ORIGINAL REPORT

RELATIONSHIP BETWEEN NUTRITIONAL STATUS AND SEVERITY OF CEREBRAL PALSY: A MULTICENTRE CROSS-SECTIONAL STUDY

Yiting ZHAO, MSc[1–3#], Hongmei TANG, MD, PhD[1,2#], Tingting PENG, MD[1,2#], Jinling LI, MD[1,2], Liru LIU, MD[1,2], Chaoqiong FU, MSc[1,2,4], Hongyu ZHOU, BSc[1-3], Shiya HUANG, MSc[1,2,4], Yuan HUANG, MD[1,2,5], Peishan ZENG, MSc[1,2], Wenda WANG, MD, PhD[1,2], Lu HE, MD[1,2], Kaishou XU, MD, PhD[1,2] and Research GROUP*

From the [1]Department of Rehabilitation, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, [2]Guangdong Provincial Clinical Research Center for Child Health, [3]Department of Sports and Health, Guangzhou Sport University, Guangzhou, [4]School of Kinesiology, Shanghai University of Sport, Shanghai and [5]School of Medicine, South China University of Technology, Guangzhou, China

[#]These authors contributed equally to this work.

**Research Group: Zhuangfei Wen (Haikou Hospital of the Maternal and Child Health), Yan Huang (Qilu Children's Hospital of Shandong University), Guanglei Tong (Anhui Province Children's Hospital), Yong Zhao (Nanhai Affiliated Maternity and Children's Hospital of Guangzhou Traditional Chinese Medicine University), Li Qiu (Quanzhou Women's and Children's Hospital), Yun Liu (Kunming Children's Hospital), Xia Cai (The First People's Hospital of Yulin), Shuyun Shang (Shenyang Children's Hospital), Yuqiong Zhang (Dongguan City Maternal and Child Health Hospital), Enci Liu (Yangjiang Maternal and Child Health Hospital, Yangjiang), Yanjuan Chen (Jiangmen Maternity and Child Health Care Hospital), Yun Jiao (Hainan Women and Children's Medical Center), Feng Zhang (Ganzhou Women and Children's Health Care Hospital), Ling Yue (Hebei Children's Hospital), Renhai Huang (Maoming Maternal and Child Health Care Hospital), Jihong Hu (Hunan Children's Hospital), Jiechao Zhou (Children's Hospital of Nanjing Medical University), Huimin Li (Boai Hospital of Zhongshan), Zhiwei Chen (The Second People's Hospital of Zhaoqing), Xiaoli Dong (Chengdu Frist People's Hospital), Jian Tang (Children's Hospital of Nanjing Medical University), Qin Gu (Soochow University Affiliated Children's Hospital) and Yanxiang Sun (Shenzhen Nanshan Maternity and Child Healthcare Hospital).*

Background: **Nutritional problems are common in children with cerebral palsy (CP), yet the relationship between nutritional status and the severity of CP is unclear.**

Objective: **To describe the nutritional status and characteristics of children with CP, and to explore the relationship between severity of CP and nutritional status in children.**

Methods: **This multicentre cross-sectional study included children with CP in China. Weight and height were measured and converted to z-scores. Gross Motor Function Classification System (GMFCS), Eating and Drinking Ability Classification System (EDACS), Subjective Global Nutritional Assessment (SGNA), social life ability, and blood indicators were tested.**

Results: **All 1,151 participants were given oral-feeding and 50.8% of them demonstrated undernutrition. Compared with those in GMFCS or EDACS levels I–III, the odds of moderate and severe undernutrition were 2.6 and 8.9 times higher in GMFCS levels IV and V, and 4.3 and 12.6 times higher in EDACS levels IV and V, respectively. Except for serum 25-hydroxyvitamin D, no significant differences were found in blood indicators among normal, undernourished and overnourished groups.**

Conclusion: **Degrees of undernutrition in children with CP are correlated with the severity of eating and drinking dysfunction and with gross motor impairment. Blood indicators may not reflect nutritional status in children with CP.**

Key words: undernutrition; cerebral palsy; motor dysfunction; dysphagia; children.

LAY ABSTRACT

Cerebral palsy is the most common physical disability in children in the world. Children with cerebral palsy may have a high risk of having malnutrition as a result of the high energy consumption and/or low energy intake. The former is mainly caused by the abnormal muscular tone, and the latter may emerge from the dysphagia and gastrointestinal problems. As for the optimization of nutritional status is integral to the overall health and clinical management of children with cerebral palsy, the nutritional status stands out for its clinical importance in this group. Children with cerebral palsy are affected by different degrees of motor dysfunction, and may also be faced with eating and drinking problems or limited daily life ability, it is not clear whether nutritional status and function are interrelated. What's more, it is believed that the blood tests may indicate the nutritional status, but it is not well understood.

In this project we will look at the nutritional status of children with cerebral palsy in China and investigate the relationship between nutritional status and function and blood indicators. This will then allow clinicians and caregivers to formulate future policies to improve nutritional status for this group of children.

Accepted Nov 23, 2022

J Rehabil Med 2023; 55: jrm00367

DOI: 10.2340/jrm.v55.4395

Correspondence address: Kaishou Xu and Lu He, Department of Rehabilitation, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, People's Republic of China. E-mails: xksyi@126.com; kittyhelu@126.com

Cerebral palsy (CP) is one of the major causes of physical disability among children worldwide, with an incidence of 2–3.5‰ and complex molecular aetiology, that imposes a heavy burden on families and society (1). Children with CP may be affected by 1 or more complications, such as epilepsy, gastroesophageal reflux, and undernutrition (2). Recently, emphasis has been placed on the nutritional management of children with CP. Indeed, undernutrition is a prominent comorbidity in children with CP, owing to a series of nutritional or non-nutritional factors, such as abnormal muscle tone, feeding and swallowing difficulties, and gastrointestinal problems (3). The prevalence of undernutrition in CP is as high as 57.2–76.6% (4, 5). Undernutrition may have a negative impact on health (such as stunting, pressure sores, weakened immunity, osteoporosis, and increased mortality rate) in children with CP (6).

Nutritional assessment of this group of patients is challenging, because children with CP tend to have below-average linear growth, muscle mass and fat stores compared with typically developing children. In order to provide appropriate interventions, strategies to identify and classify nutritional problems in children with CP are of utmost importance. The nutritional status of children with CP has been studied in some countries, which has provided evidence for clinical practice and public health strategies. However, in most studies, nutritional inadequacy was divided into 2 categories, moderate and severe undernutrition, without consideration of mild undernutrition (7, 8). By overlooking children with mild undernutrition, the optimal timing to provide nutritional treatment may be missed, resulting in the condition worsening into severe undernutrition. In addition, although approximately 50% of children with CP have difficulty feeding and swallowing (9), their eating and drinking ability has not attracted enough attention. Moreover, the relationship between nutritional status and blood indicators in children with CP is unknown. The correlation among gross motor function, eating and drinking ability, social life ability, age and nutritional status in children with CP is also unclear.

Thus, the aims of this study are to describe the nutritional status and characteristics of children with CP, and to explore the relationship between severity of CP (determined by Gross Motor Function Classification System (GMFCS) or Eating and Drinking Ability Classification System (EDACS)) and the children's nutritional status.

METHODS

Study design and participants

This was a multicentre cross-sectional study (ChiCTR2000033869). Written informed consent was obtained from each child's parents or guardians. The study was approved by the hospitals' ethics committee and followed the principles of the Declaration of Helsinki. A study flow chart is shown in Fig. 1.

Participants were recruited from 24 hospitals across 13 provinces in China. Children aged 1–18 years and with a diagnosis following a strict clinical definition adopted from the criteria of CP (10) were included in the study. Subjects were excluded if they had genetic or metabolic diseases that could have or had affected growth (e.g. Rett syndrome, chromosomal variation, etc.), or were clinically unstable. During the research period, the children were recruited during their regular clinic appointments after being invited to participate in the study. Nutritional assessments (consisting of nutritional screening, anthropometric measurement and laboratory tests) were conducted for participants in accordance with international guidelines (11).

Data collection

The sex, age, birth weight, gestational age, type of CP, GMFCS level, EDACS level, Subjective Global Nutritional Assessment (SGNA) level and social life ability scale scores of participants were collected. Height and weight were measured. Laboratory tests were performed for serum concentrations of 25-hydroxyvitamin D (25(OH)D), total protein, albumin, prealbumin and transferrin. The nutritional status of participants was classified into mild, moderate, severe undernutrition, overweight, obesity and normal according to the World Health Organization (WHO) child growth standards combined with the American Society for Parenteral and Enteral Nutrition (ASPEN) standards (12, 13). The data for general information, nutritional screening and anthropometric measurements were collected on the day of the visit, and laboratory tests were carried out within 3 days after the visit.

The lead hospital (Guangzhou Women and Children's Medical Center) organized online and on-site training sessions for personnel from other hospitals. All hospitals uploaded data to an electronic data capture system, which was specially developed for the study, and data were downloaded from the system for analysis.

The GMFCS was used to evaluate the severity of motor impairment in the children. This well-established tool consists of a 5-point ordinal scale, ranging from GMFCS levels I (walks without limitations) to V (transported in a manual wheelchair) (14). The severity of eating and drinking dysfunction was graded with EDACS, which divided eating and drinking ability into 5 levels, ranging from EDACS levels I (eats and drinks safely and efficiently) to V (unable to eat or drink safely: tube feeding may be considered to provide nutrition) (15). The social life

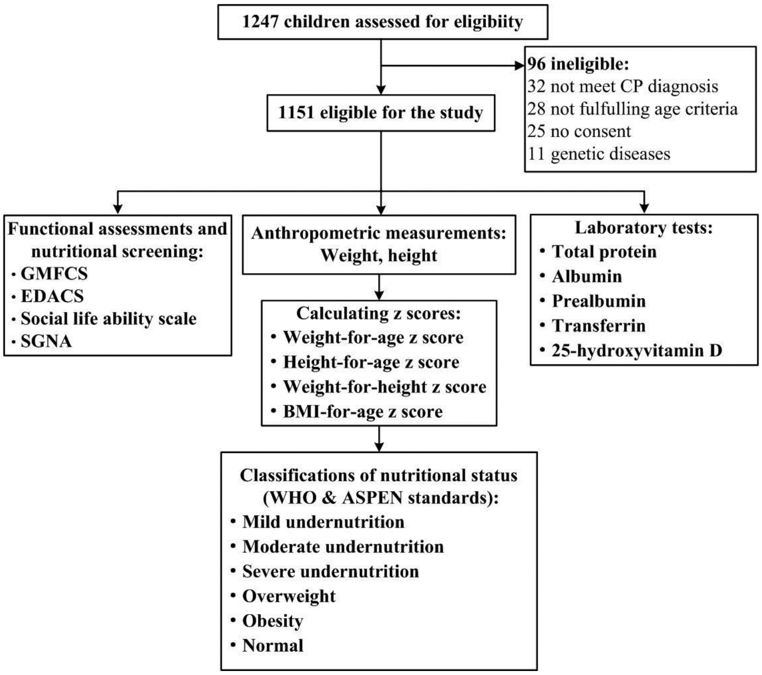

Fig. 1. Flow chart of the overall research. ASPEN: American Society for Parenteral and Enteral Nutrition; CP: cerebral palsy; EDACS: Eating and Drinking Ability Classification System; GMFCS: Gross Motor Function Classification System; SGNA: Subjective Global Nutritional Assessment; WHO: World Health Organization; 25(OH)D: 25-hydroxyvitamin D.

ability scale for Chinese infant–junior school students was performed to identify the normal (standard scores ≥ 9) or poor social life (standard scores <9) for the participants (16). The SGNA was used to screen children with good nutrition, and moderate and severe undernutrition (17).

Anthropometric measurements

The weight of the children was measured using a digital weighing scale with a precision of $\pm$ 0.1 kg following standard guidelines (e.g. bare feet, minimum clothing). The recumbent length of children under 2 years old and standing height for children over 2 years old were measured. Length/height was measured to the nearest 0.1 cm using a length board or height scale. For children who were unable to stand due to joint contracture or deformity, height was estimated by measuring tibial length (TL) according to Stevenson's equation (height (cm) $=$ (TL $\times$ 3.26) $+$ 30.8) (18). Anthropometric parameters for each child were measured in triplicate by the same trained examiner and the mean was determined. The examiners from all of the hospitals followed the same standardized anthropometric protocol.

Laboratory tests

In order to explore the relationship between nutritional status and blood indicators in the children, serum concentrations of 25(OH)D, total protein, albumin, prealbumin and transferrin were measured as per standard technique.

Classification of nutritional status

The nutritional status of each participant was defined by weight-for-age z-score (WAZ), height-for-age z-score (HAZ), weight-for-height z-score (WHZ), and BMI-for-age z-score (BAZ), which were calculated by WHO Anthro software for children under 5 years (version 3.2.2) or AnthroPlus software for children over 5 years (version 1.0.4). In this study, the nutritional status was classified into mild ($-2<$WHZ/BAZ≤ -1), moderate ($-3<$WAZ/HAZ/WHZ/BAZ≤ -2), severe undernutrition (WAZ/HAZ/WHZ/BAZ≤ -3), overweight (<5 years, BAZ>2; ≥ 5 years, BAZ>1), obesity (<5 years, BAZ>3; ≥ 5 years, BAZ>2) and normal according to the WHO growth charts and ASPEN standards.

Statistical analysis

The PASS version 11 (NCSS, UT, USA) was used to calculate sample size. A previous study reported that approximately 40% of children with CP in west China were undernourished (19). Hence, the proportion was set as 0.4. With a 2-sided 95% confidence interval (95% CI) and a width equal to 0.06, the minimum sample size required is 1,056. To maintain power for analysis on observed data, this estimate is increased by 10%. A final total of 1,161 participants was required in this study.

Continuous variables were displayed as mean (standard deviation; SD) and categorical variables were shown as numbers and percentages. Analysis of the ordinal data was performed with the χ^2 test or Fisher's exact test. Bonferroni correction with significance of $p<0.05$ was carried out as a post hoc test for subsequent multiple comparisons. To probe statistical differences between the 2 categories of motor function (GMFCS levels I–III vs IV–V) and eating and drinking ability (EDACS levels I–III vs IV–V) and the nutritional status, odds ratios (ORs) with 95% CI were calculated to measure the magnitude of association among the groups using the Mantel-Haenszel test. Spearman correlation was used to examine the association between nutritional status and GMFCS, EDACS, SGNA, social life ability and age. For Spearman correlation, nutritional status was categorized into an undernutrition group (mild, moderate and severe undernutrition) and an overnutrition group (overweight and obesity). A p-value <0.05 was considered statistically significant. Statistical analyses were conducted with SPSS version 26 (IBM, New York, NY, USA).

RESULTS

Participants' characteristics

A total of 1,151 children (749 males, 402 females) were enrolled between July 2020 and June 2021; they were mainly 1–6 years old and had spastic CP. The mean age of the children was 4 years 5 months (range 1 year to 18 years 10 months). Amongst the participants, less than half were born preterm (gestational age <37 weeks) and with a low birth weight (<2.5 kg). According to SGNA, 40.0% of the children were categorized into undernourished. The demographic and clinical characteristics of participants are shown in Table I.

Table I. Demographic and clinical characteristics of participants ($n=1,151$)

Characteristics	*n* (%)
Sex	
Male	749 (65.1)
Female	402 (34.9)
Gestation age	
<37 weeks	509 (44.2)
≥37 weeks	642 (55.8)
Birth weight	
<2.5 kg	496 (43.1)
≥2.5 kg	655 (56.9)
CP subtype	
Spasticity	948 (82.4)
Dyskinesia	119 (10.3)
Ataxia	23 (2.0)
Mixed	61 (5.3)
Age group	
1–3 years	644 (56.0)
4–6 years	343 (29.8)
7–12 years	118 (10.3)
13–18 years	46 (4.0)
GMFCS level	
I	321 (27.9)
II	284 (24.7)
III	230 (20.0)
IV	181 (15.7)
V	135 (11.7)
EDACS level	
I	690 (59.9)
II	266 (23.1)
III	147 (12.8)
IV	39 (3.4)
V	9 (0.8)
SGNA	
Well nourished	691 (60.0)
Moderate undernourished	396 (34.4)
Severe undernourished	64 (5.6)
Social Life Ability Scale	
Normal	558 (48.5)
Poor	593 (51.5)

CP: cerebral palsy; EDACS: Eating and Drinking Ability Classification System; GMFCS: Gross Motor Function Classification System; SGNA: Subjective Global Nutritional Assessment.

Prevalence of undernutrition in different levels of GMFCS, EDACS and age groups

Overall, children with CP showed a high prevalence of undernutrition, with 585 (50.8%) participants classified as having undernutrition and 78 (6.8%) as having overnutrition (Fig. 2). From GMFCS levels I to V, the prevalence of undernutrition increased gradually, accounting for 30.8%, 42.6%, 62.2%, 61.9% and 81.5%, respectively. Similarly, the prevalence of undernutrition in children with EDACS leves I-V was 30.8%, 42.6%, 62.2%, 61.9% and 81.5%, respectively.

Children were divided into 4 age groups: early childhood (1–3 years), preschool age (4–6 years), school age (7–12 years), and adolescence (13–18 years). Among the 4 age groups, the rate of overnutrition was increasing, while there was no significant difference in the rate of undernutrition (Fig. 2). The prevalence of overnutrition in the early childhood group was significantly lower than the other 3 groups ($p<0.05$) (Fig. 2).

Odds of undernutrition in different severities of cerebral palsy

The rate of undernutrition in children with GMFCS or EDACS levels IV–V was much higher than in those with GMFCS or EDACS levels I–III ($p<0.001$) (Table II). The odds of being moderately and severely undernourished for children in GMFCS levels IV–V were higher than those in GMFCS levels I–III, and it is more obvious in severe undernutrition than moderate undernutrition. In addition, the odds of being mildly, moderately, and severely undernourished were also higher for children with EDACS levels IV–V compared with those with EDACS levels I–III, and the odds increased with the aggravation of undernutrition.

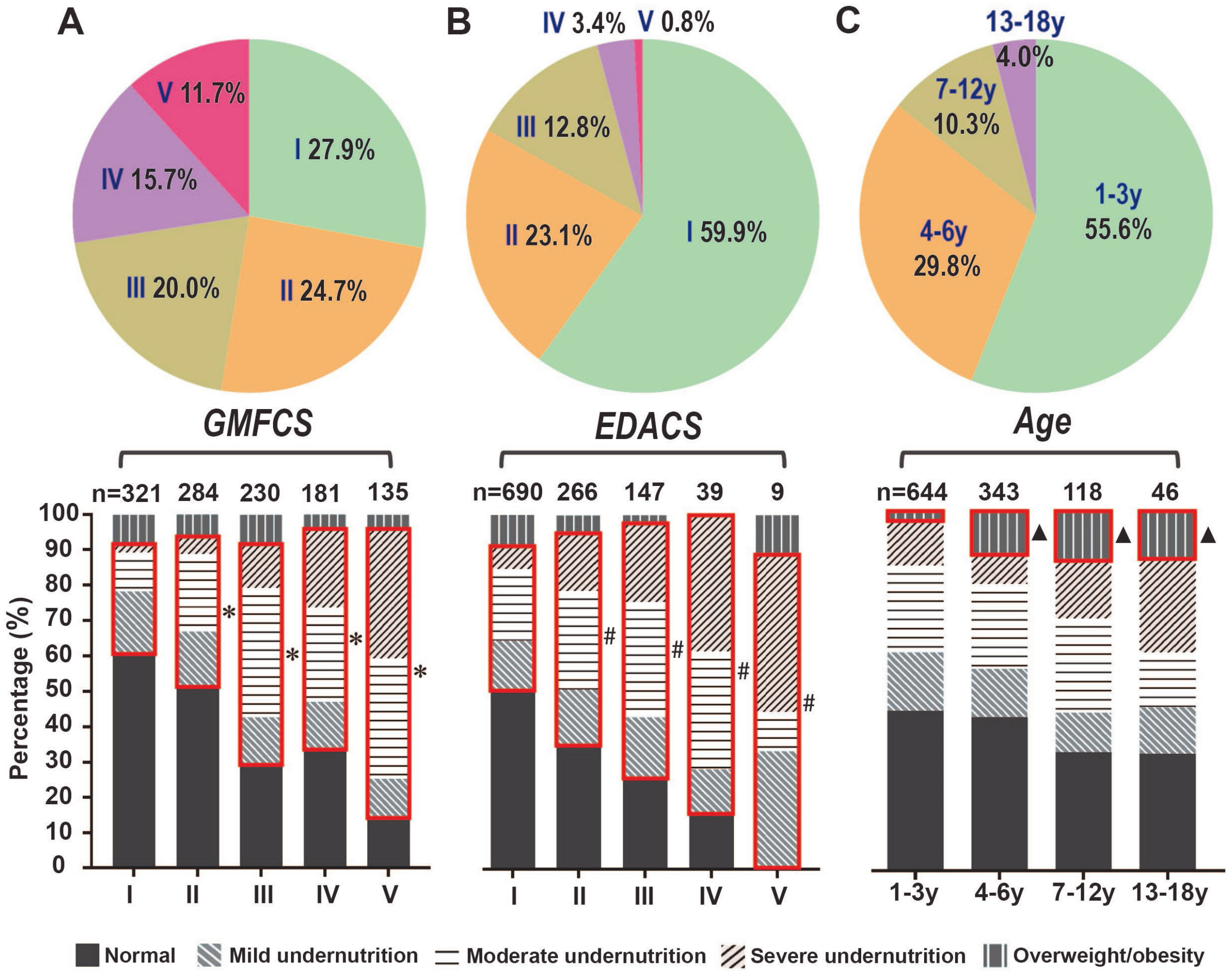

Fig. 2. Pie charts showing the distribution of participants in different (A) GMFCS levels (B) EDACS levels, and (C) age groups. The corresponding prevalence of each nutritional status is shown in bar charts below (*vs GMFCS I, $p<0.05$; #vs EDACS I, $p<0.05$; ▲vs Group 1–3 years, $p<0.05$). EDACS: Eating and Drinking Ability Classification System; GMFCS: Gross Motor Function Classification System.

Correlation between nutritional status and GMFCS, EDACS, SGNA, social life ability and age

Higher GMFCS, EDACS levels (such as levels IV and V) were linearly correlated with worse undernutrition ($p<0.001$). In addition, there was a linear association between increased SGNA levels and worse undernutrition ($p<0.001$). Worse undernutrition was correlated with better social life ability ($p<0.001$). Furthermore, there was a linear association between severe overnutrition and increased age ($p<0.001$). There was no correlation between undernutrition and age, or between overnutrition and GMFCS, EDACS, SGNA and social life ability ($p<0.05$). Spearman's correlation coefficients are shown in Table III.

Laboratory tests

Of all the participating children, 412 (35.79%) underwent laboratory testing. The mean values of their serum concentrations of 25(OH)D, total protein, albumin, prealbumin and transferrin are shown in Table IV. The 25(OH)D deficiency (<50 nmol/L) was found in 21.8% of participants according to the paediatric test reference values from the Mayo Clinic Laboratories. Moreover, the proportion of 25(OH)D below normal range in the overnourished group was higher than that in normal or undernourished group ($p=0.028$). No significant differences were found in serum concentrations of total protein, albumin prealbumin and transferrin among normal, undernourished and overnourished groups ($p>0.05$).

DISCUSSION

To our knowledge, this is the first multicentre cross-sectional study to systematically investigate the nutritional status of children with CP from a wide area of

Table II. Odds ratio (95% confidence interval; 95% CI) of malnutrition in children with cerebral palsy between Gross Motor Function Classification System (GMFCS) or Eating and Drinking Ability Classification System (EDACS) levels IV and V vs I–III

		GMFCS					EDACS				
Nutritional status	*n*	I–III, *n* (%)	IV and V, *n* (%)	OR	95% CI	*p*-value	I–III, *n* (%)	IV and V, *n* (%)	OR	95% CI	*p*-value
Normal	488	408 (48.9)	80 (25.3)	Reference			482 (43.7)	6 (12.5)	reference		
Mild undernutrition	170	131 (15.7)	39 (12.3)	1.5	1.0–2.3	0.056	162 (14.7)	8 (16.7)	4.0	1.4–11.6	0.017
Moderate undernutrition	275	181 (21.7)	94 (29.7)	2.6	1.9–3.7	< 0.001	261 (23.7)	14 (29.2)	4.3	1.6–11.3	0.001
Severe undernutrition	140	51 (6.1)	89 (28.2)	8.9	5.9–13.5	< 0.001	121 (11.0)	19 (39.6)	12.6	4.9–32.3	< 0.001
Overweight/obesity	78	64 (7.7)	14 (4.4)	1.1	0.6–2.1	0.732	77 (7.0)	1 (2.1)	1.0	0.1–8.8	1.000

EDACS: Eating and Drinking Ability Classification System; GMFCS: Gross Motor Function Classification System; OR: odds ratio; 95% CI: 95% confidence interval; WAZ: weight-for-age z-score; HAZ: height-for-age z-score; WHZ: weight-for-height z-score; BAZ: BMI-for-age z-score. Mild undernutrition: −2 < WHZ/BAZ ≤ −1. Moderate undernutrition: −3 < WAZ/HAZ/WHZ/BAZ ≤ −2. Severe undernutrition: WAZ/HAZ/WHZ/BAZ ≤ −3. Overweight: < 5 years; BAZ > 2; ≥ 5 years; BAZ > 1. Obesity: < 5 years; BAZ > 3; ≥ 5 years; BAZ > 2. Normal: except for the above situations.

Table III. Spearman correlation between nutritional status and severity and age of children with cerebral palsy

	Undernutrition		Overnutrition	
	r	*p*-value	r	*p*-value
GMFCS	0.415	< 0.001	0.062	0.138
EDACS	0.296	< 0.001	−0.043	0.312
SGNA	0.605	< 0.001	−0.004	0.928
Social life ability	−0.312	< 0.001	−0.044	0.292
Age	0.025	0.405	0.288	< 0.001

EDACS: Eating and Drinking Ability Classification System; GMFCS: Gross Motor Function Classification System; r: correlation coefficient; SGNA: Subjective Global Nutritional Assessment.

China. In addition, the study provides evidence of nutritional data for children with CP who have eating and drinking disabilities or mild undernutrition, which may help to guide clinical practice and health policy. The degrees of undernutrition were positively associated with the severity of CP. Moreover, blood samples were collected and analysed, and the relationship between nutritional status and blood indicators, which has rarely been studied previously, indicated that blood markers may not identify nutritional status in children with CP.

In this study, the prevalence of undernutrition in children with CP was 50.8%, similar to previous studies reported in Turkey, Ghana and Indonesia, which ranged from 57.2% to 85.9% (4, 8, 20). In contrast, a lower prevalence of undernutrition in developed countries was observed, with 34% in Belgium and 22% in Portugal (21, 22). A study of 377 children with CP in Southwest China in 2013 showed that 42.4% were stunting, 12.7% underweight, and 21.5% thin (19).The prevalence of undernutrition in the current study was different from that in other studies, which may be due to differences in the criteria applied to identify undernutrition, socioeconomic status, and in the areas covered by study (the current study covered more areas, e.g. Central-south, East, North, Northeast, and Southwest China). With a lack of reference for mild undernutrition, nutritional insufficiency was usually classified as moderate and severe undernutrition (23), which would result in underestimation of undernutrition. In the current study, the criteria for mild undernutrition from ASPEN were used to identify undernourished children, which might compensate for the previous shortcomings and prevent exacerbation of undernutrition. Moreover, the current study showed that the incidence of overweight and obesity together is 5.4%, which may be explained by limited mobilization, low energy consumption and over-feeding in some participants. This might increase the difficulty of making transfers, causing decreased social participation, and increasing the difficulty of nursing and the likelihood of cardiovascular diseases in adulthood (24). Therefore, accepting health education, changing lifestyle, and improving physical activity levels may be necessary for overnourished children.

This study found that the severity of CP was associated with a compromise in growth attainment; as motor or eating and drinking dysfunction increased, undernutrition became more serious, in accordance with the results of previous studies (23, 25). The current study also revealed that children with GMFCS or EDACS levels IV and V had a higher possibility of having undernutrition than those with GMFCS or EDACS levels I–III. In other words, participants with severe dysfunction were more likely to have undernutrition, compared with those with mild-moderate dysfunction. This might be explained by the hypertonia and involuntary movements of children with severe CP, which increase energy expenditure and reduce aerobic capacity. On the other hand, eating and drinking dysfunction would aggravate insufficient intake of nutrients and nutritional deficiency, resulting in an imbalance of energy consumption and intake (26, 27). Although all participants in the current study were completely orally fed according to their guardians' report, 9 children (0.8%) were in EDACS levels V (i.e. tube feeding may be needed to provide nutrition). Thus, it is important for them to be referred to the Department of Gastroenterology for further consideration of naso-gastric or gastrostomy tube placement. It is suggested that the eating and drinking ability of children with CP should not be ignored and more detailed measures should be taken to enhance awareness of this ability in children with CP. In addition, the current study found

Table IV. Laboratory tests in children with cerebral palsy ($n = 412$)[a]

	Overall ($n = 412$)		Normal ($n = 198$)		Undernutrition (n=188)		Overnutrition ($n = 26$)			
Serum concentration tests	Mean (SD)	*n* (%)	Mean (SD)	*n* (%)	Mean (SD)	*n* (%)	Mean (SD)	*n* (%)	χ^2	*p*-value
25-hydroxyvitamin D (nmol/L)	74.6 (34.7)	90 (21.8)	69.3 (28.8)	43 (21.7)	82.7 (39.6)	36 (19.1)	56.7 (20.5)	11 (42.3)	7.179	0.028
Total protein (g/L)	68.3 (4.5)	19 (4.6)	68.2 (4.7)	11 (5.6)	68.3 (4.3)	8 (4.3)	69.2 (5.1)	0	1.712	0.425
Albumin (g/L)	45.3 (2.6)	1 (0.2)	45.3 (2.6)	0	45.2 (2.7)	1 (0.5)	45.8 (2.6)	0	2.179	0.519
Prealbumin (mg/L)	198.0 (34.5)	4 (9.7)	198.6 (36.0)	2 (1.0)	194.8 (30.6)	2 (1.1)	215.6 (44.2)	0	0.329	1.000
Transferrin (g/L)	2.5 (0.4)	10 (2.4)	2.6 (0.4)	5 (2.5)	2.5 (0.4)	5 (2.7)	2.6 (0.2)	0	0.152	1.000

[a]Data presented as mean (SD) and *n* (%) for below normal range.
Reference value: 25-hydroxyvitamin D: 75–375 mmol/L; total protein: 65~85 g/L; albumin: 40~55 g/L; prealbumin: 200–400 mg/L; transferrin: 2.0~3.6g/L.
SD: standard deviation.

that children with poor eating and drinking abilities had a tendency to have worse undernourished status. This highlights the importance of screening and management of eating and drinking disability in children with CP in order to prevent further nutritional disorders.

Undernutrition has an influence on performance of activities of daily living resulting in caregiver burden (28). Similar results were also observed in the current study, the poorer the social life ability, the worse the undernutrition. It is hypothesized that children with disability in self-care would have restricted self-feeding skills, difficulty expressing hunger and limited availability of nutritional foods, which may result in insufficient energy intake and inadequate growth. Nutritional inadequacy would also exacerbate primary diseases and contribute to impaired social life. This is a vicious circle, and further research is needed into how to best help these children. The current study also found that overnutrition was positively associated with age. This could be explained by excessive caloric intake and reduced physical activities as the children grew up.

Notwithstanding that not all participants underwent laboratory testing because of the non-cooperation of some children and limited conditions in some individual hospitals, 21.8% of the 412 children in the current study were found to have 25(OH)D deficiency, implying poor bone mineral status in children with quadriplegic CP. Another study involving 59 quadriplegic CP found that 8.5% had osteoporosis and 74.6% had low bone mineral density (29). Children with CP are prone to low bone mineral density because of lack of weight-bearing, use of anticonvulsant medication, and low calcium and vitamin D intake, which can lead to osteoporosis and even fracture (30). The current results showed that the probability of 25(OH)D deficiency in the overnutrition group was higher than in the undernutrition and normal groups. This may result from lack of exercise and weight-bearing in the overnourished children. No differences were found in other blood indicators among the 3 groups. This also indicated that awareness of bone health in CP should be emphasized, and that blood indicators may not reflect nutritional status in CP, which validated that the blood tests were less reliable indicators of nutritional status and there was no single laboratory biomarker indicating adequate or inadequate nutrition (11).

This study has some limitations: *(i)* the cross-sectional nature of the study precludes interpretations of causality among nutritional status, GMFCS and EDACS; *(ii)* the sample size in EDACS IV and V and age >13 years is relatively small; *(iii)* the low proportion of severe dysphagia and older children in the study sample might not be representative of the whole CP population; *(iv)* the study did not collect all participants' blood samples because of limited conditions in a few of the hospitals involved; *(v)* the study did not calculate the trend of OR comparing each level of GMFCS and EDACS with level I; and *(vi)* the EDACS is primarily designed for children over 3 years of age, and hence its use in younger children should be further validated. Nevertheless, the study analysed data collected in several hospitals across 13 provinces of China, and included a large and sufficiently representative sample, allowing for reasonable inferences on account of its statistical power. In addition, it has been the first study to date to highlight the nutritional problems of children with CP based on their motor function and eating and drinking ability in developing countries, which makes it possible to formulate future policies for their latent improvement.

CONCLUSION

More than half of the children with CP in this study had nutritional problems, and increased degrees of undernutrition were linearly associated with more severe eating and drinking dysfunction and gross motor impairment. Blood indicators may not reflect nutritional status in children with CP. Further research is needed to analyse body composition, bone mineral density and trace elements in this group.

ACKNOWLEDGEMENTS

We thank the study participants, their families, Lingxia Sun (MS, RD, CNSC, Affiliations: Nestle Health Science, China) for her valuable advice, and Nestle Health

Science (China) for support with attending meetings and organization of training during data collection.

This work was supported by the National Natural Science Foundation of China (81902309); the Natural Science Foundation of Guangdong Province (2021A1515011303, 2021A1515012543, 2019A1515010420); Basic and Applied Basic Foundation of Guangdong Province (2020A1515110435); and grants from Science and Technology Program of Guangzhou (202102010205, 202102020581) and Featured Clinical Technique of Guangzhou (2019TS55). None of the authors have financial relationships relevant to this article to disclose.

Written informed consent was obtained from each child's parents or guardians ahead of study initiation, and they agreed to the analysis of the research data and publication of this paper.

The authors have no conflicts of interest to declare.

REFERENCES

1. Li N, Zhou P, Tang H, He L, Fang X, Zhao J, et al. In-depth analysis reveals complex molecular aetiology in a cohort of idiopathic cerebral palsy. Brain 2022; 145: 119–141. DOI: 10.1093/brain/awab209.
2. Sewell MD, Eastwood DM, Wimalasundera N. Managing common symptoms of cerebral palsy in children. BMJ 2014; 349: g5474. DOI: 10.1136/bmj.g5474.
3. Rempel G. The importance of good nutrition in children with cerebral palsy. Phys Med Rehabil Clin N Am 2015; 26: 39–56. DOI: 10.1016/j.pmr.2014.09.001.
4. Aydin K, Turkish Cerebral Palsy Study Group. A multicenter cross-sectional study to evaluate the clinical characteristics and nutritional status of children with cerebral palsy. Clin Nutr ESPEN 2018; 26: 27–34. DOI: 10.1016/j.clnesp.2018.05.002.
5. Aydın K, Kartal A, Keleş Alp E. High rates of malnutrition and epilepsy: two common comorbidities in children with cerebral palsy. Turk J Med Sci 2019; 49: 33–37. DOI: 10.3906/sag-1803-79.
6. Reyes FI, Salemi JL, Dongarwar D, Magazine CB, Salihu HM. Prevalence, trends, and correlates of malnutrition among hospitalized children with cerebral palsy. Dev Med Child Neurol 2019; 61: 1432–1438. DOI: 10.1111/dmcn.14329.
7. Pinto VV, Alves L, Mendes FM, Ciamponi AL. The nutritional state of children and adolescents with cerebral palsy is associated with oral motor dysfunction and social conditions: a cross sectional study. BMC Neurol 2016; 16: 55. DOI: 10.1186/s12883-016-0573-8.
8. Polack S, Adams M, O'banion D, Baltussen M, Asante S, Kerac M, et al. Children with cerebral palsy in Ghana: malnutrition, feeding challenges, and caregiver quality of life. Dev Med Child Neurol 2018; 60: 914–921. DOI: 10.1111/dmcn.13797.
9. Speyer R, Cordier R, Kim JH, Cocks N, Michou E, Wilkes-Gillan S. Prevalence of drooling, swallowing, and feeding problems in cerebral palsy across the lifespan: a systematic review and meta-analyses. Dev Med Child Neurol 2019; 61: 1249–1258. DOI: 10.1111/dmcn.14316.
10. Rosenbaum P, Paneth N, Leviton A, Goldstein M, Bax M, Damiano D, et al. A report: the definition and classification of cerebral palsy. Dev Med Child Neurol Suppl 2007; 109: 8–14.
11. Romano C, van Wynckel M, Hulst J, Broekaert I, Bronsky J, Dall'Oglio L, et al. European Society for Paediatric Gastroenterology, Hepatology and Nutrition guidelines for the evaluation and treatment of gastrointestinal and nutritional complications in children with neurological impairment. J Pediatr Gastroenterol Nutr 2017; 65: 242–264. DOI: 10.1097/MPG.0000000000001646.
12. World Health Organizatio (WHO) Multicentre Growth Reference Study Group. WHO Child Growth Standards based on length/height, weight and age. Acta Paediatr Suppl 2006; 450: 76–85. DOI: 10.1111/j.1651-2227.2006.tb02378.x.
13. Becker PJ, Nieman Carney L, Corkins MR, Monczka J, Smith E, Smith SE, et al. Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: indicators recommended for the identification and documentation of pediatric malnutrition (undernutrition). J Acad Nutr Diet 2014; 114: 1988–2000. DOI: 10.1016/j.jand.2014.08.026.
14. Palisano RJ, Rosenbaum P, Bartlett D, Livingston MH. Content validity of the expanded and revised Gross Motor Function Classification System. Dev Med Child Neurol 2008; 50: 744–750. DOI: 10.1111/j.1469-8749.2008.03089.x.
15. Sellers D, Mandy A, Pennington L, Hankins M, Morris C. Development and reliability of a system to classify the eating and drinking ability of people with cerebral palsy. Dev Med Child Neurol 2014; 56: 245–251. DOI: 10.1111/dmcn.12352.
16. Zhang ZX, Zuo QH, Lei ZW. Re-standardization of social life ability scale for Chinese infant-junior school student. Chin J Clin Psychol 1995; 3: 12–15.
17. Peng T, Zhao Y, Fu C, Huang S, Zhou H, Li J, et al. A study of validity and reliability for Subjective Global Nutritional Assessment in outpatient children with cerebral palsy. Nutr Neurosci 2021; 12: 2570–2576. DOI: 10.1080/1028415X.2021.1990463.
18. Stevenson RD. Use of segmental measures to estimate stature in children with cerebral palsy. Arch Pediatr Adolesc Med 1995; 149: 658–662. DOI: 10.1001/archpedi.1995.02170190068012.
19. Wang F, Cai Q, Shi W, Jiang H, Li N, Ma D, et al. A cross-sectional survey of growth and nutritional status in children with cerebral palsy in west China. Pediatr Neurol 2016; 58: 90–97. DOI: 10.1016/j.pediatrneurol.2016.01.002.
20. Jahan I, Muhit M, Hardianto D, Karim T, Al Imam MH, Das MC, et al. Nutritional status of children with cerebral palsy in remote Sumba Island of Indonesia: a community-based key informants study. Disabil Rehabil 2021; 43: 1819–1828. DOI: 10.1080/09638288.2019.1676833.
21. Leonard M, Dain E, Pelc K, Dan B, De Laet C. Nutritional status of neurologically impaired children: impact on comorbidity. Arch Pediatr 2020; 27: 95–103. DOI: 10.1016/j.arcped.2019.11.003.
22. Caselli TB, Lomazi EA, Montenegro M, Bellomo-Brandão MA. Assessment of nutritional status of children and adolescents with spastic quadriplegic cerebral palsy. Arq Gastroenterol 2017; 54: 201–205. DOI: 10.1590/S0004-2803.201700000-32.
23. Ruiz Brunner M, Cieri ME, Rodriguez Marco MP, Schroeder AS, Cuestas E. Nutritional status of children with cerebral palsy attending rehabilitation centers. Dev Med Child Neurol 2020; 62: 1383–1388. DOI: 10.1111/dmcn.14667.
24. Heyn PC, Tagawa A, Pan Z, Thomas S, Carollo JJ. Prevalence of metabolic syndrome and cardiovascular disease risk factors in adults with cerebral palsy. Dev Med Child Neurol 2019; 61: 477–483. DOI: 10.1111/dmcn.14148.
25. Benfer KA, Weir KA, Bell KL, Nahar B, Ware RS, Davies PSW, et al. Oropharyngeal dysphagia in children with cerebral palsy: comparisons between a high- and low-resource country. Disabil Rehabil 2017; 39: 2404–2412. DOI: 10.1080/09638288.2016.1229363.

26. Speyer R, Cordier R, Kim JH, Cocks N, Michou E, Wilkes-Gillan S. Prevalence of drooling, swallowing, and feeding problems in cerebral palsy across the lifespan: a systematic review and meta-analyses. Dev Med Child Neurol 2019; 61: 1249–1258.
27. Huysentruyt K, Geeraert F, Allemon H, Prinzie P, Roelants M, Ortibus E, et al. Nutritional red flags in children with cerebral palsy. Clin Nutr 2020; 39: 548–553. DOI: 10.1016/j.clnu.2019.02.040.
28. Martínez de Zabarte Fernández JM, Ros Arnal I, Peña Segura JL, García Romero R, Rodríguez Martínez G. Caregiver burden in patients with moderate-severe cerebral palsy. The influence of nutritional status. An Pediatr (Engl Ed) 2021; 94: 311–317. Spanish. DOI: 10.1016/j.anpedi.2020.06.020.
29. Alvarez Zaragoza C, Vasquez Garibay EM, García Contreras AA, Larrosa Haro A, Romero Velarde E, Rea Rosas A, et al. Bone mineral density and nutritional status in children with quadriplegic cerebral palsy. Arch Osteoporos 2018; 13: 17. DOI: 10.1007/s11657-018-0434-8.
30. Jesus AO, Stevenson RD. Optimizing nutrition and bone health in children with cerebral palsy. Phys Med Rehabil Clin N Am 2020; 31: 25–37. DOI: 10.1016/j.pmr.2019.08.001.