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Determinants of Higher GMFCS Levels in Children with Cerebral Palsy: A Retrospective Single-Centre Study

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Abstract

Objective

To identify factors associated with higher Gross Motor Function Classification System (GMFCS) levels in children with cerebral palsy.

Methods

This retrospective single-centre study included children with cerebral palsy aged 2–18 years who were assessed between January 2017 and December 2023. Gross motor function was classified using the five-level GMFCS. Demographic, perinatal, maternal, clinical, socioeconomic, and rehabilitation-related variables were collected from medical records and caregiver interviews. Factors associated with higher GMFCS levels were examined using univariable and multivariable ordinal logistic regression.

Results

A total of 424 children were included. In the adjusted ordinal logistic regression model, breastfeeding was associated with lower odds of higher GMFCS levels (adjusted odds ratio [AOR] = 0.378, 95% confidence interval [CI]: 0.260–0.551, p < 0.001). Low smoking exposure during pregnancy (AOR = 1.841, 95% CI: 1.236–2.742, p = 0.003), moderate/high smoking exposure during pregnancy (AOR = 2.773, 95% CI: 1.204–6.388, p = 0.017), occasional alcohol exposure during pregnancy (AOR = 1.621, 95% CI: 1.019–2.578, p = 0.041), and neonatal asphyxia (AOR = 1.970, 95% CI: 1.359–2.855, p < 0.001) were independently associated with higher GMFCS levels. CP subtype and topographical distribution were not independently associated with higher GMFCS levels after adjustment.

Conclusion

Maternal smoking exposure, occasional alcohol exposure during pregnancy, and neonatal asphyxia were associated with greater gross motor impairment in children with cerebral palsy, whereas breastfeeding was associated with lower GMFCS levels. These findings should be interpreted as associations rather than causal effects.

Clinical trial registration

Not applicable.

1. Introduction

Cerebral palsy (CP) describes a group of permanent disorders of movement and posture caused by non-progressive disturbances in the developing fetal or infant brain (1, 2). Although the primary manifestation of CP is motor dysfunction, affected children frequently present with additional impairments, including epilepsy, cognitive impairment, communication disorders, sensory deficits, feeding difficulties, and secondary musculoskeletal problems (3, 4). CP is one of the leading causes of childhood-onset physical disability worldwide, with substantial long-term effects on mobility, self-care, education, social participation, caregiver burden, and healthcare resource use (5, 6). Therefore, beyond diagnosis itself, the assessment of functional severity is essential for prognosis, treatment planning, rehabilitation allocation, and family counselling.

The Gross Motor Function Classification System (GMFCS) is widely used to classify gross motor function in children with CP (7–9). Unlike descriptive motor subtype or topographical classification, GMFCS provides a five-level functional classification based on self-initiated movement, sitting, transfers, walking ability, and use of mobility devices (8, 9). Higher GMFCS levels indicate greater limitation in gross motor function and are associated with greater dependence, higher need for assistive devices, increased rehabilitation demand, and greater family and social burden (4, 10, 11). Longitudinal studies have shown that GMFCS levels are useful for describing motor developmental trajectories and predicting functional prognosis in children with CP (10, 12). Accordingly, identifying factors associated with higher GMFCS levels may help clinicians recognise children at greater risk of severe motor limitation and support earlier, more targeted management.

A large body of literature has examined risk factors for the development of CP, including prematurity, low birth weight, fetal growth restriction, pregnancy infection, neonatal encephalopathy, perinatal hypoxic–ischaemic injury, and maternal exposures during pregnancy (13–15). However, factors associated with the occurrence of CP are not necessarily the same as factors associated with motor severity among children who already have CP (15). This distinction is clinically important. For example, prematurity and low birth weight are well-established risk factors for CP, but their independent relationship with GMFCS severity after a diagnosis of CP remains less consistent. Similarly, neonatal asphyxia, maternal smoking, alcohol exposure, infection during pregnancy, breastfeeding, comorbidities, socioeconomic conditions, and access to rehabilitation may influence functional severity directly or indirectly through different biological, developmental, and healthcare pathways (3, 15).

Previous studies on functional outcomes in CP have several limitations. First, some studies have focused mainly on the aetiology of CP rather than on determinants of motor severity within CP populations(16, 17). Second, GMFCS has often been dichotomised into broad “mild” and “severe” categories, which may lead to loss of information and reduced statistical power(8, 18). Third, important clinical and social confounders, such as CP subtype, topographical distribution, epilepsy, cognitive impairment, parental socioeconomic status, and access to rehabilitation services, have not always been considered(19, 20). Fourth, some perinatal and maternal variables have been measured using simple binary categories, although the timing, severity, and dose of exposure may be clinically relevant. These

limitations may partly explain inconsistencies in reported associations between early-life factors and motor outcomes in children with CP.

To address these gaps, the present study investigated demographic, maternal, perinatal, clinical, socioeconomic, and rehabilitation-related factors associated with GMFCS levels in children with CP. GMFCS was retained as a five-level ordinal outcome rather than dichotomised, allowing a more detailed assessment of factors related to increasing motor severity. We aimed to identify factors associated with higher GMFCS levels among children with CP, with the goal of providing evidence for risk stratification, rehabilitation planning, and future prospective research on motor outcomes in this population(21, 22) .

2. Materials and Methods

2.1 Study subjects

This retrospective single-centre study included children with cerebral palsy who were assessed at the Cerebral Palsy Centre of the Second Affiliated Hospital of Xinjiang Medical University between January 2017 and December 2023. Children were eligible if they met the established diagnostic criteria for cerebral palsy, were aged 2–18 years at the time of gross motor function assessment, and had available clinical, perinatal, and rehabilitation assessment data. Children were excluded if they had progressive neurological disorders, neurodegenerative diseases, inherited metabolic diseases mimicking cerebral palsy, or cerebral palsy acquired after the neonatal period. Children who had undergone major spasticity-reducing surgery or major orthopaedic reconstructive surgery within 6 months before assessment were also excluded. Cases with missing GMFCS assessment data or insufficient key clinical and perinatal information were excluded from the final analysis. The final analytic cohort included 424 children.

2.2 Motor function evaluation

Gross motor function was assessed using the Gross Motor Function Classification System (GMFCS), which classifies motor function in children with cerebral palsy into five ordered levels (8, 9). GMFCS level I indicates the least limitation in gross motor function, whereas level V indicates the most severe limitation. In the present study, GMFCS level was retained as a five-level ordinal outcome rather than dichotomised.

GMFCS assessment was performed at the time of clinical evaluation by trained rehabilitation physicians. When necessary, information from medical records, rehabilitation assessments, and caregiver reports was reviewed to support classification. The primary outcome was higher GMFCS level, indicating greater gross motor impairment.

2.3 Data collection and definition of variables

Data were collected from hospital medical records, perinatal records, rehabilitation assessment records, and caregiver interviews. Medical records were used as the primary data source, whereas caregiver-reported information was used only when medical records were unavailable or incomplete. Demographic

and clinical variables, including sex, age at GMFCS assessment, CP subtype, topographical distribution, epilepsy, cognitive impairment, and GMFCS level, were extracted from admission records and rehabilitation assessments. Perinatal variables, including gestational age, birth weight, Apgar score, neonatal resuscitation, neonatal asphyxia, and hypoxic ischaemic encephalopathy, were extracted from birth records and neonatal medical records when available. Neonatal asphyxia was defined as a clinically documented diagnosis of neonatal asphyxia in birth or neonatal medical records. When available, the diagnosis was supported by one or more of the following findings: low Apgar score at 1 or 5 minutes, need for neonatal resuscitation, evidence of respiratory depression after birth, metabolic acidosis, or a documented diagnosis of hypoxic–ischaemic encephalopathy. Because umbilical cord blood gas data were not available for all children, neonatal asphyxia was analysed as a binary variable based on documented clinical diagnosis rather than uniformly confirmed biochemical criteria.

Maternal pregnancy-related variables, including infection during pregnancy, nutritional status, smoking exposure, and alcohol exposure, were extracted from antenatal care records and supplemented by caregiver interviews when necessary.

Maternal nutritional status during pregnancy was defined using clinically documented maternal undernutrition or malnutrition-related indicators. When available, pre-pregnancy or early-pregnancy body mass index, gestational weight gain, hemoglobin level, and physician-documented malnutrition were recorded. Maternal undernutrition was defined as pre-pregnancy or early-pregnancy BMI < 18.5 kg/m² or a documented clinical diagnosis of undernutrition or malnutrition during pregnancy. If only caregiver-reported poor nutrition was available, it was recorded as self-reported nutritional insufficiency rather than clinically confirmed malnutrition.

Maternal smoking exposure during pregnancy was categorized into three groups: no exposure, low exposure, and moderate/high exposure. No exposure was defined as no active smoking and no regular passive smoking during pregnancy. Low exposure was defined as passive smoking exposure or active smoking of 1–5 cigarettes per day. Moderate/high exposure was defined as active smoking of more than 5 cigarettes per day. When available, the timing of smoking exposure was recorded by trimester.

Maternal alcohol exposure during pregnancy was defined as any reported or clinically documented alcohol consumption by the mother from conception to delivery. Alcohol exposure was classified into three categories according to the reported frequency and amount of intake. No exposure was defined as complete abstinence from alcohol throughout pregnancy. Occasional exposure was defined as alcohol consumption less than once per week, without daily drinking or binge-drinking episodes. Regular/heavy exposure was defined as alcohol consumption at least once per week, daily alcohol use, or any episode of binge drinking during pregnancy. Binge drinking was defined as consuming four or more standard drinks on one occasion. One standard drink was defined as approximately 10 g of pure alcohol. Because the number of children with regular/heavy alcohol exposure was small, regular and heavy alcohol exposure were combined into one category for statistical analysis.

Access to rehabilitation services was assessed using residence, travel distance or travel time to the hospital or rehabilitation facility, regular rehabilitation before GMFCS assessment, and age at rehabilitation initiation. One point was assigned for each access barrier: rural residence, travel distance > 50 km or travel time > 1 hour, no regular rehabilitation before GMFCS assessment, defined as less than one rehabilitation session per week, and rehabilitation initiation after 12 months of age. The total score ranged from 0 to 4 and was categorized as good access (0–1 point), moderate access (2 points), and poor access (3–4 points).

Parental occupation was recorded for both parents when available and classified according to the highest parental occupational class. Occupation was categorized into three groups: stable/non-manual occupation, service/self-employed/skilled work, and agricultural/manual/unstable employment. Stable/non-manual occupation included professional, administrative, managerial, and office-based occupations. Service/self-employed/skilled work included service workers, self-employed workers, sales workers, drivers, and skilled manual workers. Agricultural/manual/unstable employment included agricultural workers, unskilled manual workers, temporary workers, unemployed parents, and parents without stable employment.

Parental education was recorded for both parents when available. The highest parental education level was used as the socioeconomic education indicator for analysis. Education level was categorized into three groups: junior high school or below, senior high school or technical secondary school, and college or above. When the number of cases in individual categories was limited, education level was further collapsed into two groups: junior high school or below and senior high school or above.

Socioeconomic status was classified into high, middle, and low categories based on the highest parental education level and highest parental occupational class. High socioeconomic status was defined as college-level parental education or stable/non-manual parental occupation. Middle socioeconomic status was defined as senior high school or technical secondary school education or service/self-employed/skilled work. Low socioeconomic status was defined as junior high school or below education or agricultural/manual/unstable employment. When parental education and occupational class were inconsistent, the lower socioeconomic category was used for conservative classification.

Pregnancy infection was defined as a clinically documented maternal infection occurring from conception to delivery. Medical records and antenatal care records were used as the primary sources, whereas caregiver-reported information was used only when records were unavailable or incomplete. When available, infection type and timing were recorded for descriptive purposes; infection type was classified as respiratory tract, urinary tract, genital tract, gastrointestinal, TORCH-related, other, or unspecified infection, and timing was categorized by trimester. Because the number of infection cases was limited, infection type and trimester-specific variables were not included separately in the main bivariate or multivariable analyses; instead, any documented pregnancy infection was used as the main infection variable in the regression models.

2.4 Statistical analysis

Continuous variables were assessed for distribution. Non-normally distributed continuous variables were presented as median and interquartile range and compared across GMFCS levels using non-parametric tests. Categorical variables were presented as number and percentage and compared using the chi-square test or Fisher's exact test, as appropriate. Because GMFCS is an ordered five-level classification, ordinal logistic regression was used to examine factors associated with higher GMFCS levels. Univariable ordinal logistic regression was first performed to estimate crude odds ratios (CORs) and 95% confidence intervals (CIs). Variables with clinical relevance or $p < 0.20$ in bivariate analysis were considered for inclusion in the multivariable ordinal logistic regression model. Adjusted odds ratios (AORs), 95% CIs, and p-values were reported. Multicollinearity among candidate independent variables was assessed before multivariable modelling using the variance inflation factor. Missing data were evaluated before analysis. The primary analysis was conducted using complete cases, and no statistical imputation was performed. A two-sided p-value < 0.05 was considered statistically significant. Statistical analyses were performed using standard statistical software.

3. Results

3.1. Baseline characteristics :

A total of 424 children with cerebral palsy were included in the final analysis. Among them, 240 were male (56.6%) and 184 were female (43.4%). The median age at GMFCS assessment was 7 years (interquartile range, 5–10 years). Regarding cerebral palsy subtype, spastic cerebral palsy was the most common type, observed in 232 children (54.7%), followed by mixed cerebral palsy in 178 children (42.0%) and athetoid cerebral palsy in 14 children (3.3%). When grouped for regression analysis, 232 children (54.7%) were classified as having spastic CP and 192 (45.3%) as having non-spastic or mixed CP. Bilateral involvement was observed in 256 children (60.4%), and unilateral involvement in 168 (39.6%). The distribution of GMFCS levels was as follows: 39 children (9.2%) were classified as level I, 175 (41.3%) as level II, 78 (18.4%) as level III, 67 (15.8%) as level IV, and 65 (15.3%) as level V. GMFCS level II was the most frequent classification in this cohort, whereas level I was the least frequent (Table. 1).

3.2. Bivariate analysis

The distribution of candidate variables across GMFCS levels I–V is shown in Table 2. In bivariate analysis, significant differences across GMFCS levels were observed for age at GMFCS assessment ($p = 0.003$), CP subtype ($p < 0.001$), gestational age ($p = 0.001$), birth weight ($p = 0.005$), breastfeeding history ($p < 0.001$), smoking exposure during pregnancy ($p < 0.001$), alcohol exposure during pregnancy ($p < 0.001$), and neonatal asphyxia ($p < 0.001$).

Table 1
Baseline data .

Variable	Total cohort (n = 424)
Sex, n (%)	
Male	240 (56.6%)
Female	184 (43.4%)
Age at GMFCS assessment, years, median (IQR)	7 (5, 10)
Cerebral palsy classification, n (%)	
Spastic cerebral palsy	232 (54.7%)
Mixed cerebral palsy	178 (42.0%)
Athetoid cerebral palsy	14 (3.3%)
Topographical distribution, n (%)	
Bilateral involvement	256 (60.4%)
Unilateral involvement	168 (39.6%)
GMFCS, n (%)	
Level I	39 (9.2%)
Level II	175 (41.3%)
Level III	78 (18.4%)
Level IV	67 (15.8%)
Level V	65 (15.3%)

Table 2
Distribution of candidate variables across GMFCS levels I–V.

Factors(self-variable name)	GMFCS I (n = 39)	GMFCS II (n = 175)	GMFCS III (n = 78)	GMFCS IV (n = 67)	GMFCS V (n = 65)	p-Value
Gender, n (%)						0.116
Male (240, 56.6%)	18	96	51	43	32	
Female (184, 43.4%)	21	79	27	24	33	
CP subtype, n (%)						< 0.001
Spastic CP (232, 54.7%)	8	117	37	38	32	
Non-spastic or mixed CP (192, 45.3%)	31	58	41	29	33	
Topographical distribution, n (%)						0.857
Bilateral involvement (256, 60.4%)	24	102	51	39	40	
Unilateral involvement (168, 39.6%)	15	73	27	28	25	
Age at GMFCS assessment (7, 5–10)	9	8	6	7	6	0.003
2-<4 years (46, 10.8%)	2	14	11	11	8	
4-<6 years (103, 24.3%)	6	40	20	13	24	
6-<12 years (216, 50.9%)	22	93	40	37	24	
12–18 years (59, 13.9%)	9	28	7	6	9	
Age of mother (24, 22–28)	23	25	24.5	24	24	0.808
Age of father (26, 22–28)	25	25	26	26	26	0.572
Gestational age, n (%)						0.001
>=37 weeks (280, 66.0%)	24	125	48	39	44	

Factors(self-variable name)	GMFCS I (n = 39)	GMFCS II (n = 175)	GMFCS III (n = 78)	GMFCS IV (n = 67)	GMFCS V (n = 65)	p-Value
32–37 weeks (74, 17.5%)	13	18	21	10	12	
< 32 weeks (70, 16.5%)	2	32	9	18	9	
Birth weight, n (%)						0.005
>=2500 g (305, 71.9%)	30	123	52	48	52	
1500–2499 g (99, 23.3%)	8	49	22	10	10	
< 1500 g (20, 4.7%)	1	3	4	9	3	
Breast milk, n (%)						< 0.001
Yes (212, 50.0%)	26	117	24	24	21	
No (212, 50.0%)	13	58	54	43	44	
Smoking during pregnancy, n (%)						< 0.001
No exposure (258, 60.8%)	24	140	30	32	32	
Low exposure (149, 35.1%)	15	33	42	29	30	
Moderate/high exposure (17, 4.0%)	0	2	6	6	3	
Drinking during pregnancy, n (%)						< 0.001
No exposure (347, 81.8%)	33	159	46	53	56	
Occasional exposure (70, 16.5%)	3	15	30	13	9	
Regular/heavy exposure (7, 1.7%)	3	1	2	1	0	
Neonatal asphyxia, n (%)						< 0.001
Yes (181, 42.7%)	17	54	31	45	34	
No (243, 57.3%)	22	121	47	22	31	
Delivery mode, n (%)						0.800

Factors(self-variable name)	GMFCS I (n = 39)	GMFCS II (n = 175)	GMFCS III (n = 78)	GMFCS IV (n = 67)	GMFCS V (n = 65)	p-Value
Vaginal delivery (274, 64.6%)	23	118	48	42	43	
Cesarean section (150, 35.4%)	16	57	30	25	22	
Infection during pregnancy, n (%)						0.252
Yes (25, 5.9%)	5	8	5	2	5	
No (399, 94.1%)	34	167	73	65	60	
Malnutrition during gestation, n (%)						0.071
Yes (28, 6.6%)	6	8	8	3	3	
No (396, 93.4%)	33	167	70	64	62	
Family genetic history, n (%)						0.396
Yes (9, 2.1%)	2	2	2	1	2	
No (415, 97.9%)	37	173	76	66	63	
Epilepsy, n (%)						0.977
Yes (54, 12.7%)	6	22	9	8	9	
No (370, 87.3%)	33	153	69	59	56	
Cognitive impairment, n (%)						0.486
Yes (23, 5.4%)	4	7	6	3	3	
No (401, 94.6%)	35	168	72	64	62	
Socioeconomic status, n (%)						0.628
High (138, 32.5%)	15	53	25	21	24	
Middle (142, 33.5%)	13	67	23	18	21	
Low (144, 34.0%)	11	55	30	28	20	
Rehabilitation access, n (%)						0.399
Good (106, 25%)	6	44	19	20	17	
Moderate (127, 30%)	18	46	26	20	17	

Factors(self-variable name)	GMFCS I (n = 39)	GMFCS II (n = 175)	GMFCS III (n = 78)	GMFCS IV (n = 67)	GMFCS V (n = 65)	p-Value
Poor (191, 45%)	15	85	33	27	31	

Table 3
Multicollinearity diagnosis of candidate independent variables included in the final model

Factors	VIF
Age	2.867
Gender	1.043
Gestational age	1.824
Birth weight	1.574
Breast milk	1.047
Smoking during pregnancy	1.122
Drinking during pregnancy	1.048
Neonatal asphyxia	1.045
Malnutrition during gestation	1.042
CP subtype	1.059
Topographical distribution	1.037

Children with higher GMFCS levels tended to have lower rates of breastfeeding and higher proportions of maternal smoking exposure, alcohol exposure, and neonatal asphyxia. Very preterm birth and very low birth weight were also more frequently observed among children with higher GMFCS levels.

No significant differences across GMFCS levels were found for sex (p = 0.116), maternal age (p = 0.808), paternal age (p = 0.572), delivery mode (p = 0.800), topographical distribution (p = 0.857), infection during pregnancy (p = 0.252), malnutrition during gestation (p = 0.071), family genetic history (p = 0.396), epilepsy (p = 0.977), cognitive impairment (p = 0.486), socioeconomic status (p = 0.628), or rehabilitation access (p = 0.399).

3.3. Multivariable ordinal logistic regression :

Before multivariable modelling, multicollinearity among candidate independent variables was assessed using the variance inflation factor. All VIF values were below 3, indicating no substantial multicollinearity among the variables included in the final model.

The results of multivariable ordinal logistic regression analyses are shown in Table 4. In the adjusted model, breastfeeding was independently associated with lower odds of higher GMFCS levels (AOR = 0.378, 95% CI: 0.260–0.551, $p < 0.001$). In contrast, low smoking exposure during pregnancy (AOR = 1.841, 95% CI: 1.236–2.742, $p = 0.003$), moderate/high smoking exposure during pregnancy (AOR = 2.773, 95% CI: 1.204–6.388, $p = 0.017$), occasional alcohol exposure during pregnancy (AOR = 1.621, 95% CI: 1.019–2.578, $p = 0.041$), and neonatal asphyxia (AOR = 1.970, 95% CI: 1.359–2.855, $p < 0.001$) were independently associated with higher GMFCS levels.

Table 4
Univariable and multivariable ordinal logistic regression analyses of factors associated with higher GMFCS levels.

Factors	COR	95% CI	p-Value	AOR	95% CI	p-Value
Age						
2-<4 years	Ref			Ref		
4-<6 years	0.838	0.455–1.543	0.570	1.007	0.527–1.925	0.983
6-<12 years	0.531	0.304–0.926	0.026	0.590	0.328–1.061	0.078
12–18 years	0.392	0.194–0.791	0.009	0.580	0.275–1.220	0.151
Gender						
Male	Ref			Ref		
Female	0.854	0.601–1.214	0.379	0.944	0.655–1.361	0.759
Gestational age						
>=37 weeks	Ref			Ref		
32-<37 weeks	1.083	0.677–1.734	0.738	1.176	0.690–2.005	0.550
< 32 weeks	1.279	0.805–2.034	0.298	1.371	0.731–2.571	0.326
Birth weight						
>=2500 g	Ref			Ref		
1500–2499 g	0.727	0.484–1.093	0.126	0.642	0.380–1.083	0.097
< 1500 g	2.305	1.083–4.906	0.030	1.437	0.584–3.533	0.430
Breast milk						
Yes	0.315	0.219–0.453	< 0.001	0.378	0.260–0.551	< 0.001
No	Ref			Ref		
Smoking during pregnancy						
No exposure	Ref			Ref		

Factors	COR	95% CI	p-Value	AOR	95% CI	p-Value
Low exposure	2.402	1.653–3.491	< 0.001	1.841	1.236–2.742	0.003
Moderate/high exposure	3.948	1.762–8.843	< 0.001	2.773	1.204–6.388	0.017
Drinking during pregnancy						
No exposure	Ref			Ref		
Occasional exposure	1.741	1.127–2.689	0.012	1.621	1.019–2.578	0.041
Regular/heavy exposure	0.308	0.065–1.465	0.139	0.334	0.075–1.483	0.149
Neonatal asphyxia						
Yes	2.017	1.414–2.877	< 0.001	1.970	1.359–2.855	< 0.001
No	Ref			Ref		
Malnutrition during gestation						
Yes	0.677	0.331–1.386	0.286	0.605	0.283–1.294	0.195
No	Ref			Ref		
CP subtype						
Spastic CP	Ref			Ref		
Non-spastic or mixed CP	0.995	0.702–1.411	0.980	1.040	0.720–1.502	0.836
Topographical distribution						
Bilateral involvement	Ref			Ref		
Unilateral involvement	0.947	0.665–1.348	0.762	1.025	0.708–1.483	0.897

After adjustment, age at GMFCS assessment, sex, gestational age, birth weight, regular/heavy alcohol exposure during pregnancy, maternal malnutrition during pregnancy, CP subtype, and topographical distribution were not significantly associated with GMFCS level. Specifically, non-spastic or mixed CP was not associated with higher GMFCS levels compared with spastic CP (AOR = 1.040, 95% CI: 0.720–1.502, p = 0.836), and unilateral involvement was not associated with higher GMFCS levels compared with bilateral involvement (AOR = 1.025, 95% CI: 0.708–1.483, p = 0.897).

4. Discussion

In this retrospective study, we examined factors associated with higher GMFCS levels among children already diagnosed with cerebral palsy. By analysing GMFCS as an ordinal five-level outcome, this study focused on the severity of gross motor impairment rather than the risk of developing cerebral palsy (8, 10, 15). The main findings showed that maternal smoking exposure during pregnancy, occasional alcohol exposure during pregnancy, and neonatal asphyxia were independently associated with higher GMFCS levels, whereas breastfeeding was associated with lower GMFCS levels. CP subtype and topographical distribution were not independently associated with higher GMFCS levels in the adjusted model. These results suggest that prenatal exposure, perinatal hypoxic events, and early postnatal feeding status may be related to the severity of motor impairment in children with cerebral palsy.

An important interpretation of these findings is that the identified factors should not be viewed as isolated predictors. Rather, they may represent different stages of early-life vulnerability (23). Maternal smoking and alcohol exposure reflect potentially adverse prenatal environments, neonatal asphyxia reflects perinatal compromise, and breastfeeding may reflect both early nutritional support and the child's functional ability to feed. Together, these factors may indicate that children exposed to cumulative prenatal and perinatal stressors are more likely to present with higher GMFCS levels (15, 23). However, because this study was retrospective and observational, these associations cannot establish causal effects.

Maternal smoking exposure during pregnancy and neonatal asphyxia were independently associated with higher GMFCS levels in this cohort. This finding is broadly consistent with previous studies reporting associations between prenatal or perinatal adverse exposures and worse neurodevelopmental or functional outcomes in children with CP, including evidence from the Canadian Cerebral Palsy Registry showing a greater disability burden among children with CP after neonatal encephalopathy or suspected asphyxia (24–26). However, these associations should be interpreted cautiously. Maternal smoking may reflect not only prenatal toxic exposure but also broader unmeasured environmental, socioeconomic, antenatal-care, or familial factors(27). Similarly, neonatal asphyxia may represent a marker of overall perinatal compromise rather than a single uniform causal exposure (28–30). In addition, unrecognised monogenic or chromosomal causes of CP may have influenced motor severity and confounded the observed associations (31–33). Therefore, these findings should be interpreted as associations with higher GMFCS levels rather than direct causal effects.

Alcohol exposure during pregnancy was also associated with higher GMFCS levels in the adjusted model, but only occasional exposure reached statistical significance. This finding requires cautious interpretation(26, 34). The lack of a significant association for regular/heavy alcohol exposure may be explained by the small number of children in that category, under-reporting of alcohol intake, or unstable estimates. Therefore, the present results do not support a clear dose–response relationship for alcohol exposure. Future studies should quantify alcohol intake more precisely, including timing, frequency, and cumulative exposure during pregnancy (34).

Breastfeeding was associated with lower odds of higher GMFCS levels. This may reflect potential benefits of early nutrition and bioactive components in breast milk for neurodevelopment(35–37). However, reverse causation is also possible. Children with more severe motor impairment may have early sucking, swallowing, or feeding difficulties, making breastfeeding less likely or shorter in duration (38, 39). Breastfeeding may also be associated with caregiver involvement, maternal education, access to health information, neonatal health status, and socioeconomic conditions. Therefore, breastfeeding should not be interpreted as a direct protective treatment for motor impairment in cerebral palsy. Instead, it may be a marker of a more favourable early-life clinical and caregiving context.

Gestational age and birth weight differed significantly across GMFCS levels in the bivariate analysis but were not independently associated with GMFCS level after adjustment. Prematurity and low birth weight are established risk factors for the occurrence of cerebral palsy (13–15), but their role in determining motor severity among children who already have cerebral palsy may be less direct (15). Their effects may be mediated by neonatal complications, hypoxic injury, infection, brain injury pattern, and postnatal care. This distinction is important: the present study does not evaluate why cerebral palsy develops, but rather why some children with cerebral palsy have higher GMFCS levels than others.

Age at GMFCS assessment differed across GMFCS levels in the bivariate analysis but was not independently associated with GMFCS level after adjustment. Age in this study reflects the timing of functional assessment rather than age at diagnosis, disease duration, or natural recovery. Therefore, the results should not be interpreted as evidence that motor function improves with age. Differences across age groups may be partly explained by referral patterns, survival bias, rehabilitation exposure, developmental trajectories, or the accumulation of musculoskeletal complications over time (10, 12). Longitudinal studies are needed to clarify how GMFCS levels change with age in children with CP.

Several limitations should be noted. First, the retrospective design limits causal inference. Second, data were obtained from a single centre, which may limit generalisability. Third, some variables, including smoking, alcohol exposure, breastfeeding, infection during pregnancy, and rehabilitation access, may have been affected by recall bias or incomplete documentation. Fourth, although CP subtype and broad topographical distribution were included in the adjusted model, detailed brain imaging findings, fine-grained topographical patterns, severity of cognitive impairment, nutritional status after birth, and rehabilitation intensity were unavailable or incompletely measured(3, 40). Fifth, although socioeconomic and rehabilitation-related variables were collected, residual confounding remains possible. Finally, complete-case analysis may have introduced selection bias if children with missing data differed systematically from those included in the analysis. Another limitation is the lack of systematic genetic evaluation. Genetic and chromosomal causes of CP are increasingly recognised and may influence clinical phenotype, motor severity, comorbidities, and prognosis (31, 32, 41). Because genetic testing was not routinely performed, unidentified monogenic or chromosomal disorders may have affected patient stratification and confounded associations between perinatal exposures and GMFCS severity.

In conclusion, maternal smoking exposure during pregnancy, occasional alcohol exposure during pregnancy, and neonatal asphyxia were associated with higher GMFCS levels among children with cerebral palsy, whereas breastfeeding was associated with lower GMFCS levels. These findings should be interpreted as associations with motor severity, not as causal determinants of cerebral palsy onset. Further prospective multicentre studies using standardised exposure definitions, detailed neuroimaging data, and longitudinal GMFCS assessment are needed to validate these findings.

5. Conclusion

In this retrospective study of children with cerebral palsy, maternal smoking exposure during pregnancy, occasional alcohol exposure during pregnancy, and neonatal asphyxia were independently associated with higher GMFCS levels, whereas breastfeeding was associated with lower GMFCS levels. These associations persisted after adjustment for CP subtype and topographical distribution, neither of which was independently associated with higher GMFCS levels. These findings suggest that prenatal, perinatal, and early postnatal factors may be related to the severity of gross motor impairment in children with cerebral palsy. Given the observational design, these associations should not be interpreted as causal effects. Further prospective multicentre studies with standardised exposure assessment and longitudinal GMFCS evaluation are needed to validate these findings.

Abbreviations

CP Cerebral palsy

GMFCS Gross Motor Function Classification System

Declarations

Interests and conflicts

The authors declare that there are no competing financial interests or personal relationships with other people or organisations.

Ethical Statements

This study was conducted in accordance with the Declaration of Helsinki. The study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Xinjiang Medical University (Approval No. 20211012-14C). Informed consent was obtained from all patients and their legal guardians/families for the collection and use of their data.

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Author Contribution

The authors' contributions to the study and the manuscript include the following: conception of experimental ideas, data analysis and writing of the initial manuscript: Hongjia Tian, Chunyu Zhang, Linli Zhang; data organisation and statistical analysis: Hong Zhao, Xinping Luan and Baofeng Yan ; visualisation of the experimental results: Songhai Biedelehan, Mingbo Hu and Kaidiriye Abolaiti; experimental supervision, guidance, capital acquisition, review and revision of the initial manuscript: Aikebaier Halike. All authors gave critical comments and approved the submission.

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Data Availability

The datasets generated and analyzed during the present study are available from the corresponding author upon reasonable request

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