Prevalence of comorbidities and their relationship to functional status of children with cerebral palsy

Sruthi Rameshan[1], Pankaj M Buch[2]

From [1]Senior Resident, [2]Professor, Department of Pediatrics, Trivandrum Medical College, Thiruvananthapuram, Kerala, India, Department of Pediatrics, M. P. Shah Government Medical College, Jamnagar, Gujarat, India

Correspondence to: Dr. Pankaj M Buch, Professor of Pediatrics, Department of Pediatrics, M. P. Shah. Government Medical College, Jamnagar - 361 008, Gujarat, India. E-mail: drpankajbuch@yahoo.com

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ABSTRACT

Background: Cerebral palsy (CP) is the most common motor disorder in children. Associated comorbidities are very common. Gross motor functional classification system (GMFCS), manual ability classification system (MACS), and communication function classification system (CFCS) are used to decide functional ability. Functional ability and comorbidities have the greatest impact on the child with CP. There is a paucity of data regarding the functional level and their correlation with comorbidity. **Objective:** The aim of the study was to find the prevalence of comorbidities in CP and their correlation to functional status in children. **Materials and Methods:** A total of 154 consecutive children with CP attending district early intervention center and pediatric department from the period of January to December 2018 were enrolled. Cases were evaluated by history, clinical examination, and investigations. CP was classified in subtypes. Cases were screened for comorbidities. Functional assessment was done as per GMFCS-ER, MACS, and CFCS. **Results:** Study showed that 76% of children had spastic CP, 7% dyskinetic, 6% hypotonic/ataxic, and 11% of them had mixed CP. Mean age was 4 years. Perinatal asphyxia was the most common insult. Comorbidities were intellectual disability (81%), epilepsy (50%), visual problems (70%), hearing problems (12%), malnutrition (36%), and drooling (61%). About 63% were having GMFCS level ≥3. About 60% had MACS and CFCS level ≥3 with significant correlation. Comorbidities were dichotomously distributed across GMFCS levels. There was a strong correlation between comorbidity burden and GMFCS level. **Conclusion:** Comorbidities were significantly observed and disproportionally distributed across GMFCS levels. The burden of comorbidities was more in higher levels of GMFCS.

Key words: *Cerebral palsy, Comorbidities, Gross motor functional classification system, Spastic*

The term "cerebral palsy" (CP) describes a group of permanent disorders of the development of movement and posture attributed to non-progressive damage that occurred in the developing fetal or infant brain. The motor disorders are often accompanied by a disturbance in sensation, perception, cognition, communication, and behavior [1]. Most of the children with CP have lifelong impairments. A systemic screening and management of these impairments are essential for improving functional status, to ensure optimum participation and integration of these children in the family and community. CP is accompanied by various comorbidities which have major impact on the quality of life of children and their families [2]. Population-based studies report that the prevalence estimates of CP range from 1.5 to more than 4/1000 live births or children [3]. CP is more common in boys compared to girls [3-5].

The gross motor function classification system (GMFCS), the manual ability classification system (MACS), and the communication function classification system (CFCS) have been widely used to decide functional status and proved to have good reliability and validity in CP [6-8]. The combination of these three classification systems provides a profile of the overall functional status of a child with CP. Especially, GMFCS has good uptake internationally for use in research and clinical practice [9-12].

The prevalence of comorbidities in children with CP varies widely. Common comorbidities affecting various systems are intellectual disability/global developmental delay (GDD) in the range of 30–50%, epilepsy (15–55%), vision (10–100%) and hearing deficits (30–40%), gastrointestinal (75%), and bony problems (40–50%) [2,9,10,13]. The prevalence of comorbidities across various functional levels is dichotomous. The study between comorbidities and functional status in CP might be helpful for the application of appropriate screening tools [10-12].

Children in GMFCS Level 1 can perform all the activities of their age-matched peers, although with some difficulty with speed, balance, and coordination. Children in Level V have difficulty achieving any voluntary control of the movement [14]. Similarly, MACS describes how the children aged 4–18 years with CP use their hands with objects during activities of daily living [7]. CFCS also has five levels depending on the child's ability to communicate [8]. The aim of the study was to find

the prevalence of comorbidities in CP and their correlation to functional status in children. This might help to plan suitable intervention at the earliest for a better outcome. The data on this aspect from developing countries are limited.

MATERIALS AND METHODS

This cross-sectional study was conducted in children with CP presenting to the Department of Paediatrics and District Early Intervention Centre (DEIC), attached to medical college hospital, for a period of 1 year from January 2018 to December 2018. The study was approved by the Institutional Ethical Committee. Children with CP in the age range of 0–18 years receiving services at Paediatrics Department and DEIC were included in the study. The diagnosis was made/confirmed by pediatric faculty. Children with regression of milestones and history of head injury were excluded from the study. Parents of the children fulfilling inclusion criteria were explained about the nature of the study, and written informed consent was obtained.

The parents were interviewed for the socio-demographic characteristics; antenatal, intranatal, and postnatal history was recorded and verified with available documents. Developmental history, comorbidities, and other pertinent information such as feeding history and clinical presentation were obtained. Children were subjected to thorough general examination including anthropometry and systemic examination. Neurological examination was done by developmental pediatrician attached to DEIC or pediatric faculty, and CP was topographically classified into quadriplegia, diplegia, hemiplegia, or monoplegia depending on limb involvement [1]. CP was also classified into spastic, athetoid, mixed (spastic+athetoid), hypotonic, and ataxic based on an assessment of tone. Anthropometry was interpreted by the WHO charts, [15] Fenton growth charts [16] and Z score [17].

Intelligence/developmental quotient and behavior problems were assessed by trained psychologist attached with DEIC with the help of Developmental Assessment Scale for Indian Infants (DASII) which yields motor and mental developmental quotients based on more than 200 items and applicable up to the age of 3 years [18]. Bharat Raj adaptation of Vineland Social Maturity Scale (VSMS) was used in children who were not cooperative for DASII on repeated attempts or in whom DASII was not possible due to older age and who were not able to undergo intelligence quotient (IQ) testing. VSMS signifies social quotients based on locomotion, self-help, and direction, language and communication skills to a major extent and is applicable for the entire pediatric age group [19].

In the present study, either Malin's Intelligence Scale (MISIC) [20] or Seguin Form Board (SFB) test [21] was used in older children, based on the cooperation of child for IQ assessment. MISIC is an intelligence test for children from the ages of 6 to 15 years 11 months**.** It is administered individually and takes about 2–2½ h. The test comprises subtests divided into two groups, verbal and performance. Verbal scale consists of six subtests and performance scale consists of five subsets. SFB has a performance scale and is culture and language free. DQ and IQ <70 were considered as developmental delay/intellectual disability.

The GMFCS, MACS, and CFCS were used to evaluate functional status. GMFCS which is most studied functional assessment system is a five level clinical classification system that describes the gross motor function of people with CP on the basis of self-initiated movement abilities. These assessments grade severity from level 1 (most able) to level 5 (least able). All the children were screened for visual problems.

Detailed ophthalmological examination was performed by an ophthalmologist in suspected cases. Strabismus, refractive errors, and nystagmus were considered as moderate visual impairment, whereas optic atrophy and blindness were considered as severe visual impairment. Hearing was assessed in a quiet room with handheld audiometer as a screening tool, and suspected cases were confirmed by brain stem evoked response audiometry by the audiologist. No response to 70 dB was considered as significant hearing impairment. Orthopedic examination was sought for children with contractures, bony deformities, and/or suspected bony problems.

Data were entered in Microsoft Excel 2007. Data were analyzed using Epi info version 7 and SOFA software. Continuous data were presented as mean±SD. Spearmen's R correlation test was used to measure the relationship between comorbidities and types of CP, between GMFCS, MACS, and CFCS as well as functional level (GMFCS) and comorbidities.

Table 1: Frequency of comorbidities according to topographical subtypes of cerebral palsy

Comorbidities	Monoplegia	Hemiplegia	Diplegia	Quadriplegia
n (%)	(n=4)	(n=18)	(n=25)	(n=107)
Intellectual disability/GDD	1 (25)	13 (70)	17 (68)	92 (86)
Epilepsy	0	10 (55)	5 (20)	61 (57)
Moderate visual impairment¥	0	18 (100)	22 (88)	90 (84)
Severe visual impairment*	0	0	0	3 (3)
Hearing impairment	0	2 (11)	1 (4)	5 (5)
Behavioral problem	1 (25)	4 (22)	2 (8)	9 (8)
Drooling	0	8 (44)	5 (20)	67 (63)
Need of feeding tube	0	0	0	9 (8)
Hip dislocation	0	0	4 (16)	13 (12)

¥Strabismus, refractive error, and nystagmus had been included in moderate visual impairment. *Optic atrophy and blindness included in severe visual impairment

RESULTS

Of the 154 children with CP who were enrolled in the study, the mean age was 4.80±3.61 in years. The median age was 4 years. In the present study, male to female ratio was 1.71:1. About 97% of parents of children with CP belonged to the lower and lower-middle of socioeconomic class. About 82% of children were born at term whereas 16% were born preterm. In about 2% (three children), maturity at birth was not ascertained from records. Significant perinatal events were present in the majority (86%) of children with CP. Perinatal asphyxia was present in 63% of children and hypoglycemia in 5%. About 26% of children with a history of perinatal events had either jaundice requiring exchange transfusion, pyogenic meningitis or pneumonia/hyaline membrane disease requiring ventilator care in the neonatal period.

Microcephaly was a significant finding in 65% of children whereas 35% of children had normal head circumference. Macrocephaly was observed in only one child with CP. Based on the topographical classification of CP, 69% of children had quadriplegia, whereas 17% had diplegia and 12% had hemiplegia. Monoplegia was least with 2% of children. In the present study as per physiological classification, 117/154 (76%) of children had spastic CP as predominant type, whereas dyskinetic, hypotonic, and mixed type were observed in 7%, 6%, and 11%, respectively. Malnutrition/undernutrition was observed in 36%.

As decipted in Table 1, comorbidities were dichotomously distributed across topographical subtypes of CP. Intellectual disability/GDD, epilepsy, visual problems, drooling, and other gastrointestinal problems as well as bony and muscular problems were more common in quadriplegic CP compared to other CP types. Intellectual disability/GDD, epilepsy, and visual problems were also seen in many of the children with hemiplegic and diplegic CP. As shown in Table 2, based on physiological classification of CP children, comorbidities were most common in dyskinetic and mixed (spastic+dyskinetic) CP.

On linear regression analysis, we found a strong correlation (Spearman's r> 0.8) between hearing impairment and dyskinetic/mixed CP. Similarly, there was moderate to high correlation (r≥0.7) between GERD and mixed/quadriplegic CP. Refractive errors were seen more commonly (r≥0.7) in hemiplegic (17%) and diplegic CP (16%). Epilepsy was more common in spastic hemiplegic and spastic quadriplegic CP compared to other types.

The functional status from Level I to V for each scale in the children with CP is demonstrated in Fig. 1. GMFCS, MACS, and CFCS levels were distributed disproportionately. About 57% of children with CP had a level of IV or V in CFCS suggesting significant impairment in communication.

As shown in Fig. 2, the functional level distribution of each classification system in the quadriplegic, diplegic, hemiplegic, and monoplegic CP was statistically significant ($p<0.001$). Quadriplegic CP had most of children in Level IV or V as per GMFCS, as shown in Fig. 1 and based on Spearmen's correlation test there was moderate correlation between levels in GMFCS and CFCS (R stat 0.459) and strong correlation between GMFCS and MACS (R stat 0.782).

Table 2: Distribution of comorbidities in different physiological subtypes of cerebral palsy

Comorbidity (%)	Spastic	Dyskinetic	Hypotonic /ataxic	Spastic +Dyskinetic
	(n=117)	(n=11)	(n=9)	(n=17)
GDD/ID*	79	82	67	100
Epilepsy	50	54	33	65
Visual impairment	75	91	78	88
Hearing impairment	5	9	11	6
Drooling	43	64	78	88
GERD[¥]	7	18	0	41

*GDD: Global developmental delay, ID: Intellectual disability, [¥]GERD: Gastroesophageal reflux disease

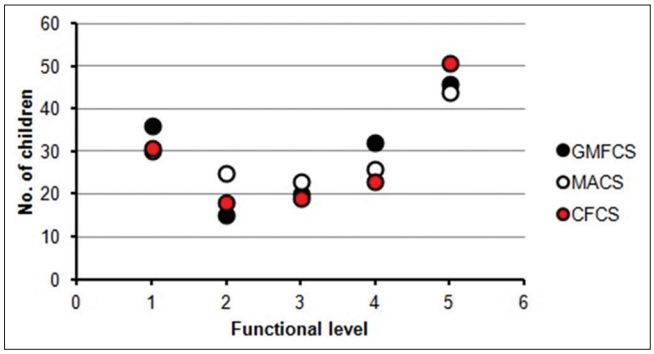

Figure 1: Correlation between gross motor function classification system, manual ability classification system, and communication function classification system in cerebral palsy

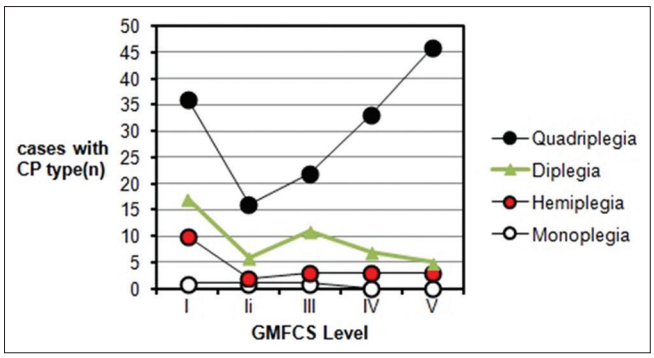

Figure 2: Distribution of gross motor functional classification system levels by types of cerebral palsy

In the present study, as shown in Table 3, we tried to find out the association between GMFCS level and burden of comorbidity and found moderate correlation between most of the comorbidities and GMFCS level.

As shown in Fig. 3, there was strong correlation between increasing GMFCS level and burden of comorbidities.

DISCUSSION

The mean and median age of children with CP in the present study at the time of registration was 57 months (range 3–192 months) and 48 months. The presenting age of CP varies significantly

Table 3: Comorbidity and its association with GMFCS level

Comorbidity	p-value	R stat	Linear correlation
SAM/under nutrition	<0.001	0.460	Moderate positive
Epilepsy	0.67	−0.03	No correlation
Hip dislocation	<0.001	0.488	Moderate positive
Intellectual disability/GDD	<0.001	0.455	Moderate positive
Behavioral problems	<0.001	0.344	Weak positive

GDD: Global developmental delay, SAM: Severe acute malnutrition

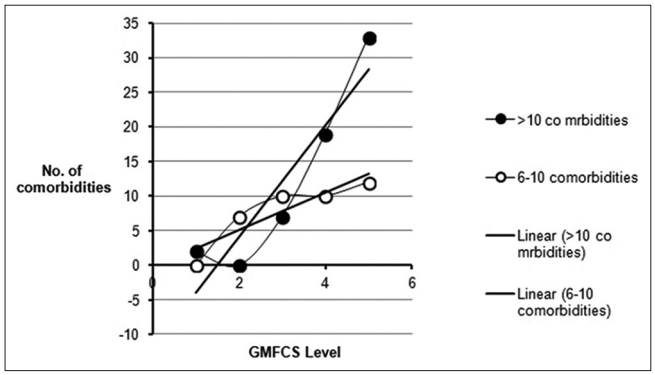

Figure 3: Gross motor function classification system levels and burden of comorbidities in cerebral palsy

across different studies as in studies by Amoghimath *et al*. [2], Mohamed and Ali [9], Venkateswaran and Shevell [22]. This is mainly because of the difference in sociodemographic and referral characteristics. In the present study, referred patients who had been diagnosed earlier were included which increased the possibility of variable age of presentation of CP. Awareness regarding developmental disabilities including CP is increasing in society, but there is a need for early referral and intervention for a better outcome.

Different studies have demonstrated different sex ratio among children with CP. Sex ratio observed in our study of 1.7:1 is correlating with a study by Mohamed and Ali [9]. In a study by Amoghimath *et al*. from South India [2] and Venkateswaran and Shevell from Canada [22], the sex ratio of 1.2–1.48:1 was observed. It is well known that all developmental disabilities are more common in boys compared to girls. The study done in a hospital setting might have different sex ratio than population-based study. Majority of the parents in the present study were of lower and lower-middle socioeconomic class. Similar findings were observed in studies done by Amoghimath *et al*. and Mohamed and Ali [2,9]. Diplegic CP was found to be more common among lower socioeconomic class in a study by Dowding and Barry [23]. No such correlation was found in the present study.

A total of 55% of children in the present study were first-order child whereas 29% were born on the second-order. This finding is comparable with the study by Gowda *et al*. [24]. One of the reasons for this might be better perinatal care-seeking behavior in consecutive pregnancy. We did not find a significant correlation between preterm birth and specific CP type notably diplegia (p>0.05), though periventricular leukomalacia is more common in preterm birth leading to diplegic CP. In the present study, prematurity was documented in 16% of children, which is in accordance with the study by Gowda *et al*. [24]. In our study, perinatal asphyxia was present in 63% of children. In studies by Amoghimath *et al*. and Mohamed and Ali [2,9], birth asphyxia was observed in 43–48% of children with CP. This finding highlights that perinatal asphyxia is the major cause for CP in developing country like India.

In our study, 76% of the cases constituted spastic variety of CP which was comparable with studies across the developing countries notably by Eyong *et al*. [25] and Gowda *et al*. [24]. In the present study, mixed (spastic+dyskinetic) CP was observed in 11% of cases. Spastic or mixed type of CP is more common in term newborn who had suffered perinatal asphyxia/hypoxic ischemic encephalopathy (HIE). In our study, 63% of term newborn suffered perinatal asphyxia/HIE, which usually leads to spastic/mixed type of CP. We observed spastic quadriplegia in 69% of children. The prevalence of 7% cases of dyskinetic CP was comparable with the study by Amoghimath *et al*. and Gowda *et al*. [2,24].

GMFCS, MACS, and CFCS classification system used in the present study are evidence-based, helpful to predict prognosis, help to guide intervention and are standardized systems to measure the severity of movement and communication disability in children with CP [6-10]. Very few studies have correlated the relationship between burden of morbidity and functional status in CP [11-12,14].

Comorbidities were disproportionally distributed across various subtypes and GMFCS levels. Intellectual disability/GDD, visual problems, epilepsy, gastrointestinal problems, drooling, and bony as well as musculoskeletal problems were common. Similar findings have been noted by Venkateswaran and Shevell and Gowda *et al*. [22,24]. Burden of comorbidities was significantly higher among children with bilateral spastic and mixed (spastic+dyskinetic) CP. We did not find a significant association of increasing age with the burden of comorbidities. Management of CP is multidisciplinary and many times burden of comorbidities decides the quality of life rather than diseases itself. Consultants and therapist need to keep a constant vigil on the development of new comorbidities and its prevention for a better outcome.

Good correlation between GMFCS, MACS, and CFCS was observed in the present study. Similar findings have been observed in different CP subtypes in a study by Compagnone *et al*. [26]. We found a strong correlation (R stat 0.782) between GMFCS and MACS levels. We also observed that 62% of cases with quadriplegic CP had GMFCS Level of IV or V whereas 66% cases with hemiplegic CP had GMFCS Level of I or II. This finding can be helpful for counseling of parents regarding expectation about locomotion based on the type of CP. Main concern of parents is usually about the mobility of a child with CP. GMFCS level remains unchanged after 5 years of age so findings of GMFCS level and CP types may be used for counseling of parents. Correlation between GMFCS levels and CP types can also help to understand age-appropriate realistic outcome in CP and about use of assistive mobility devices.

There was a very strong correlation (R stat 0.9) between increasing GMFCS level and increasing the burden of

comorbidities. We also found a moderate correlation between increasing GMFCS level with certain comorbidities such as hip dislocation, severe acute malnutrition/undernutrition, and intellectual disability/GDD. Similar findings were observed in a study by Abas *et al*. [10] and Türkoğlu *et al*. [12] demonstrating a strong correlation between global functional disability profile/GMFCS level and IQ as well as other comorbidities. This finding proves that there is a relationship between motor function disorder and intelligence level, particularly at Stage IV-V, and severe ID. In a study by Venkateswaran and Shevell [22], no significant correlation was found between GMFCS level and comorbidities burden except for feeding difficulty [26].

In a study by Gabis *et al*., 72.4% of patients with CP at GMFCS Level IV-V had ID; this ratio was 0% for patients at the Level I and 40.9% for patients at Level II-III [27]. In a study by Himmelmann *et al*., evaluation of 411 children with CP was done and concluded that with higher levels of GMFCS, the frequency of problems such as comorbid learning disability, visual disorders, and hearing disorders also increased [28]. These findings highlight the need for proper counseling of parents about the high burden of comorbidities with increasing GMFCS level and possible ways to prevent/minimize it for a better outcome and improved quality of life of CP children.

The present study was limited by the collection of data from hospital settings and not community settings and including referred children, which made the age ascertainment difficult.

CONCLUSION

Intellectual disability, malnutrition, epilepsy, bony problems, vision, and hearing problems were the most common comorbidities in CP. Comorbidities were distributed disproportionally across various types of CP. There is a strong correlation between increasing GMFCS level and burden of comorbidities. Inclusion of functional status and screening for comorbidities in every child with CP might improve overall prognosis in children and family with CP.

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