

ORIGINAL ARTICLE

COMORBIDITIES IN CHILDREN WITH CEREBRAL PALSY

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ABSTRACT

Aim: To study comorbidities in children with cerebral palsy (CP).

Methods: This cross-sectional study was conducted over a period of four months, from December 10, 2019 to March 24, 2020 in 88 children with CP aged 6 months to 15 years without other associated chronic pathologies. All data were collected through parental interviews, medical records and physical examination. To assess motor impairment, Gross Motor Function Classification System score (GMFCS) was used. The association between the etiologies of CP, the types of CP, the level of disability and comorbidities were analysed.

Results: The most common morbidity of CP was intellectual impairment in 84 (95.5%), microcephaly in 66 (75%), epilepsy in 61 (69.3%) and nutritional disorders in 48 (54.6%) of which 40 (83.3%) of the patients had stunting, 36 (75%) were underweight, 9 (18.75%) were acutely malnourished and 3 (6.2%) were obese. Digestive disorders were seen in 33 cases of which 31 (93.9%) had constipation, 13 (39.39%) had dysphagia, 6 (18.2%) had gastroesophageal reflux and 22 (66.7%) had oro-facial dyspraxia. Visual impairment was present in 18 cases of which strabismus was present in 10 (55.5%), nystagmus in 6 (33.3%) and blindness in 7 (38.9%) children. Respiratory tract infections were present in 17 (19.3%), urinary tract infections were present in 8 (9%). Orofacial dyspraxia [OR=4.93(95% CI 1.74-13.94)] and nutritional disorders [OR=7.2 (95% CI (2.65-19.57))] were associated with GMFCS V. Intellectual impairment was mild in GMFCS I and severe in GMFCS V (p=0.001). Those with a GMFCS II [OR= 9.44(95% CI (1.99-44.81))] were more likely to have a respiratory infection.

Conclusion: Cerebral palsy is associated with higher prevalence of comorbidities. Improved preventive strategy through adequate perinatal care may reduce incidence of CP.

Introduction

Cerebral palsy (CP) describes a group of permanent disturbances in the development of movement and posture resulting in a limitation of activity, attributed to non-progressive disturbances in the developing brain of the fetus or infant 1. Motor disturbances in CP are often accompanied by disturbances in sensation, perception, cognition, communication and behavior, as well as epilepsy and secondary musculoskeletal disorders.¹ CP is the most common cause of physical disability in children.² It is a real public health problem due to its medical, socio-cultural and economic consequences. In Europe, the prevalence of cerebral palsy is about 2 per 1000 live births.² This prevalence has changed little over the last 10 years with an upward trend despite the

improvement in the quality of obstetric and perinatal care. This is attributed to a high survival rate of newborns, premature and low birth weight babies.² In Cameroon, prevalence of CP has been 18.35% of the neuropediatric pathologies in a tertiary center.³

Although CP is primarily an impairment of motor function, several comorbidities occur in these children due to the brain damage associated with CP and multiple disabilities. This further affects their quality of life and life expectancy. Previous studies have shown epilepsy prevalence of 41.5% and intellectual impairment of 42.96% in CP patients in Cameroon.⁴ In children with CP, the presence or absence of an associated comorbidity is a major determinant of their life quality, functional capacity, and prognosis. A better understanding of these associated disorders is an important contribution to improving their management. Hence, we undertook this study to determine incidence of various comorbidities in children with CP and their associated etiologies.

Methods & Materials

This cross-sectional study was conducted in a

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neuropediatrics unit in a tertiary referral center in Cameroon over a 4-month period from December 10, 2019 to March 24, 2020 in 88 children with CP aged 6 months and 15 years of age. Patients were included in the study after informed consent of the parents and institutional ethical committee approval (N° 986/CIERSH/DM/2020). We excluded child with chronic diseases such as human immunodeficiency virus (HIV) infection, sickle cell disease, asthma and malignancy. Assessment of comorbidities has been made through parent interviews, evaluation of medical records, examination of child. All data were collected on data sheet. The international definition and classification system for CP was used to diagnose children.¹ Data recorded included sociodemographic factors, pregnancy details, birth history, post-natal history, growth and comorbidities. Sought comorbidities were intellectual impairment, epilepsy, microcephaly, motor disability, visual and hearing impairment, nutritional disorders, digestive disorders and acute infections (respiratory and urinary infections). World Health Organization (WHO) child growth standards were used to assess growth using the following growth parameters: weight, height/length, mid-arm circumference, body mass index, weight-for-height, weight-for-age, height-for-age.⁵ It was used for children under 5 years. For those over 5 years we used WHO reference 2007 which is a growth reference data for children and adolescents from 5 to 19 years.⁶ The length of a large number of infants could not be measured exactly because of deformities. According to the anthropometric parameters obtained, the children were classified into 4 groups: good nutritional status, stunted growth, underweight, obesity. To evaluate mental development, we used two tools: DENVER II scale for children aged 0 to 6 years old⁷ and BINET-SIMON intelligence scale for children over 6 years.⁸ Intellectual impairment was considered when children had not achieved common developmental milestones for age on time, according to DENVER II scale. It was also considered in the absence of reasoning, poor working memory and severe behavioral disorders. Visual impairment was evaluated during neurologic examination by testing the response to light contrast with a black and white contrasted target. The test was based on the child's ability to show steady fixation of a target and to follow the target using smooth pursuit movements. Strabismus was considered when the eyes did not look in the same direction at the same time. Nystagmus was considered when child presented rapid oscillating eye movements. Hearing impairment was considered when child failed to respond to mild level spoken voice or deafness diagnosed by hearing test. Evoked otoacoustic emissions and tympanometry were used to assess hearing impairment. To assess motor impairment we used Gross Motor Function Classification System score (GMFCS). It was classified as 'walking without restriction'(GMFCS I -II), 'walking with hand-held mobility device'(GMFCS III), 'wheeled mobility '(GMFCS IV), 'self-mobility severely limited'(GMFCSV). The variables were subdivided into sociodemographic variables (age, sex), clinical variables: maternal history, prenatal history, birth history, postnatal history, age of diagnosis of CP, level of disability according to GMFCS, types of cerebral palsy,

etiologies of CP. The comorbidities associated with CP were intellectual impairment, epilepsy, microcephaly, visual impairment, deafness, digestive disorders, oro-facial dyspraxia, nutritional disorders, respiratory tract infection and urinary tract infection. Digestive disorders sought were various: swallowing disorders, gastroesophageal reflux (GER), vomiting, chronic constipation and abdominal pain. We also considered chronic pulmonary aspiration as a frequent complication of digestive disorder. Diagnosis of GER was clinical due to unavailability of pH studies and based on history of reflux, arching, vomiting, and/or chronic pulmonary aspirations. Other digestive disorders were diagnosed during parents interview and physical examination.

Statistical analysis

The study data were entered and analysed using Epi Info 7.2.2.6 and excel 2016. The chi-square test and Fisher's exact test were used to compare the association between the etiologies of CP, the types of CP, the level of disability and comorbidities. The Odd's ratio and the 95% confidence interval were used to assess the strength of association between the variables. The significance threshold was $p < 0.05$.

Results

Of 88 children, male: female ratio was 49:39. The median age of children was 38 months. (IQR:15.5-68). Etiologies of CP were found in 85 (96.6%) cases. Perinatal asphyxia was the most frequent etiology in 48 (54.6%), followed by epileptic disorders in 11 (12.1%), kernicterus and embryofetopathy in 8 (9.1%) each, congenital brain malformation in 7 (7.9%), prematurity and meningitis in the first month in 5 (5.7%) children each and in 3 (3.4%), the etiology was unknown. Spastic quadriplegia was the commonest type of CP in 66 (75.8%) followed by spastic hemiplegia in 8 (9.2%), choreoathetosis in 6 (6.9%), mixed form of CP in 3 (4.6%), spastic diplegia in 2 (2.3%) and cerebellar ataxia in 1 (1.2%). GMFCS V disability was present in 26 (40.6%), GMFCS IV was seen in 13 (20.3%), GMFCS III and II was seen in 8 (12.5%) each and GMFCS I was seen in 9 (14.1%) patients. The most common morbidity of CP was intellectual impairment in 84 (95.5%), microcephaly in 66 (75%), epilepsy in 61 (69.3%) of which 30 (49.2%) had focal epilepsy, 14 (23%) had West syndrome, 12 (19.7%) had generalised epilepsy and 5 (8.2%) had indetermined epilepsy. Nutritional disorders were seen in 48 (54.6%). Among them, 40 (83.3%) had stunting, 36 (75%) were underweight, 9 (18.75%) were acutely malnourished and 3 (6.2%) were obese. Digestive disorders were seen in 33 (37.5%). Among them, 31 (93.9%) had constipation, 13 (39.39%) had dysphagia, 6 (18.2%) had gastroesophageal reflux and 22 (66.7%) had oro-facial dyspraxia. Visual impairment was present in 18 (20.5%) of which strabismus was present in 10 (55.5%), nystagmus in 6 (33.3%) and blindness in 7 (38.9%) children. Three (3.4%) children were deaf. Respiratory tract infections were present in 17 (19.3%), urinary tract infections were present in 8 (9%).

Co-morbidities and association with GMFCS score are depicted in Tables 1 and 2.

Orofacial dyspraxia [OR=4.93(95% CI 1.74-13.94)]

and nutritional disorders [OR=7.2 (95% CI (2.65-19.57))] were associated with GMFCS V. Intellectual impairment was mild in GMFCS I and severe in GMFCS V (p=0.001).

Co-morbidities found were commoner in children with

spastic quadriplegia type compared to the others type: 77% epilepsy, 78.8 % microcephaly, 73.8 % intellectual impairment, 94.4% visual impairment, 75 % nutritional disorders, 81.8% digestive disorders, 81.8 % oro-facial dyspraxia, 76.5% respiratory infection and 50% urinary tract infection (Table 3).

Table 1. Relationship between comorbidities (nutritional disorders, digestive disorders, oro-facial dyspraxia, respiratory infection, urinary tract infection) and degree of disability

Degree of disability	Comorbidities		OR (95% CI)	p value
	Yes (%)	No (%)		
Nutritional disorders (n=48)				
GMFCS 1	2 (16.7)	10 (83.3)	0.13 (0.03-0.64)	0.001
GMFCS 2	2 (20)	8 (80)	0.17 (0.03-0.85)	
GMFCS 3	3 (27.3)	8 (72.7)	0.27 (0.07-1.1)	
GMFCS 4	12 (63.2)	7 (36.8)	1.57 (0.55-4.46)	
GMFCS 5	29 (80.5)	7 (19.5)	7.2 (2.65-19.57)	
Digestive disorders (n=33)				
GMFCS 1	2 (12.5)	14 (87.5)	0.19 (0.04-0.9)	0.014
GMFCS 2	2 (13.3)	13 (86.7)	0.21 (0.04-1)	
GMFCS 3	8 (53.3)	7 (46.7)	2.19 (0.71-6.74)	
GMFCS 4	6 (46.2)	7 (53.8)	1.52 (0.46-4.99)	
GMFCS 5	15 (51.7)	14 (48.3)	2.44 (0.98-6.09)	
Oro-facial dyspraxia (n=22)				
GMFCS 1	1 (9.1)	10 (90.9)	0.27 (0.03-2.24)	0.009
GMFCS 2	1 (4.8)	20 (95.2)	0.11 (0.01-0.87)	
GMFCS 3	1 (11.1)	8 (88.9)	0.35 (0.04-2.97)	
GMFCS 4	4 (33.3)	8 (66.7)	1.61 (0.43-5.98)	
GMFCS 5	15 (42.9)	20 (57.1)	4.93 (1.74-13.94)	
Respiratory infection (n=17)				
GMFCS 1	1 (5.3)	18 (94.7)	0.18 (0.02-1.46)	0.002
GMFCS 2	5 (62.5)	3 (37.5)	9.44 (1.99-44.81)	
GMFCS 3	1 (12.5)	7 (87.5)	0.57 (0.07-4.97)	
GMFCS 4	5 (38.5)	8 (61.5)	3.28 (0.92-11.76)	
GMFCS 5	5 (12.5)	35 (87.5)	0.43 (0.14-1.35)	
Urinary tract infection (n=8)				
GMFCS 1	0 (0)	9 (100)	-	0.508
GMFCS 2	1 (14.3)	6 (85.7)	1.76 (0.18-16.77)	
GMFCS 3	0 (0)	8 (100)	-	
GMFCS 4	3 (18.75)	13 (81.25)	3.09 (0.66-14.55)	
GMFCS 5	4 (8.3)	44 (91.7)	0.82 (0.19-3.51)	

Table 2. Relationship between comorbidities (epilepsy, mental retardation, microcephaly, visual impairment) and degree of disability

Degree of disability	Comorbidities		p value
	Yes (%)	No (%)	
	Epilepsy (n=61)		
GMFCS 1	7 (36.8)	12 (63.2)	0.003
GMFCS 2	7 (87.5)	1 (12.5)	
GMFCS 3	4 (50)	4 (50)	
GMFCS 4	10 (76.9)	3 (23.1)	
GMFCS 5	33 (82.5)	7 (17.5)	
	Intellectual Impairment (n=84)		
GMFCS 1	6 (60)	4 (40)	0.001
GMFCS 2	8 (100)	0 (0)	
GMFCS 3	8 (100)	0 (0)	
GMFCS 4	13 (100)	0 (0)	
GMFCS 5	49 (100)	0 (0)	
	Microcephaly (n=66)		
GMFCS 1	6 (40)	9 (60)	0.014
GMFCS 2	7 (87.5)	1 (12.5)	
GMFCS 3	6 (75)	2 (25)	
GMFCS 4	18 (85.7)	3 (14.3)	
GMFCS 5	29 (73.1)	7 (19.5)	
	Visual impairment (n=18)		
GMFCS 1	2 (12.5)	14 (87.5)	0.001
GMFCS 2	1 (6.7)	14 (93.3)	
GMFCS 3	0 (0)	10 (100)	
GMFCS 4	0 (0)	13 (100)	
GMFCS 5	15 (44.1)	19 (55.9)	

Table 3. Comorbidities in different type of CP.

Comorbidities	PC type						Total n(100%)
	Spastic quadriplegia n (%)	Spastic hemiplegia n (%)	Spastic diplegia n (%)	Choreo-athetosis n (%)	Cerebellar Ataxia n (%)	Mixed Form n (%)	
Epilepsy	47 (77.1)	7 (11.5)	1 (1.6)	3(4.9)	2 (3.3)	1(1.6)	61(100)
Microcephaly	52 (78.8)	6 (9.1)	1 (1.5)	4(6.1)	1 (1.5)	2(3)	66(100)
Intellectual impairment	62 (73.8)	6 (7.1)	4 (4.8)	6(7.1)	2 (2.4)	4(4.8)	84(100)
Visual impairment	17 (94.4)	1 (5.6)	0	0	0	0	18(100)
Nutritional disorders	36 (75)	2 (4.2)	2 (4.2)	6(12.4)	1 (2.1)	1 (2.1)	48(100)
Digestive disorders	17 (81.8)	1 (3)	0	0	2 (6.1)	3 (9.1)	33(100)
Oro-facial dyspraxia	18 (81.8)	1 (100)	0	0	1 (100)	2 (100)	22(100)
Respiratory infection	13 (76.5)	0	1 (5.9)	3(17.6)	0	0	17(100)
Urinary infection	4 (50)	0	1 (12.5)	3(37.5)	0	0	8(100)

Discussion

In our study population, we had a slight male predominance. This is in line with Mbonda et al⁴ who obtained a sex ratio of 1.3 with a male predominance, as well as Nguefack et al³ also noted a male predominance with a sex ratio of 1.62. This male dominance may be related to the fact that the interaction between hormonal modulation and genetically determined apoptotic mechanisms offers girls a certain degree of protection against hypoxic-ischaemic perinatal brain damage compared to boys.⁹

In our study, the main aetiologies were perinatal asphyxia followed by epileptic disorders and embryofetopathy. Similarly, Bhati et al¹⁰ in India in 2019 also found perinatal asphyxia as a major cause in 67.4% of cases. Minocha et al¹¹ in India in 2017 noted seizure disorder as a second cause of CP. Mbonda et al⁴ noted perinatal asphyxia in 43.8% of cases, and neonatal infections in 22.5% of cases. The predominance of perinatal asphyxia may be due to the low socio-economic level of the population, the absence of pregnancy monitoring and deliveries in health centres without trained personnel.

Spastic quadriplegia was the main clinical form of CP in our study followed by spastic hemiplegia, choreoathetosis, and spastic diplegia. These data are similar to those of Nguefack et al³ who noted 67.9% and 17.2% respectively for spastic tetraparesis and spastic hemiplegia. These findings are significantly higher than those of Bearden et al¹² in Botswana in 2016 who showed 46% with spastic quadriplegia and 24% with spastic hemiplegia respectively, 4% with spastic hemiplegia. The predominance of spastic quadriplegia may be due to the fact that it is strongly correlated with the presence of ischaemic lesions due to perinatal asphyxia, which is the main aetiology of CP in our context. More than half of the children had a severe disability with 40.6% and 20.3% respectively with a GMFCS V and IV. This result is in agreement with Bearden et al¹², who revealed that severe motor disability was predominant, with 41% with GMFCS V and 16% with a GMFCS IV. The majority of severe disability is due to the preponderance in our study of spastic quadriplegia, the most severe CP clinical type.

Intellectual impairment (95.4%) is the most frequent comorbidity. Similarly, Bearden et al¹² found a frequency of intellectual impairment of 82%. This is much higher than the frequency found by Mbonda et al⁴, which was 42.9%. Similarly, Moifo et al¹³ reported intellectual impairment in 40.2% of cases. This significant difference may be due to the fact that the patients with severe intellectual impairment are those with spastic quadriplegia, which is widely represented in our study in almost 76% of cases.

Microcephaly occurred in 75% of patients. This frequency is much higher than that found by Moifo et al¹³ who showed 40.1%, and Kakooza et al¹⁴ noted 33.7%. This can be explained by the fact that in our study the major aetiology was perinatal asphyxia with major destruction of neurons.

Epilepsy had a frequency of 69.3%, this finding is not very far from that of Nguefack et al³ who found epilepsy in 57.5% , however Mbonda et al⁴ found epilepsy in

41%. This high frequency may be due to the high proportion of spastic quadriplegia in our study, which may be related to the cortical damage and the severity of the brain lesions.

In our study, more than half of the population had nutritional disorders (54.6%), almost 83.3% of the patients had stunting, 75% were underweight and 18.75% were acutely malnourished. These results are similar to those of Kakooza et al¹⁵, who noted the presence of nutritional disorders in 52% of cases, underweight in 42%, and 38% were stunted. Nguefack et al³ found 22.2% of children to be underweight, and 31.3% to be stunted. Poor growth is multifactorial.¹⁶ This is due to inadequate nutrient intake (poor head posture, gastroesophageal reflux, oro-facial dyspraxia), environmental factors, and endocrine factors including growth hormone deficiency. Studies revealed that children with choreoathetosis and mixed forms had and an accelerated metabolism with energy needs not covered by losses, due to uncontrolled jerky movements and hypertonia of spastic forms.¹⁶

Concerning digestive disorders (37.9%), constipation was seen in 35.6% of cases, this result is not very far from that of Park et al¹⁷ in the United States who found 26.3%. Thus a delay in transit is due to an alteration in the motility of the smooth muscles of the colon and the activity of the striated muscles of the anal sphincter, associated with the permanent immobility of these children.¹⁷ Oro-facial dyspraxia was seen in 25.6% of cases, dysphagia was seen in 14.9% and gastroesophageal reflux was seen in 6.9% of cases. These digestive disorders were also found by Caramico-Favero et al¹⁸ but dysphagia was the most frequent digestive disorder, seen in 82.5% and all symptoms were associated with different food intake patterns. Damage to the developing central nervous system may result in significant dysfunction in the gastrointestinal tract and is reflected in impairment in oral-motor function, gastro-oesophageal reflux, delayed gastric emptying, and constipation.¹⁹

Furthermore, visual impairment was observed in 18 cases (20.45%): strabismus in 10 (55.5%), blindness in 7 (38.9%), and nystagmus in 6 (33.3%). Some children had more than one visual impairment type. Nguefack et al³ also found that strabismus was the most frequent visual impairment (21.6%), followed by blindness (8.2%) and nystagmus (2.2%). Most often, visual disorders in children with CP are due to a lesion in the retro chiasmatic pathway and other cerebral areas involved in the perception and processing of visual stimuli.²⁰

The occurrence of a respiratory tract infection has been recorded in 19.54% of the population, in agreement with Chen et al²¹ who found 28.6% of cerebral palsy patients with a respiratory infection. Excessive secretions due to GER or swallowing disorders, inefficient coughing will lead to an inefficient clearance of secretions and thus favour respiratory infections.²²

UTI was revealed in 9% of cases, which is not very different from the prevalence of Ryakitimbo et al²³ in Tanzania in 2018, which was 13.1%. Constipation would have an impact on the occurrence of urinary tract infection.²⁴ Factors that increase the risk of acquiring

urinary tract infection in CP include low cognition, limited ability to communicate the need to void, impaired mobility, and bladder dysfunction.²³

Patients with GMFCS V were at greater risk of developing nutritional disorders and orofacial dyspraxia. Indeed, Bearden et al¹² found that malnutrition is more frequent in subjects with GMFCS \geq IV. The more severe the motor disability, the more difficult it will be for the child to feed himself properly, which will inevitably lead to malnutrition.

We noticed that a GMFCS \geq II was a risk of respiratory infection. For Prastiya et al²⁵ pneumonia was the main cause of death. Similarly, they found that the GMFCS score was an important factor in mortality. GMFCS I had lesser incidence of intellectual impairment in our study compared to other GMFCS scores where it was 100%. Bearden et al¹² demonstrated that brain performance is highly correlated with the GMFCS Score. The results of systematic review suggest that severe motor impairments are associated with higher intellectual disability. Hamid et al²⁶ found that children with GMFCS I to IV had a higher intellectual level in comparison with children at level V.

Conclusion

Perinatal asphyxia was the leading cause of CP. Spastic quadriplegia was the main clinical form, causing severe disability. Comorbidities found were commoner in children with spastic quadriplegia type compared to the others type. Intellectual impairment, epilepsy, microcephaly and nutritional disorders were the main comorbidities. Patients with spastic hemiplegia were less likely to be mentally retarded. We found that severe motor disability was associated to nutritional disorders and oro-facial dyspraxia. The less severe the motor disability, the less mental impairment is observed.

Authors Contribution

SN, DE, DN, RB, FND conceived, designed and organized the study. SN, FND, DK, EM coordinated and monitored the study. RB, CANK collected and analysed anthropometrics data and wrote the initial manuscript. CANK, DK, SN critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Compliance with Ethical Standards

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