

Causes, functional outcomes and healthcare utilisation of people with cerebral palsy in Singapore

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ABSTRACT

Introduction: A voluntary cerebral palsy (CP) registry was established in 2017 to describe the clinical characteristics and functional outcomes of CP in Singapore.

Methods: People with CP born after 1994 were recruited through KK Women's and Children's Hospital, National University Hospital and Cerebral Palsy Alliance Singapore. Patient-reported basic demographics, service utilisation and quality of life measures were collected with standardised questionnaires. Clinical information was obtained through hospital medical records.

Results: Between 1 September 2017 and 31 March 2020, 151 participants were recruited. A majority (n=135, 89%) acquired CP in the pre/perinatal period, where prematurity (n=102, 76%) and the need for emergency caesarean section (n=68, 50%) were leading risk factors. Sixteen (11%) of the total participants had post-neonatal acquired CP. For predominant CP motor types, 109 (72%) had a spastic motor type; 32% with spastic mono/hemiplegia, 41% diplegia, 6% triplegia and 21% quadriplegia. The remaining (42, 27.8%) had dyskinetic CP. Sixty-eight (45.0%) participants suffered significant functional impairment (Gross Motor Functional Classification System levels IV–V). Most participants (n=102, 67.5%) required frequent medical follow-up (≥4 times a year).

Conclusion: Optimisation of pre- and perinatal care to prevent and manage prematurity could reduce the burden of CP and their overall healthcare utilisation.

Ann Acad Med Singap 2021;50:111-8

Keywords: Cerebral palsy, functional outcomes, neonatal, registry

INTRODUCTION

Cerebral palsy (CP) describes a group of permanent, but often changing, disorders that affect movement and posture, causing activity limitation, attributed to non-progressive disturbances that occurred in the developing fetal or infant brain.¹ The birth prevalence of CP is estimated to be 1.4–2.2 per 1,000 in high-income countries. It is one of the most common and severe disabilities in childhood, with high individual and societal demands on health, educational and social services.^{2–4}

Since the first population-based CP registry was set up in Denmark in 1950, over 40 registries have been

established, mainly in European countries, Canada and Australia.⁵ These large databases provide a wealth of information on prevalence, aetiology, risk factors, temporal trends and treatment strategies. This forms a basis upon which to plan services, conduct research and act as a springboard for advances in therapeutics and rehabilitation. Historically, there has been limited data on CP in both Asia and in low- and middle-income countries worldwide. However, with the establishment of new surveillance programmes in the region in the last 2 decades, this is beginning to change. The Korean Database of Cerebral Palsy was developed in 2009 and a CP

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registration system has been developed in Japan.^{6,7} Epidemiology of CP has also been studied in different parts of China, Pakistan and Nepal based on population-based surveys, local disability registration systems and hospital-based studies.⁸⁻¹² New CP registers have also been formed in Bangladesh, Sri Lanka, Vietnam and other Asian countries.^{4,13,14} These CP registers are beginning to identify both the birth prevalence of CP in these regions, which is essential to understand service requirements, and also to identify region-specific opportunities for prevention. Singapore, despite being a developed country in Asia, lacks comprehensive data on the burden of disease for this common lifelong neurological condition.

The Cerebral Palsy Registry in Singapore (SingCPR) was established in September 2017. The key objectives of the Registry are: (1) to determine the clinical characteristics and functional outcomes of people with CP in Singapore; (2) to assist in planning, development and provision of resources and services for CP locally; and (3) to identify areas for further research to improve clinical outcomes of people with CP. In this article, we report the preliminary data of the CP Registry, specifically the demographics, clinical data and functional outcomes of people with CP in Singapore.

METHODS

Design and study population

Participation was voluntary. Cases were identified from outpatient clinics, therapy sessions and inpatient admissions at KK Women's and Children's Hospital (KKH) and National University Hospital (NUH), the only tertiary paediatric hospitals in Singapore. Participants were also identified from those attending the Cerebral Palsy Alliance Singapore (CPAS), one of the largest local social service organisations that provides educational and therapy services to people with CP. Recruitment materials were also sent to community providers such as private paediatricians, early intervention centres and special schools. Cases were referred to and screened by the study team of therapists and doctors who had undergone standardised training of the case definition, classification and functional outcome assessments.

In the pilot phase, children born in 2011 and later (6 years and younger) were included. From 2019, people with CP born in 1994 and later were included.

The main inclusion criterion for SingCPR is a diagnosis of CP made by a paediatrician. Our case definition of CP contains 5 key elements common to the definitions published by Bax,¹⁵ Mutch¹⁶ and Rosenbaum,¹ as adopted

by the Surveillance of Cerebral Palsy in Europe² and Australian Cerebral Palsy Register.⁴

Under our definition, cerebral palsy:

- (1) is an umbrella term for a group of disorders
- (2) is a condition that is permanent but not unchanging
- (3) involves a disorder of movement and/or posture and of motor function
- (4) is due to a non-progressive interference, lesion, or abnormality
- (5) the interference, lesion, or abnormality originates in the immature brain

Based on information from the hospital medical records, CP was sub-divided into 2 categories: pre/perinatal CP (defined as an injury to the developing brain throughout pregnancy and the first 28 completed days after birth) and post-neonatal CP (defined as an injury to the developing brain occurring after 28 days of life and before 3 years of age). Under pre/perinatally acquired CP, data collected for risk factors included: (1) gestation (prematurity was defined as birth that occurs less than 37 completed weeks of gestation); (2) birth weight; (3) small for gestational age; (4) meconium-stained liquor; (5) mode of delivery; (6) multiple births; (7) neonatal encephalopathy; (8) intrauterine infection; (9) congenital anomaly; and (10) unknown. Neonatal encephalopathy is defined as a clinical syndrome in an infant born at or beyond 35 weeks of gestation, manifested by a subnormal level of consciousness or seizures, and often accompanied by difficulty with initiating and maintaining respiration, and depression of tone and reflexes. Under post-neonatally acquired CP, causes consisted of infection, head trauma, cardiovascular accident, anoxic brain injury and others.

Those with progressive neurological conditions as the sole aetiology of their abnormal neurology were excluded, as were people with hypotonia but no other neurological signs, risk factors or abnormal brain imaging.

Clinical data and comorbidities were obtained through hospital medical records. Detailed information on demographics, service utilisation and quality-of-life measures were collected via a standardised questionnaire administered to the family by a study member. Quality-of-life measures included screening questions on general well-being and function using the World Health Organization International Classification of Functioning, Disability and Health, Children and Youth version (ICF-CY) in the domains of Body Structure/Function, Activities and Participation, and Environmental factors.¹⁷ Levels of ICF-CY impairment was graded according to frequency, intrusiveness or severity from 0 (no impairment/ difficulty) to 4 (complete/ constant

CLINICAL IMPACT

What is New

- The new cerebral palsy (CP) registry in Singapore provides objective data on the causes, functional outcomes and healthcare utilisation of people with CP.
- Pre/perinatally acquired CP accounted for majority of cases, with prematurity as the main risk factor.
- Almost half of participants in this registry suffer from severe motor functional impairment.

Clinical Implications

- Optimisation of pre- and perinatal care to prevent and manage prematurity, together with early diagnosis and intervention, is important to reduce the incidence, severity and lifelong burden of CP in Singapore.

impairment/ difficulty/ intensity totally disruptive).¹⁸ Functional outcome scales including the Gross Motor Function Classification System (GMFCS),¹⁹ Manual Ability Classification System (MACS),²⁰ Eating and Drinking Ability Classification System (EDACS)²¹ and Communication Function Classification System (CFCFS),²² were assessed by healthcare providers at the respective institutions. The diagnosis of CP was verified by the study team based on hospital medical records, prior to the final registration and data entry. All data were entered into REDCap, a secure web-based database platform.

Statistical analysis

For ordinal outcome measures, Wilcoxon Signed-rank Test was used with results presented as frequencies and percentages. For outcome measures with continuous scores, paired t-tests were performed with results in mean and standard deviations. Statistical significance was indicated by a *P* value <0.05. Statistical analysis was conducted with SPSS Statistics software version 19 (IBM Corp, Armonk, US).

Ethics

Ethics approval for the study was obtained from the SingHealth Institution Review Board (CIRB number: 2016/2266). Informed consent was obtained from all caregivers/participants in accordance with the review board.

RESULTS

A total of 153 participants were identified during a 31-month period from 1 September 2017 to 31 March 2020. Of these, 2 were excluded for not fulfilling the diagnostic criteria for CP, leaving 151 participants for analysis.

Of the 151 participants, 106 (70.2%) were males, with a median age of 6.2 years old at recruitment (range 1.2–24.3 years old) and majority were of Chinese ethnicity (Table 1). Ninety (59.6%) were diagnosed in the first 2 years of life and 117 (77.5%) before 3 years old. Ninety-six of all participants (63.6%) had a brain magnetic resonance imaging (MRI). The most common abnormal MRI finding was white matter injury (49.5%), including periventricular leukomalacia and periventricular haemorrhage.

Participants with pre/perinatally acquired CP accounted for 89.4% (135) of all CP, while participants with post-neonatally acquired CP accounted for 10.7% (16) of the total group. In the pre/perinatally acquired group (*n*=135), the majority of participants were born preterm (75.6%) and required emergency caesarean section (50.4%) while 10.4% (14/135) were born small for gestational age (Table 2). In the post-neonatally acquired group (*n*=16), the most common cause was infection (37.5%), followed by head trauma (25.0%) (Table 3).

Predominant CP motor type and gross motor function

In terms of the predominant CP motor type, 109 participants (72.2%) had a spastic motor type while 42 (27.8%) had dyskinesia (Table 4). None had choreoathetoid or ataxic CP motor types. Among those with pre/perinatally acquired CP, 44 had spastic diplegia, 30 had spastic monoplegia/hemiplegia, 6 had spastic triplegia and 19 had quadriplegia. Dyskinetic CP constituted 26.7% of those with pre/peri-neonatally acquired CP and 37.5% of those with post-neonatally acquired CP.

For gross motor function (*N*=151), 50 participants were able to walk independently (GMFCS I–II), 33 were able to walk with assistive devices (GMFCS III) and the remaining 68 were wheelchair-dependent (GMFCS IV–V).

Associated co-morbidities

Of the 151 participants, 63 (41.7%) had visual impairment, 13 (8.6%) had hearing impairment, 38 (25.2%) had epilepsy and 38 (25.2%) had cognitive impairment (Intelligence Quotient ≤70). In terms of hip surveillance, 117 (77.5%) had at least 1 pelvis

Table 1. Baseline characteristics for all cerebral palsy (N=151)

Characteristics	n (%)
Sex	
Male	106 (70.2)
Female	45 (29.8)
Race	
Chinese	91 (60.3)
Malay	31 (20.5)
Indian	17 (11.3)
Other	12 (7.9)
Age at recruitment, median (range), years	6.2 (1.2–24.3)
Age at diagnosis	
0–6 months	22 (14.6)
7–12 months	25 (16.6)
13–24 months	44 (29.1)
25–36 months	27 (17.9)
37–48 months	13 (8.6)
49–60 months	6 (4.0)
Age > 5 years	8 (5.3)
Not stated	6 (4.0)
MRI brain finding (n=101)^a	
Normal	10 (9.9)
White matter injury (PVH, PVL)	50 (49.5)
Diffuse cortical injury	15 (14.9)
Focal cortical injury	7 (6.9)
Basal ganglia pattern	8 (7.9)
Malformation	9 (8.9)
Missing information	2 (2.0)

MRI: magnetic resonance imaging; PVH: periventricular haemorrhage; PVL: periventricular leukomalacia

^a Of 96 participants with MRI brain, 5 had 5 or more dominant MRI findings

X-ray, of whom 24 (20.5%) had hip subluxation and 8 (6.8%) had hip dislocation (Table 4).

Other functional outcomes

For hand function, 69 (45.7%) participants were able to handle most objects easily (MACS I–II), 29 (19.2%) could handle objects independently with modified activities (MACS III) while 53 (35.1%) needed continuous or total assistance (MACS IV–V) (Table 4).

Table 2. Characteristics and risk factors of pre/perinatally acquired cerebral palsy (n=135)

Characteristics	n (%)
Gestational age (weeks)	
23–27	33 (24.4)
28–31	39 (28.9)
32–36	30 (22.2)
≥37	33 (24.4)
Birth weight (grams)	
<1000	28 (20.7)
1000–1499	36 (26.7)
1500–2499	41 (30.3)
>2500	30 (22.3)
Mode of delivery	
Normal vaginal delivery	43 (31.8)
Assisted vaginal delivery	14 (10.4)
Elective caesarean section	10 (7.4)
Emergency caesarean section	68 (50.4)
Plurality	
Singleton	105 (77.8)
Twins	27 (20.0)
Triplets	3 (2.2)
Risk factors	
Meconium-stained liquor	4 (3.0)
Congenital anomaly	16 (11.9)
Neonatal encephalopathy	22 (6.3)
Intrauterine infection	0
Unknown risk factor	8 (5.9)

For feeding, most participants were on oral feeding while 19 (12.7%) were on tube feeding (EDACS V) of which, 10 had undergone gastrostomy and fundoplication. Approximately half the participants (70/149, 47.0%) were mostly effective in everyday communication (CFCS I–II) while 60/147 (40.2%) had inconsistent and limited communication even with familiar partners (CFCS IV–V).

Healthcare utilisation

Most participants (102, 67.5%) had frequent medical follow-up (≥4/year). Only a third (52, 34.4%) had dental care in the past year. More than half of Singaporeans/

permanent residents (80/140, 57.9%) attended or were attending community early intervention programmes, while the rest received or were receiving hospital-based

or private therapies. In terms of equipment, 86 of the total participants (57.0%) had ankle-foot-orthoses, 31 (20.5%) used walkers or gait trainers, and 17 of 100 (17.0%) participants in GMFCS III–V owned standing frames.

Table 3. Post-neonatal causes (n=16)

Causes	n (%)
Infection	6 (37.5)
Group B Streptococcus meningoen­cephalitis/ non-meningoen­cephalitis with bacteraemia	2
<i>Streptococcus pneumoniae</i> meningoen­cephalitis with bacteraemia	1
HSV type 2 meningoen­cephalitis	2
Aseptic meningitis with hydrocephalus	1
Head trauma	4 (25.0)
Non-accidental injury	3
Road traffic accident	1
Cardiovascular accident	2 (12.5)
Event resulting in hypoxia	2 (12.5)
Other post-neonatal event	2 (12.5)

HSV: herpes simplex virus

Quality of life outcomes

Most participating parents (102, 67.5%) perceived their child to be happy or very happy in general at the point of assessment. The majority of participants reported no or little problem with sleep or pain while 9 (6.0%), 8 (5.3%) and 5 (3.3%) complained of difficulty in onset of sleep, difficulty in maintaining sleep and generalised pain, respectively. Sleep disturbances and generalised pain were associated with higher GMFCS levels ($P<0.05$ and $P=0.04$, respectively).

DISCUSSION

This first SingCPR report provided data on the demographics, clinical profiles and functional outcomes of people with CP in Singapore. In our Registry, prematurity is a major risk factor of pre/perinatally

Table 4. Predominant cerebral palsy motor type, functional motor severity classifications and comorbidities

	All CP n (%)	Pre/perinatally acquired CP n (%)	Post-neonatally acquired CP n (%)
	(N=151)	(n=135)	(n=16)
Predominant CP motor type and subtype			
Spastic	109 (72.2)	99 (73.3)	10 (62.5)
Monoplegia/ Hemiplegia	35 (32.1)	30 (30.3)	5 (50.0)
Diplegia	45 (41.2)	44 (44.4)	1 (10.0)
Triplegia	6 (5.5)	6 (6.0)	0
Quadriplegia	23 (21.1)	19 (19.3)	4 (40.0)
Dyskinetic	42 (27.8)	36 (26.7)	6 (37.5)
Ataxic	0	0	0
GMFCS			
I–II	50 (33.1)	49 (36.3)	1 (6.2)
III	33 (21.9)	29 (21.5)	4 (25.0)
IV–V	68 (45.0)	57 (42.2)	11 (68.8)
MACS			
I–II	69 (45.7)	67 (49.6)	2 (12.5)
III	29 (19.2)	25 (18.5)	4 (25.0)
IV–V	53 (35.1)	43 (31.8)	10 (62.5)
Comorbidities			
Visual impairment	63 (41.6)	57 (42.2)	6 (37.5)
Hearing impairment	13 (8.6)	11 (8.1)	2 (12.5)
Epilepsy	38 (25.2)	30 (22.2)	8 (50.0)
Cognitive impairment	38 (25.2)	32 (23.7)	6 (37.5)
Hip subluxation/ dislocation	33 (21.9)	28 (20.7)	4 (25.0)

CP: cerebral palsy; GMFCS: Gross Motor Function Classification System; MACS: Manual Ability Classification System

acquired CP while infection is the most common post-neonatal cause. Spastic CP is the predominant CP motor type. Almost half were in severe impairment groups (GMFCS levels IV–V).

Compared with established CP registries from other developed countries, we share similar findings of predominant male gender, age of diagnosis typically by 2 years of age and a higher proportion of pre- or perinatally acquired CP. In the group with pre- or perinatally acquired CP, prematurity and the need for emergency caesarean section were the 2 most common risk factors. While recent literature has shown that there was a decreasing prevalence of CP in moderately preterm as well as moderately and very low birth weight (VLBW) infants, we found preterm birth and birth weight <2,500g in almost two-thirds of our study population, compared with 40–50% in Western countries.^{2,4,23,24} This figure is consistent with reported Asian data of 70% in Okinawa, Japan and 60% in South Korea.^{6,7} This is likely related to our increasing rates of premature birth and decreasing mortality rate of VLBW in Singapore.²⁵ Our robust surveillance and follow-up programme in the VLBW cohort has likely also contributed to the high proportion of CP associated with prematurity.²⁶

Among participants with post-neonatally acquired CP, infection and non-accidental head trauma were the commonest aetiologies. Some of these infections were potentially preventable causes. Vaccination against pneumococcal disease was recently included as one of the nationally recommended vaccines, with enhanced subsidy in Singapore. We hope that this will further reduce the risk of pneumococcal meningoenzephalitis that may result in severe neurological sequelae. In terms of non-accidental head injury in infants, there needs to be further education for parents and carers in the risks of shaking a baby as well as identifying families who may require additional support.

In our Registry, spasticity was the most common dominant motor type, similar to other registries. However, unlike in Canada and in Australia, spastic diplegia is more common than spastic hemiplegia in Singapore.^{4,24} This is related to the higher rate of premature birth, low birth weight and associated periventricular leukomalacia in our Registry.^{27,28}

Similar to registries from Europe and Canada, we classified CP into 3 motor types: spastic, dyskinetic and ataxic.²⁹ In our Registry, dyskinetic CP represent a larger proportion (27.8% overall) as compared to 7–12% in Europe and Australia.^{4,30,31} This may be related to specialist recognition of dyskinesia in our hospital-based cohort. Separately, due to a rigorous national

neonatal hyperbilirubinemia screening and treatment programme, we had no local choreoathetoid CP associated with kernicterus.

We recorded no cases of hypotonic or ataxic CP in our Registry while other registries reported <10% of hypotonic or ataxic CP.^{4,13,32} In our case definition, hypotonic children with no other neurological sign, risk factor or abnormal brain imaging were excluded and we performed metabolic and genetic investigations in children with hypotonia and/or early-onset ataxia in line with recommendations.³⁴ Furthermore, the description and definition of ataxic CP is generally lacking. A high proportion of people with ataxic CP can have an incorrect initial diagnosis.³³ Thus, it is rare to make a diagnosis of ataxic or hypotonic CP in our clinical practice.

With regards to comorbidities, we reported similar findings in epilepsy, visual impairment, cognitive impairment and hip displacements as most other registries.^{4,13,23,24,31,32} In terms of gross motor function, our Registry reported higher proportions (45%) of participants with severe impairments (GMFCS IV–V, 25–28% in established CP registries).^{4,24} This may be explained by our Registry being hospital- and centre-based, as compared to other community registries.

Unique to our Registry, we collected comprehensive data on measures related to quality of life. It is heartening to know that most parents perceived their child to be happy in general and majority of the participants had no or little problem with sleep or pain. However, those with higher GMFCS levels were more likely to complain of sleep disturbances and pain, comparable with studies that indicated that sleep disorders are positively associated with impaired gross motor function.^{35,36} Participants with higher GMFCS were more likely to experience pain from muscle spasms, hip dislocation and difficulties in changing sleep positions, which worsen sleep disturbances.³⁷ There is a pressing need to look into the practical management of these specific issues to improve the quality of life of these patients.

Strengths and limitations

The strength of our Registry is active recruitment from the 2 main paediatric hospitals and 1 of the largest CP service providers in Singapore. We also had strict case definitions of CP and the participants' diagnoses were verified by paediatricians using hospital medical records before final recruitment. Moreover, data in our Registry were extensive and included measures for quality of life and service utilisation. At the same time, information was complete for the motor subtypes and functional classification scales of the participants.

The main limitation of the Registry comes from likely selection bias, due to the process of voluntary recruitment through tertiary hospitals, increasing the likelihood of recruiting participants with more severe disabilities and missing participants with mild disabilities who are not assessing these services. Such selection bias could have contributed a higher proportion of severe CP and a lower proportion of hemiplegic CP in our Registry.

Moving forward, we hope to expand community recruitment so that we could include more participants with less severe disabilities. In addition, the registry has planned for regular review and update of our patients' information. With time, this will allow us to track the burden of the disease locally, to allow policymakers and administrators to better plan health resources allocation and management.

CONCLUSION

This is the first report of the newly established CP Registry in Singapore that provided objective data on the causes, functional outcomes and healthcare utilisation of people with CP locally. Pre/perinatally acquired CP accounted for the majority of all cases, with prematurity being the main risk factor. Almost half of the registry is in the severe motor functional impairment groups. Optimisation of pre- and perinatal care to prevent and manage prematurity, together with early diagnosis and intervention, remains an important strategy to reduce the incidence, severity and chronic burden of the condition locally. As the Registry continues to grow in the future, we are confident this work will provide important new insights into our understanding of this common lifelong neurodevelopmental disorder.

Acknowledgements

The authors would like to acknowledge Ms Latha Kuthy and all staff of Cerebral Palsy Alliance Singapore for their support in setting up the Registry. We thank Ms Su Bing for maintaining the database, Ms Melody Por for recruitment efforts, Dr Dhivya Muthiah and Dr Teo Tong Lin for their inputs in data interpretation, as well as the patients and their families who contributed to the Registry.

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