity and Acceptability of an Early Diagnosis Clinic for Cerebral Palsy : A Single Site Implementation Study.***Brain Sci.* 1–14 (2021).

90. Strøm, M., Tollånes, M., Lie, R. T., Forthun, I. & Moster, D. **Risk of cerebral palsy in**

relation to parental chronic diseases : Mother or father , does it.*Rev. d'Epid?®miologie Sant?® Publique***66**, S321 (2018).

91. Nelson, K. B. **Infection in pregnancy and cerebral palsy**. *J Am Med Womens Assoc* 2008–2009 (2009).

92. Albahri, A. H., Abushibs, A. S. & Abushibs, N. S. **Barriers to effective communication between family physicians and patients in walk-in centre setting in Dubai : a cross-sectional survey**. *BMC Health Serv. Res.* 1–13 (2018).

93. Sabherwal, N., Mittal, A., Pandey, N., Kaushal, G. & Kaustav, P. **A Study of Patient-Physician Communication and Barriers in Communication**. *Int. J. Res. Found. Hosp. Healthc. Adm.***3**, 71–78 (2015).

94. Alruwaished, A. *et al.***Knowledge and attitude of caregivers of cerebral palsy children in Riyadh city**. *Int. J. Med. Dev. Ctries.***4**, 12–17 (2020).

95. Kyei, E. A. & Dogbe, J. **Perceptions of Primary Caregivers about Causes and Risk Factors of Cerebral Palsy in Ashanti Region , Ghana**. *Disabil. CBR Incl. Dev.* (2019) doi:10.5463/DCID.v30i2.840.

96. Eyong, K. I., Asindi, A. A. & Torty, C. **Aetiology and comorbidities of cerebral palsy in a developing country**. *Int. J. Res. Med. Sci.***6**, 3246–3250 (2018).

97. Lawson, R. D. & Badawi, **N. Etiology of cerebral palsy**. *hand Clin.***19**, 547–556 (2003).

98. Badawi, N. & Keogh, J. M. **Causal pathways in cerebral palsy**. *J. Pediatr. child Heal.***49**, 5–8 (2013).

99. Nelson, K. B. **Causative factors in cerebral palsy**. *Clin. Obstet. Gynecol.***51**, 749–762 (2008).

100. Issayeva, R., Aliakparova, A., Abzaliyeva, S. & Kassenova, G. **Cerebral palsy experience risk factors : international**. *web Conf.***08006**, 159 (2020).

101. Sogbossi, E. S., Houekpetodji, D., Kpadonou, T. G. & Bleyenheuft, Y. **A Cross-sectional Study of the Clinical Profile of Children With Cerebral Palsy in Benin , a West African Low-Income Country.***J. Child Neurol.* (2019) doi:10.1177/0883073819864516.

102. Karim, T. *et al.* D**ata on cerebral palsy in Vietnam will inform clinical practice and policy in low and middle- income countries**. *Disabil. Rehabil.***0**, 1–8 (2021).

103. Manlongat, E. **Congenital anomalies in children with cerebral palsy in rural Bangladesh**. *Dev. Med. Child Neurol.* 1–7 (2019) doi:10.1111/dmcn.14456.

104. Garne, E., Dolk, H., Kra, I., Holst, S. & Cans, C. **Review article Cerebral palsy and congenital malformations**. *Eur. J. Paediatr. Neurol.***12**, 82–88 (2008).

105. Rankin, J. *et al.* C**ongenital anomalies in children with cerebral palsy : a population-based record linkage study**. *Dev. Med. Child Neurol.* (2009) doi:10.1111/j.1469-8749.2009.03415.x.

106. Buckley, D., Fehlings, D., Kirton, A. & Koclas, L. **Congenital Malformations in Children with Cerebral Palsy: Is Prematurity Protective?***Pediatr. Neurol.* (2020) doi:10.1016/j.pediatrneurol.2020.02.002.

107. Goldsmith, S., Hons, B., Mcintyre, S., Hansen, M. & Badawi, N. **Congenital Anomalies in Children With Cerebral Palsy : A Systematic Review**. *J. Child Neurol.* 1–8 (2019) doi:10.1177/0883073819854595.

108. Simard-tremblay, E. & Shevell, M. **Determinants of Ambulation in Children With Spastic Quadriplegic Cerebral Palsy : A Population-Based Study**. *J. bone Jt. Surg.***25**, 669–673 (2010).

109. Shea, T. M. O. **Diagnosis , Treatment , and Prevention of Cerebral Palsy**. *Clin. Obstet. Gynecol.***51**, 816–828 (2008).

110. Bhatia, M. & Joseph, B. **Rehabilitation of cerebral palsy in a developing country : the need for comprehensive assessment**. *Pediatr. Rehabil.***4**, 0–3 (2001).

111. Anaby, D. *et al.***Current Rehabilitation Practices for Children with Cerebral Palsy: Focus and Gaps**. *Phys. Occup. Ther. Pediatr.***2638**, (2016).

112. Chin, E. M., Gwynn, H. E., Robinson, S. & Jr, A. H. H. **Principles of Medical and Surgical Treatment of Cerebral Palsy**. *Neurol. Clin. NA***38**, 397–416 (2020).

113. Balcı, N. Ç. **Current Rehabilitation Methods for Cerebral Palsy**. *Intechopen* (2016).

114. Upadhyay, J., Tiwari, N. & Ansari, M. N. **Cerebral Palsy: Etiology, Pathophysiology and Therapeutic Interventions**. *Clin. Expermental Pharmacol.* 1891–1901 (2020) doi:10.1111/1440-1681.13379.

115. Meehan, E. *et al.***Therapy service use in children and adolescents with cerebral palsy : An Australian perspective**. *J. Pediatr. child Heal.***52**, 308–314 (2016).

116. Faraz, S. *et al.***Effectiveness of Treatment in Children With Cerebral Palsy**. *cureus***13**, (2021).

117. Theroux, M. C. **Major Surgical Procedures in Children with Cerebral Palsy**. *Anesthesiol. Clin.***32**, 63–81 (2014).

118. Urileanu, A. L. I. N. H. O. B., Allatah, S. A. F. & Hiuţu, L. U. C. R. C. **Cerebral Palsy . Considerations Upon 249 Consecutive Patients and Review of Literature**. *Curr. Heal. Sci. J.*45, 405–411 (2019).

APPENDICES

APPENDIX I: DATA COLLECTION TOOL

PATIENT DEMOGRAPHY

1. Date of initial visit [……/…. /……..] Date of Discharge […../……./…….]

   [DD/MM/YYYY] [DD/MM/YYYY]

2. Patient ID number……

3. Gender: Male □ Female □

4. Date of Birth [……/…. /……..]

   [DD/MM/YYYY]

DURING PRREGNANCY

1. Pregnancy Single □ Multiple □ Specify

2. Fever □

3. Bleeding □

4. Chronic disease:…

5. Other:….

DURING DELIVERY

1. Mode of delivery: Spontaneous vaginal delivery □ Induced labor □ Cesarean □

2. Place of birth: Health center□ District hospital □ Referral hospital □ Home □ Other□

3. Gestational Age: Term (>37wks) □ Moderate Preterm (32-37wks) □ Very preterm (28-32wks) □ Extremely Preterm (<28wks) □

4. Birth weight : Normal birth weight (2500-4000g) □ Low birth weight (<2500g) □ very low birth weight (<1500g) □ Extremely low birth weight (<1000g) □

5. Fetal distress: No □ Yes □

NEONATAL CONDITIONS

1. Neonatal Jaundice No □ Yes □
2. Neonatal admission No □ NICU □
3. Congenital malformation No □ Yes □ specify…..

POST NEONATAL CONDITIONS

1. Physical injuries No □ Yes □
2. Infection No □ Yes □ Specify……
3. Brain imaging No □ Yes □ CT scan □ MRI □ Finding:…..

ASSOCIATED CONDITIONS

1. Visual impairments No □ Yes □
2. Epilepsy No □ Yes □
3. Intelligence: Normal □ Discreet □ Mediocre □

PYSCHOMOTOR DEVELOPMENT

1. Eating Self □ with support □ Starting Age:
2. Head control No □ Yes □ Starting Age
3. Sitting No □ Yes □ Starting Age:
4. Stand up No □ Yes □ Starting Age:
5. Crawling No □ Yes □ Starting Age:
6. Independent walking No □ Yes □ Starting Age:
7. Incomprehensible words No □ Yes □ Starting Age
8. Comprehensible words No □ Yes □ Starting Age:
9. First sentences No □ Yes □ Starting Age:

CEREBRAL PALSY CLASSIFICATION

A. MOTOR TYPE (Physiological Classification)

1. Spastic □
2. Athetoid □
3. Hypotonic □
4. Ataxic □
5. Mixed □

B. TOPOGRAPHIC DISTRIBUTION (Geographic Classification)

1. Monoplegia □
2. Hemiplegia □
3. Diplegia □
4. Quadriplegia □

C. MOTOR SEVERITY (Gross Motor Function Classification System)

1. GMFCS L-1 □
2. GMFCS L-2 □
3. GMFCS L-3 □
4. GMFCS L-4 □
5. GMFCS L-5 □

TREATMENT PLAN

1. Conservative

a) Gait training No □ Yes □
b) Sitting No □ Yes □
c) Serial casting No □ Yes □
d) Other □ specify:….

2. Surgery:

a) Tenotomy/myotomy No □ Yes □
b) Tendon lengthening No □ Yes □
c) Tendon transfer No □ Yes □
d) other □ Specify:….

APPENDIX II: Institutional Review Board Approval Letter

Dr UWIZEYIMANA Eugene
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 397/CMHS IRB/2021

Your Project Title ***"Assessment Of Preventable Causes And Predictors Of Independent Ambulation For Cerebral Palsy In Rwanda"*** has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Involved in the decision		
		Yes	No (Reason)	
			Absent	Withdrawn from the proceeding
Prof Kato J. Njunwa	UR-CMHS	X		
Dr Stefan Jansen	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 9th December 2021, **Approval has been granted to your study.**

Please note that approval of the protocol and consent form is valid for **12 months**.

APPENDIX III: CCO RILIMA Approval Letter

CENTRE DE CHIRURGIE ORTHOPEDIQUE PEDIATRIQUE ET DE REHABILITATION, SAINTE MARIE DE RILIMA (CCO RILIMA)
TIN 101312420

RILIMA SECTOR - BUGESERA DISTRICT
Tel. 0788323310 – 0788681666
stmarie.rilima@gmail.com
ad.stmarierilima@gmail.com
www.rilimaorthopaedic.rw
P.o. Box 1949 KIGALI

Rilima, 30th December 2021

Ref. 373/2021/MGT/NE

Dr. Eugene UWIZEYIMANA
Resident in rotation in CCO Rilima
Tel: 0788878988
Email: jimmyson007@gmail.com

RE: ***Your request for data collection approval in CCO Rilima***

Dear Sir,

Reference made to your letter of December 22nd, 2021 requesting for our approval for data collection in CCO Rilima as part of your research project on "ASSESSMENT OF PREVENTABLE CAUSES AND PREDICTORS OF INDEPENDENT AMBULATION FOR CEREBRAL PALSY IN RWANDA",
Reference also made to the evaluation report of the CCO Rilima Ethics & Education Committee recommending us to approve your research project,

We would like to tell you that your research project in our Centre is approved.

Furthermore, we formally urge you to reserve a copy of your final research document to CCO Rilima.

Sincerely,

Dr. NZAYISENGA Albert

Director General