

Frequency and risk factors of scoliosis in Malaysian children with cerebral palsy

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Abstract

Background: Scoliosis is a common musculoskeletal co-morbidity seen in children with cerebral palsy (CP). **Objective:** To describe the frequency of scoliosis and analyze the risk factors for scoliosis to propose a surveillance program for children with cerebral palsy in Malaysia. **Methods:** Cross-sectional study of children with cerebral palsy between 5 to 18 years old recruited from July 2017 to March 2018. A clinical examination was done, and Cobb's angle was measured on all spine radiographs. Gross Motor Function Classification System (GMFCS) level, cerebral palsy subtype, age at clinical diagnosis of scoliosis, and the Cobb angle at the first radiography examination were registered. **Results:** Eighty-one children were recruited. 46/81 (56.8%) had clinical scoliosis and were subjected to spine radiograph. 41/81 (50.6%) had scoliosis with a Cobb angle >10°, of which 9/81 (11.1%) had a Cobb angle >40°. The risk of scoliosis was related to the GMFCS level with 4/81(4.9%) at GMFCS I-III and 37/81(45.7%) at GMFCS IV-V. More than half of the children with bilateral spastic cerebral palsy (52.3%) and dystonic cerebral palsy (60%) had scoliosis. Children with GMFCS levels IV-V developed scoliosis by ten years old. **Conclusion:** In our cohort, more than half had scoliosis. The frequency of scoliosis increased with GMFCS level and bilateral spastic cerebral palsy subtypes. The proposed simple spine surveillance based on the occurrence of scoliosis and GMFCS levels will lead to early detection, improved care, and timely intervention of the scoliosis deformity in children with cerebral palsy in Malaysia.

Keywords: scoliosis, cerebral palsy, children, frequency, risk factors, GMFCS, Cobb angle.

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Introduction

Cerebral Palsy (CP) is a group of permanent but not unchanging disorders of movement, posture, and motor function due to a non-progressive interference, lesion, or abnormality of the developing/immature brain [1]. Children with CP have an increased risk of developing scoliosis in their early years and adolescence [2, 3, 4]. Madigan *et al.* [5] and Saito *et al.* [2] describe the frequency of scoliosis in the spastic CP group to be above 60%, with most scoliosis occurring before ten years. The natural history of scoliosis progression is closely related to the severity of the CP and continues to progress beyond skeletal maturity [2].

Traditionally, scoliosis is defined as ten or more degrees of lateral curvature calculated by Cobb's method on a posterior-anterior radiograph [6, 7, 8, 9]. Two distinct curve patterns have been described in patients with CP [3]. The first group has double curves with a thoracic and lumbar component, occurring most often in patients with good ambulatory function and less severe neurological deficit [3]. The second group has single curves in either the thoracic or lumbar spines and occurred more frequently in more severely affected patients who are wheelchair-dependent and had significant pelvic obliquity [3].

The development of scoliosis in growing children with CP is due to spasticity, muscle weakness, and poor muscle tone [3]. Scoliosis leads to poor trunk balance, and the associated pelvic obliquity in ambulatory patients affects both standing balance and walking ability. Scoliosis may cause sitting intolerance, postural pain, and pressure sores in wheelchair or bed-bound patients. Patients with severe scoliosis can develop cardiopulmonary complications due to chest wall deformity, gastroesophageal reflux, swallowing disorders, and repeated aspirations with the progression of the spinal deformity.

Cobb angle is the gold standard assessment measure for scoliosis on a plain radiograph, which measure the most-tilted spine vertebrae in each curve. Scoliosis is diagnosed when the lateral spinal curvature has a Cobb angle of 10° or more. A curvature of more than 20° is defined as moderate scoliosis, and a curvature greater than 40° is considered severe scoliosis [10, 11]. Cobb angle remains the most reliable indicator for scoliosis measurement and a useful tool for initiation of intervention [10, 11, 12].

The overall incidence of scoliosis is estimated to be between 21% to 64% in patients with CP [4, 13, 5]. In studies from developed countries, this is directly proportionate to the degree of neurological deficit and their ambulatory capacity measured as gross motor function [3, 14]. There are no local published data on the prevalence and incidence of scoliosis in children with CP

in Malaysia. The main aim of this study was to determine the frequency and risk factors of scoliosis among children with CP in Malaysia, facilitate an appropriate spine surveillance program, and initiate early intervention measures.

Methods

Participants and data collection

This was a single-center, cross-sectional study involving children with CP aged 5 to 18 who attended the Paediatric Neurology clinic, CP clinic, or admitted to the paediatric ward. They were recruited into the study from July 2017 to April 2018.

All children with CP aged between 5 and 18 years old and whose parents or caregivers had given written informed consent were included. Children who have already had spinal surgery were excluded. Eighty-seven children from the clinic population were identified to participate in this study. Six of these children were further excluded as spine radiograph was not correctly done in one, and five could not comply with radiography due to positioning difficulties.

The investigators took data collection, including demographic and clinical characteristics (including cause and type of CP, number of limb involvement, hip dislocation, and wheelchair use), after obtaining written informed consent from the parent or caregiver. All children were examined for scoliosis.

The Adam's forward bending test [15] was used in a standing posture for all participants who could stand and in a sitting position for those who could not stand [16]. The angle of trunk rotation was not significantly different between standing and sitting forward bending positions [16]. The forward bending test was considered positive when there was a deviation from the midline, and the degree of clinical scoliosis [2] was graded as: (a) No scoliosis; (b) Mild scoliosis where a discrete curve is seen on forward bending; (c) Moderate scoliosis when an obvious curve is seen in upright and forward bending with the presence of rib hump; (d) Severe scoliosis when there was an obvious curve preventing upright position without external support.

Adam's forward bending test was quantified using a scoliometer. We used the scoliometer as an additional screening tool with the cutoff set to $\geq 7^\circ$ to ensure appropriate referral for spine radiographs in anteroposterior view [10]. Spinal radiographs will show C7 to the femoral heads and the entire rib cage from right to left [10, 16]. The spine radiograph is done in a standing or sitting position, otherwise in a supine position [4].

The attending investigators determined the CP subtypes following the Surveillance for CP in Europe classification into unilateral or bilateral spastic CP, dyskinetic, choreo-athetoid, and ataxic CP. The investigators ascertained the gross motor function of these children according to the age-appropriate Gross Motor Functional Classification System (GMFCS) levels. The GMFCS is a five-level clinical classification system that describes the gross motor function of children with CP. Level I corresponds to the highest function and level V to the lowest function. In this study, children with GMFCS IV and V were categorized as severe CP.

Measurement of Cobb angle

Children who had a positive clinical diagnosis of scoliosis were instructed to do a spine radiograph. The Cobb's angle was calculated manually by the attending investigators using a 2-dimensional radiographic image. The Cobb angle of a scoliotic curve is the angle formed by the intersection of two lines, one parallel to the endplate of the superior end vertebra and the other parallel to the endplate of the inferior end vertebra [17, 18].

Measurement of the angle included identifying both ends of the vertebrae plates of the curve deformity, and the angle is measured by two intersecting lines drawn along the endplates of the curve. In cases where the lines did not intersect on the film, further two lines were plotted, each at right angles to the first two and the angle measured (Figure 1).

Scoliosis is defined when the Cobb angle is 10° or more [6, 7, 8, 9]. A Cobb angle from 10 to 19 degrees is a mild curve, moderate curvature when the Cobb angle is between 20 to 39 degrees, and curvature of $\geq 40^\circ$ is a severe curvature [2, 3, 4]. Cobb angle measurement has limitations with a 5-10° intra-observer variation, minor rotation during the examination, diurnal variations, and failure to accurately document the severity of the three-dimensional deformity [18, 19].

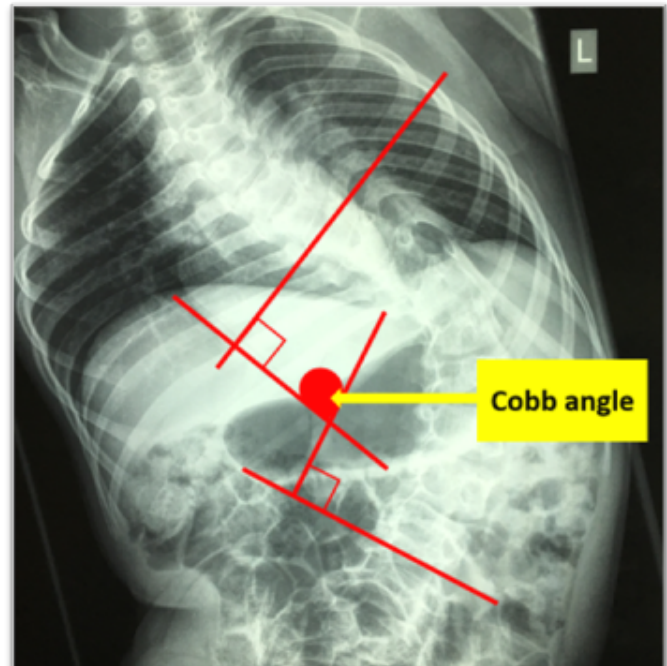


Figure 1. To calculate the Cobb angle, identify the most tilted vertebrae above and below the curve's apex. The angle between the intersecting lines is drawn perpendicular to the top of the top vertebrae and the bottom of the lower vertebrae in the Cobb angle.

Statistical analysis

The data were statistically analyzed using SPSS version 20.0 for Windows. Two-way analysis of variance (ANOVA) was used to evaluate the effect of CP subtype and GMFCS on the Cobb

angle at the latest radiological examination. The correlation between parameters was evaluated by Pearson's correlation coefficient (r). Differences were considered significant when the p -value was <0.05 . Kaplan Meier analysis was used to identify the age at diagnosis of mild to severe scoliosis. The curve illustrates the probability of having scoliosis over time at different GMFCS levels. Multivariate analysis was used to look for risk factors of scoliosis.

The study was approved by the Medical Research Ethics Committee of the Ministry of Health, Malaysia. (NMRR-17-1188-35686).

Results

General characteristics and frequency of scoliosis

Eighty-one children with cerebral palsy, with a median age of 9.5 years (IQR 4.3 years), were recruited for spine surveillance. Of these, 46 (56.8%) had clinical scoliosis, of which 22 were graded as mild and 24 as moderate to severe. Scoliosis with the latest Cobb angle measuring $\geq 10^\circ$ occurred at a mean age of 10.2 years (SD 3.4 years). Characteristics of the participants are described in Table 1.

Thirty-five children did not have clinical scoliosis, and their general characteristics are shown in Table 2. Spine radiographs were not ordered as they did not have signs of scoliosis. Of these, 24 (68.6%) children with cerebral palsy without spine radiographs were in GMFCS level I-III.

All 46 children who had clinical scoliosis were subjected to a spine radiograph. Only 41 (51%) of them had radiologically significant scoliosis with a $\geq 10^\circ$ curve, shown in Table 2.

Table 3 illustrates the distribution of children with clinical scoliosis and the corresponding Cobb angle. In children with severe CP (GMFCS IV and V), a total of 15 (32.6%) were identified with mild clinical scoliosis, and 22 (47.8%) children were identified with moderate to severe clinical scoliosis. From the group with moderate to severe clinical scoliosis, 13 (28.3%) had a Cobb angle of $20\text{--}39^\circ$, and 9 (19.6%) had a Cobb angle $\geq 40^\circ$. The positive predictive value in identifying radiologically significant scoliosis (Cobb angle 10° or more) from clinical assessment was 89%.

Frequency of scoliosis in relation to the GMFCS level

The risk of scoliosis increased proportionately with the higher GMFCS level, as shown in Figure 2. The proportion of the children with Cobb angle $\geq 40^\circ$ increased from none in GMFCS level I to 28% in GMFCS V ($p=0.001$). A two-way analysis of variance tested GMFCS level to Cobb angle and found a significant correlation ($F = 7.006$, $p = 0.010$, $n^2 = 0.088$). The Pearson correlation supported a positive relationship between GMFCS level and Cobb angle was statistically significant with ($r(81) = 0.064$, $p = .00$). Approximately 66% of the children in GMFCS V level had a Cobb angle of $\geq 20^\circ$. Children with GMFCS I and III level did not have scoliosis. In the GMFCS level II, four children had

mild scoliosis with a Cobb angle of $\geq 10^\circ$, and this could be attributed to them being of slightly older age and bilateral spastic CP subtypes.

Frequency of scoliosis in relation to cerebral palsy subtypes

The various degree of scoliosis in relation to their cerebral palsy subtypes is presented in Figure 3. It is noted that 52% ($n=34$) of children with bilateral spastic cerebral palsy had scoliosis, with 31% ($n=20$) having moderate to severe scoliosis. A two-way analysis of variance tested the CP types to Cobb angle found a significant correlation with $F= 4.86$, $p= 0.026$, $n^2= 0.048$ and similarly the Pearson correlation was ($r(81) = -.04$, $p= 0.046$). Children with dystonic cerebral palsy carry an intermediate risk of developing clinical scoliosis. In contrast, children with unilateral spastic CP in our cohort did not have scoliosis. The only child with choreo-athetoid CP had mild scoliosis.

Risk factors for scoliosis

Multivariate analysis was performed to evaluate the variables that had the greatest influence on the development of scoliosis. The factors considered were the child's age, gender, GMFCS level, type of cerebral palsy, and if there was concurrent hip surveillance, botulinum toxin injection, and use of assistive locomotive devices. GMFCS and the CP subtype were the only factors with a significant influence on the risk of scoliosis. The risk of scoliosis was significantly higher in children with severe CP (GMFCS IV-V) than in children with GMFCS I to III (adjusted OR 3.1, 95% CI 1.95-4.97, $p=0.001$). Spastic CP likewise had increased scoliosis with adjusted OR 4.6, 95% CI 1.7-3.05, $p=0.003$.

Age at first detection of significant scoliosis among children with severe cerebral palsy

Children with severe CP are at increased risk of developing scoliosis. The mean age at Cobb angle $\geq 10^\circ$ (mild) scoliosis was 9.6 years (SD 1.26 years, range 5 to 16 years). Moderate scoliosis (Cobb angle $\geq 20^\circ$) was seen at a mean age of 9.9 years (SD 0.76 years, range 5 to 14 years). The mean age of our children with severe CP developing severe scoliosis was 12.2 years (SD 1.09 years, range 9 to 17 years). Our cohort showed the incidence of severe scoliosis with Cobb angle $\geq 40^\circ$ peaked at 12 years old and was detected as early as nine years old.

Survival plot analysis of the occurrence of scoliosis in relation to the GMFCS levels

Kaplan-Meier survival plot shows the occurrence of significant radiological scoliosis in relation to the GMFCS level (Figure 4). Children in GMFCS levels I to III developed scoliosis at a median age of 11.5 years (IQR 1.1 years, age; 95% CI). In contrast, children in GMFCS levels IV to V developed scoliosis at a median age of 9.6 years (IQR 0.6 years, age; 95% CI).

FIGURE 4 HERE

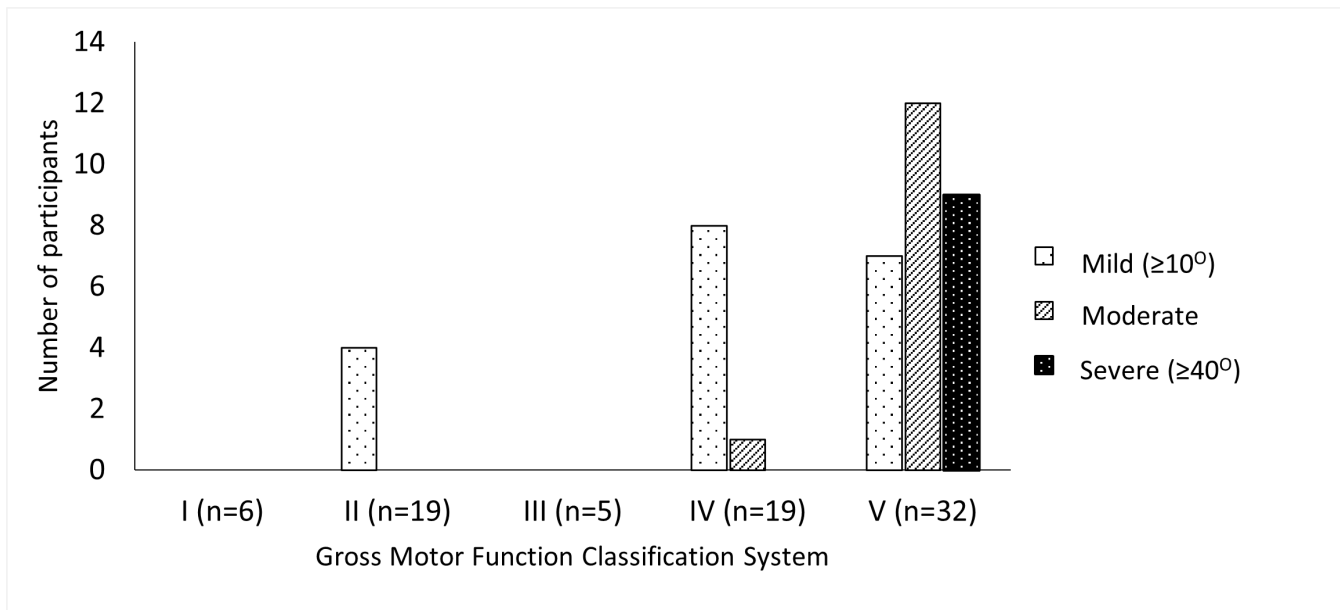


Figure 2. Proportion of children with different severity of scoliosis in relation to their GMFCS levels.

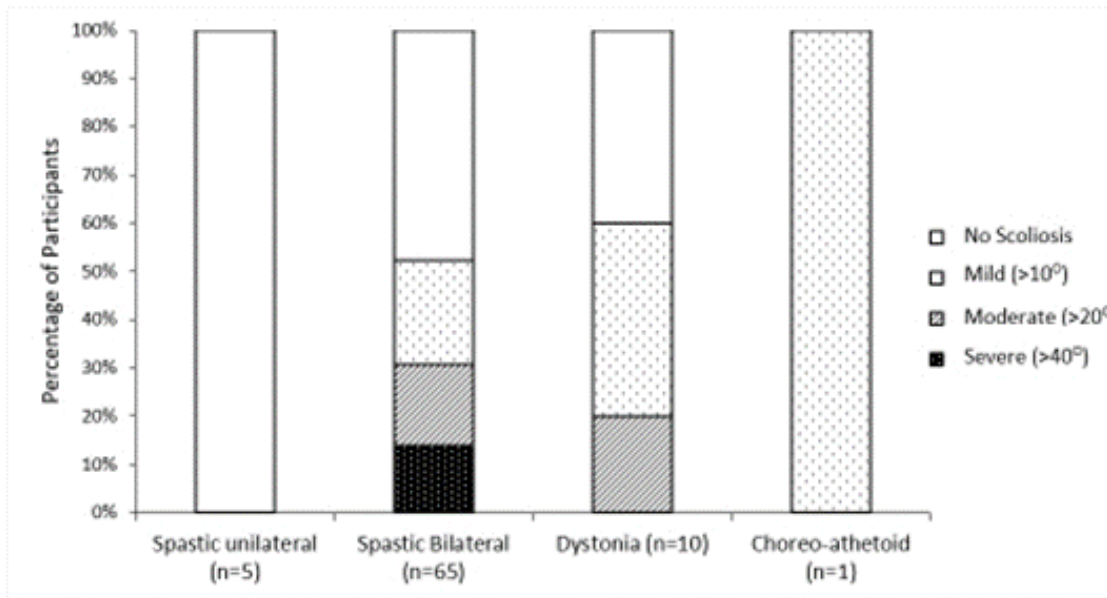


Figure 3. Proportion of children (n=81) with different severity of scoliosis in relation to their CP subtypes.

Discussion

This cross-sectional study showed the frequency of scoliosis in a total population of children with CP seen in our center aged from 5 to 18 years old. Of the 81 children in this study, 22 (27.2%) had mild scoliosis, and 24 (29.6%) had moderate to severe scoliosis based on clinical examination. The risk of developing scoliosis increased with the GMFCS level. In most children, scoliosis was diagnosed after eight years of age.

The incidence of scoliosis in children with CP, as seen in population-based studies, is directly related to GMFCS levels [4, 20, 21]. In our study, we show a similar correlation. Children with GMFCS V had a higher frequency of scoliosis, with 46% of the 46 children with clinical scoliosis having moderate

to severe scoliosis with a Cobb angle of $\geq 20^\circ$. Four children had mild scoliosis with a Cobb angle of $\geq 10^\circ$ attributed to older age and bilateral spastic CP subtype.

Spinal deformity in CP develops due to a combination of spasticity, muscle weakness, and balance [2, 3]. In our study, children at GMFCS level IV and V with Cobb angle $\geq 20^\circ$ were mostly bilateral spastic and dyskinetic CP. Children with unilateral spastic CP and GMFCS levels I to III had a low incidence of scoliosis. This is consistent with a study done in Sweden by Persson-Bunke *et al.* [10] in 2012 where 16% of 244 children with spastic bilateral CP and 15% of 66 children with dyskinetic CP had a curve of more than 20° . This may indicate that the development of scoliosis in children with CP is related primarily to the degree of neurological deficit and ambulation capacity [22, 23].

Table 1. General characteristics of participants.

Participants' Characteristics (n=81)	Total
Median age (IQR) in years	9.5 (4.3)
Sex, n (%)	
Male	50 (61.7)
Female	31 (38.3)
Cerebral palsy subtypes	
Spastic	
Unilateral	5
Bilateral	65
Dyskinetic	
Dystonic	10
Choreo-athetoid	1
GMFCS, n (%)	
Level I	6 (7.3)
Level II	19 (23.5)
Level III	5 (6.2)
Level IV	19 (23.5)
Level V	32 (39.5)
Age at scoliosis surveillance (mean \pm 2SD, year)	
Nil	8.6 \pm 2.8
Mild	9.6 \pm 1.3
Moderate	9.9 \pm 0.8
Severe	12.2 \pm 1.1
Age at the radiograph showing Cobb angle \geq 10° (mean \pm 2SD, year)	10.2 \pm 3.4
Age at the radiograph showing Cobb angle \geq 20° (mean \pm 2SD, year)	10.9 \pm 3.6
Age at the radiograph showing Cobb angle \geq 40° (mean \pm 2SD, year)	12.6 \pm 2.7

In our study, the first spine surveillance was done at a mean age of 8.6 years (SD 2.8 years). The mean age at which our cohort was detected to have a Cobb angle \geq 10° was 9.7 years (SD 3.4 years). This was fairly consistent with other case series, where most of the curvature started forming before ten years of age [6]. We also observed that many of our children in this cohort had their first spine surveillance during this study.

In addition, we also observed that the scoliosis deformity pattern seen in our cohort was similar to studies [24, 25], with increased thoracolumbar and thoracic scoliosis being the most encountered deformity pattern in cerebral palsy. This identification of deformity pattern is important for surgical correction as lumbar scoliosis is the most difficult to correct surgically. In our study, twenty-six percent (n=12) had a lumbar curvature. Flexible postural curvature develops in young children, which can become structural and rigid as the child approaches puberty.

To the best of our knowledge, our results provide preliminary local epidemiological data that could lay the groundwork for forming a simple spine surveillance guideline for children with CP in a developing country with limited resources. We propose a surveillance guideline as below:

Limitations

In this cross-sectional study, 63% of the study population of 81 children consisted of children with severe CP. The trend seen in this study can be explained as our center is a tertiary hospital and tends to see children in the more severe spectrum of CP.

The number of patients in this study was small. Some children with GMFCS I and II may have been followed up in other disciplinary clinics in our hospital and not have been referred to the neurology clinics as these children may not have demonstrated severe impairment in terms of function. Potential participants with severe CP may not have been brought to the clinic due to logistics (larger size and difficulties with transportation and ambulation) for accurately capturing the true frequency of scoliosis in our cohort.

This study also did not consider the rate and progress of the spine curvature. Unlike idiopathic scoliosis, scoliosis in CP has been shown to progress beyond skeletal maturity [3, 26]. In our study population, the participants with GMFCS III did not have clinical scoliosis, possibly due to their younger age, and were grouped into the GMFCS I and II categories on the Kaplan-Meier plot.

Table 2. General characteristics of children with and without scoliosis

Participants' Characteristics	Children with CP	
	No clinical scoliosis (n=35)	With clinical scoliosis (n=46)
Median age (IQR) in years	8.8 (4.7)	9.5 (4.3)
Sex, n (%)		
Male	20 (57)	30 (66)
Female	15 (43)	16 (34)
Subtype of cerebral palsy, n (%)		
Spastic		
Unilateral spastic/hemiplegia	4 (11.4)	1 (2.2)
Bilateral spastic	27 (77.2)	38 (82.6)
Dyskinetic		
Dystonic	4 (11.4)	6 (13.0)
Choreo-athetoid	0	1 (2.2)
GMFCS, n (%)		
Level I	6 (17.1)	0
Level II	13 (37.2)	6 (13.0)
Level III	5 (14.3)	0
Level IV	9 (25.7)	10 (21.7)
Level V	2 (5.7)	30 (65.2)

Table 3. Distribution of clinical scoliosis and Cobb angle in relation to Gross Motor Function Classification System (GMFCS);.

GMFCS	Total, n	Clinical scoliosis			Cobb Angle*			
		No curve	Mild	Moderate/ Severe	<10°	≥10°	≥20°	≥40°
I	6	6	0	0	0	0	0	0
II	19	13	6	0	2	4	0	0
III	5	5	0	0	0	0	0	0
IV	19	9	8	2	1	8	1	0
V	32	2	8	22	2	7	12	9
Total	81	35	22	24	5	19	13	9

*only 46 children with clinical scoliosis had spine radiograph done

Though a cross-sectional study can be used to assess the disease burden, a prevalence study involving a healthy cohort and a multi-centered population should be conducted, when the National CP registry is established in Malaysia.

Conclusion

In conclusion, this study showed that more than half of our cohort had scoliosis. GMFCS level and bilateral spastic CP subtype were important risk factors for deciding on an early and timely spine surveillance program. Children with GMFCS IV to V will need regular spinal examinations into adulthood. We propose a

practical and straightforward spine surveillance program be introduced in centers looking after children with CP in developing countries with limited resources, as without timely intervention, the scoliosis deformity can be severe and functionally debilitating.

Competing interests

The authors declare no potential conflicts of interest with respect to the research, authorship, and publication of this article.

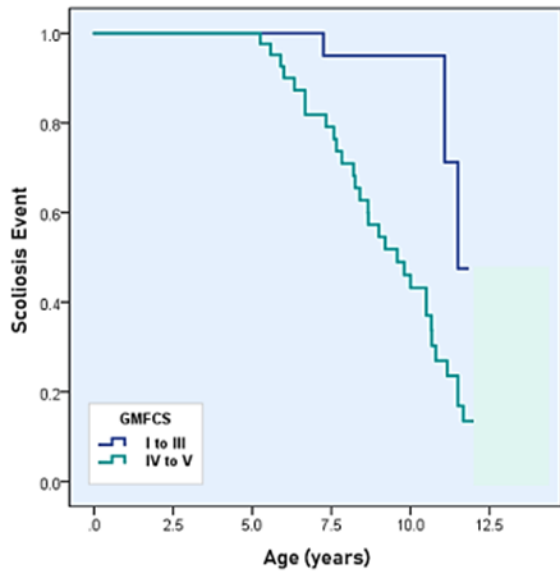


Figure 4. Kaplan-Meier survival plot showing the occurrence of significant radiological scoliosis to the GMFCS level.

GMGCS I-III
<ul style="list-style-type: none"> Adam’s forward bending test from the age of 7 years, repeat at yearly intervals
<ul style="list-style-type: none"> Spine radiograph when clinical scoliosis is detected
<ul style="list-style-type: none"> if Cobb angle is 10° – 19o, repeat spine radiograph yearly
<ul style="list-style-type: none"> if Cobb angle is ≥20°, refer to Spine Clinic
GMFCS IV-V
<ul style="list-style-type: none"> Adam’s forward bending test from the age of 5 years, repeat at six-monthly intervals
<ul style="list-style-type: none"> Spine radiograph when clinical scoliosis is detected
<ul style="list-style-type: none"> if Cobb angle is 10° – 19o, repeat spine radiograph every six months
<ul style="list-style-type: none"> if Cobb angle is ≥20°, refer to Spine Clinic

Author contributions

Dr. P Anandakrishnan: drafting manuscript, data collection, and analysis/data interpretation

Dr. Teik-Beng Khoo: revising and manuscript editing, critical analysis of data interpretation, final approval of the version to be published.

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