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Growth and minerals status in children with cerebral palsy in Shiraz, Iran during April 2012-April 2013

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ABSTRACT

Background: Growth retardation and nutritional deficiencies is common in children with cerebral palsy (CP) and can influence their motor function. This study aimed to evaluate the growth and minerals status in children with CP and determine the association between macro and micro-minerals deficiencies with some factors like age, sex, type, and severity of CP and severity of malnutrition in these children.
Methods: One hundred patients with CP underwent anthropometric measurements. Malnutrition was assessed according to Gomes, Waterlow, Cole, and WHO classifications. Ten patients were excluded from the study due to hemolysis of blood samples. Serum analysis for minerals' concentration was performed for calcium (Ca), phosphorus (P), zinc (Zn), Copper (Cu), and ferritin. Motor functions were evaluated in according to Gross Motor Function Classification System (GMFCS) and manual ability classification system (MACS) classifications. Statistical analysis of patients' data was done using Chi-square and ANOVA tests.
Results: From a total of 90 participants, 30% had severe wasting, and 38.9% had severe stunting. Zinc deficiency was common among these children. Also, there were association between serum phosphorus (P) level and age variant ($p = 0.03$) and between high grades of GMFCS and zinc (Zn) deficiency ($p = 0.04$). Correlations were significant between severe malnutrition and spastic quadriplegic type and between stunting and wasting with spastic quadriplegic CP.
Conclusion: Malnutrition and growth retardation is common in children with CP. As an improvement in nutritional status has an impact on motor function and life quality in children with CP, more attention is recommended to their nutritional status and feeding problems.

Keywords: growth, minerals, cerebral palsy
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INTRODUCTION

Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing limitation in an activity that is attributed to non-progressive disturbances and occurs in the developing fetal or infant brain.[1] It is static at the time of recognition[2] and originates from some types of cerebral insults before birth, during delivery, or in the perinatal period.[3] The incidence of CP according to recent data from the Centers for Disease control and prevention is 3.6/1000 live births and male to female ratio is 1.4/1.[4] Prevalence of CP rises to 16/1000 live births in those born below 2500 gram.[5] Unfortunately, no study has been done about incidence or prevalence of CP in Iran until now.

There is no definite curable treatment for CP and treatment is based on prevention. Some studies have shown that magnesium administration in cases of impending preterm birth protects against CP.[6] In a study, intrathecal baclofen therapy resulted in weight gain and increased growth parameters in severe spastic and malnutrition children.[7]

Prognosis of CP depends on many factors, but in this study, we specifically focused on growth and serum minerals status because growth retardation and malnutrition can increase mortality rate in these children.[8] The results of previous studies also demonstrate higher incidence and prevalence of malnutrition in these children. An investigation done by Asmah et al[9] on 29 patients in 2015 showed copper and zinc deficiencies is a common feature in Ghanaian children with CP. Same results obtained by Kalra et al[10] in India. Serum iron and copper were lower in CP cases compared to control group, and there was no difference in micronutrients levels with respect to Gross Motor Function Classification System (GMCSF) grade. Another study was done by Hillesund et al[11] in Norway on 2007 also showed low serum micronutrients in CP cases. However, no investigation has been done to find out whether there is any association between minerals deficiency and some factors like severity of disability, or type of CP or more other factors so far.

This study aimed to evaluate the growth and minerals status and to discover an association between mineral's serum levels and some factors like type of CP, the severity of CP, the severity of malnutrition, age, and sex in children with CP in Iran. Also, there was an attempt to investigate the correlation between severity of malnutrition and type of CP and severity of the disability.

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MATERIAL AND METHODS

Study design and selection criteria

One hundred children with CP (62 boys and 38 girls) with the age range from seven months to 17 years who visited children neurology clinic of Imam-Reza, Shiraz, Iran (affiliated with Shiraz University of Medical Science) were selected to participate in this cross-sectional study. Inclusion criteria were children with CP aged 6 months to 18 years old who did not have any chronic disease other than CP.

Assessment of nutritional status and gross motor function

The patients underwent anthropometric measurements including weight (wt), height/length, body mass index (BMI), weight for age, and height for age. BMI for age z-scores was calculated for each patient and compared with normal Iranian children growth charts.[12] BMI was calculated as wt (kg)/[height (m)]^2. For evaluation of the severity of malnutrition, patients were classified into normal, mild, moderate and severe groups using Gomez, Waterlow, Cole.[4] The formula to calculate according to Gomez, Waterlow, and Cole criteria described as follow:

Gomez criteria = [(patient weight) / (weight of normal child of same age)] x100
Waterlow criteria = [(height of patient) / (height of a normal child of the same age)] x100
Cole criteria = z-scores of BMI for age

Gross motor function of children was assessed and classified according to GMFCS and Manual Ability Classification System (MACS). [13]

Blood sample collection and analysis

After obtaining permission from the ethics committee and verbal consent from the parents, 5 mL venous blood sample was taken from non-fasting patients in acid washed plastic tubes and analyzed at Namazi Hospital Laboratory of Gastroenterology and Liver Disease Research Center. Ten patients were excluded from this study due to hemolysis of blood samples and no permission for resampling. We continued the study with 90 patients (55 boys and 35 girls). Analysis for serum minerals concentrations including calcium (Ca), phosphorus (P), zinc (Zn), copper (Cu), and ferritin was done on these 90 samples.

Calcium measurement performed with photometric determination with Arsenazo III method (BioSystem kit). Phosphorus measurement performed with photometric ultraviolet (UV) test (Pars azmoon kit). Measurement of zinc performed with randox colorimetric method (ZN2341). Measurement of copper performed with randox colorimetric method (CU2340), and ferritin with EIA 96 tests method (Padtan Elm kit). The results were evaluated against the reference ranges used by the respective laboratories except for calcium. Harriet Lane Handbook 19th edition's age-specific serum Ca levels were used to interpret the data.[14] According to those reference ranges, measured values were considered as high, normal, and low: For assessment of nutritional status, patients were classified into 3 groups (mild, moderate and severe) according to Gomez, Waterlow, and Cole classifications.[4] Also, the patients were classified into

Table 1 Frequency and percentages of malnutrition according to Gomez, Waterlow, and Cole grading

Grading	Severity				Total
Gomez	Normal (> 90%) n = 7 (7.8%)	Mild (75-90%) n = 32 (35.6%)	Moderate (60-74%) n = 27 (30%)	Severe (< 60%) n = 24 (26.7%)	n = 90 (100%)
Waterlow	Normal (> 90%) n = 7 (7.8%)	Mild (80-90%) n = 32 (35.6%)	Moderate (70-80%) n = 27 (30%)	Severe (< 70%) n = 24 (26.7%)	n = 90 (100%)
Cole	Normal (z-score ≥ -1) n = 29 (32.2%)	Grade 1 (z-score < -1) n = 5 (5.6%)	Grade2 (z-score < -2) n = 14 (15.6%)	Grade 3 (z-score < -3) n = 42 (46.7%)	n = 90 (100%)

Table 2 minerals status and sex and serum Ca, P, Cu, Zn, and Ferritin

Minerals	Normal	Low	Mean ± SD	F	*p*-value
Ca	n = 51 (56.7%)	n = 39 (43.3%)	8.96 ± 1.8 mg/dL	1.24	0.22
P	n = 84 (93.3%)	n = 6 (6.7%)	5.53 ± 1.9 mg/dL	1.32	0.17
Cu	n = 74 (82.2%)	n = 16 (17.8%)	120 ± 40 µg/dL	0.85	0.68
Zn	n = 67 (74.4%)	n = 23 (25.6%)	91.28 ± 37.9 µg/dl	1.49	0.09
Ferritin	n = 89 (98.9%)	n = 1 (1.1%)	179.7 ± 186.8 ng/ml	0.89	0.63

Table 3 Minerals status in different types of CP

Type of CP		Ca	P	Cu	Zn	Ferritin
Spastic diplegic	Mean	8.9927	5.0455	1.1868	1.5402	1.1995
	n	11	11	11	11	11
	Std. Deviation	1.49575	1.97958	3.90335	2.85628	1.46458
	Minimum	6.50	.70	52.50	116.30	13.50
	Maximum	11.43	8.40	162.50	208.60	471.30
Spastic quadriplegic	Mean	8.7523	5.5069	1.2043	1.3574	1.9379
	n	62	62	62	62	62
	Std. Deviation	1.93048	1.95368	3.92258	4.54213	1.87076
	Minimum	3.83	.60	50.20	2.70	5.20
	Maximum	11.77	9.90	221.20	301.00	780.30
Extrapyramidal	Mean	10.0100	5.9737	92.8375	1.3434	2.0204
	n	8	8	8	8	8
	Std. Deviation	1.32638	1.83040	3.25815	2.04442	2.20585
	Minimum	8.15	4.40	64.10	98.90	12.40
	Maximum	12.06	9.10	152.20	166.20	700.00
Hemiplegic	Mean	9.4878	5.9667	1.4402	1.5897	1.3597
	n	9	9	9	9	9
	Std. Deviation	1.62240	1.76139	4.45939	2.95734	2.07031
	Minimum	6.27	3.60	65.30	119.60	13.10
	Maximum	11.36	8.50	181.50	202.70	676.10
Total	Mean	8.9670	5.5380	1.2012	1.4017	1.7972
	n	90	90	90	90	90
	Std. Deviation	1.82704	1.91443	4.01625	4.11504	1.86801
	Minimum	3.83	.60	50.20	2.70	5.20
	Maximum	12.06	9.90	221.20	301.00	780.30

n = number of patients in each category of CP, Std. Deviation = standard deviation

grade 1,2,3 using BMI z-scores according to Cole classification, and classified to moderate and severe stunting and wasting according to WHO wasting and stunting classifications by using weight for age and height for age z-scores.[4]

Data analysis

Statistical analysis was performed using SPSS for Windows (version 11, SPSS Inc.). Data with normal distribution presented as mean ± standard deviation (SD), while data without normal distribution presented as median (minimum-maximum). Prevalence of each mineral (Ca, P, Cu, Zn, and ferritin) deficiencies and the association between minerals serum level and type of CP, the severity of CP, the severity of malnutrition, age, and sex of the patients were assessed and interpreted using Chi-square and ANOVA tests. A *p*-value below 0.05 was considered statistically significant.

RESULTS

This study included 90 children (55 males and 35 females) with CP, aged ranged from seven months until 17 years old (mean 5.43 ± 4.2 years).

From a total of 90 patients with CP, 52 patients (57.7%) had a weight below the 5th percentile for their age and gender. 87 patients (96.6%) had a weight below the 50th percentile. 25 patients (27.8%) had moderate wasting, and 27 patients (30%) had severe wasting according to WHO wasting classification.[3] In the evaluation of height, 50 patients (55.5%) had height below the 5th percentile, and 81 patients (90%) had height below the 50th percentile. According to WHO stunting classification, 15 patients (16.7%) had moderate, and 35 patients (38.9%) had severe stunting. The result of Gomez, Waterlow, and Cole classifications shown in Table 1.

The results of minerals status shown in Table 2. No association was found between sex and level of serum minerals (table 2).

No correlation was found between sex and type of CP. Also, no association was found between sex and severity of malnutrition using Chi-square test. We found an association between serum P level and age variant using ANOVA test ($p = 0.03$) showing that low serum P level was more common in younger ages (mostly below 4 years old). No association was found between Ca, Zn, Cu, and Ferritin levels and age variant. Minerals status in different types of CP is displayed in Table 3.

In the evaluation of malnutrition and types of CP, it was revealed that patients with spastic quadriplegic CP were significantly malnutrition. According to Gomez grading, 91.7% of the patients with severe (grade 3) malnutrition were those with spastic quadriplegic type, and there was a significant association between the type of CP and severe Gomez grading (p=0.002). However, there was no association between the type of CP and Waterlow grading (p=0.16). Also, 92.6% of the patients with severe wasting and 85.7% with severe stunting were those with spastic quadriplegic type, and there was a significant correlation between wasting, stunting, and type of CP (p-values are 0.01 and 0.005 respectively). As to the severity of gross motor dysfunction, 78.3% of patients with low serum Zn had GMCSF grade 5, and we found a negative correlation between Zn level and GMFCS grading with p=0.04. No significant association was found between other mineral's serum levels and GMFCS and MACS grading. In the assessment of the association between Gomez, Waterlow and Cole classifications and mineral's level, no association was found.

DISCUSSION

In our study children with CP significantly had lower anthropometric measurements (height, weight, BMI) than normal. Total prevalence of wasting was 57.8% in our study. 52 patients (57.7%) had a weight below the 5th percentile for their age and gender. 54 males (98.1%) and 33 females (94.2%) had a weight below the 50th percentile. More than half of these patients (n = 50) were stunted (-2 > HFA z-score) according to WHO stunting and wasting classification.[4] Previous studies also confirm these results. In a study that was done by Samson-Fang et al[15] at North America in 2002, 225 of 235 cases with CP (95.7%) had mean WFA Z-score below -2. Campanozzi et al[16] study in 2006 found that 62% had the height for age below the 5th percentile. Kakooza-Mwesige et al[17] study at Uganda in 2015 also revealed that over half of cases (52%) were malnourished with underweight (42%) being the most common category followed by stunting (38%), thinness (21%), and wasting (18%). Another cross-sectional study done by Wang et al[18] in 2016 at West China showed that 42.4% of cases were stunted. All these results reveal that malnutrition and growth deviation is significantly common in children with CP.

Some studies also found a correlation between prevalence of malnutrition and severity of motor impairment. As in Wang et al[18] study, a significant negative correlation was found between nutritional status and age, GMFCS, and MACS levels. Also in our study, most of the children with grade 3 or severe malnutrition were the spastic quadriplegic type (91.7%). Another study from Greece noticed that stunting and wasting z-scores were aggravated in spastic quadriplegic cases.[19] Also a cross-sectional investigation of 90 children with CP at Brazil in 2013 revealed that children with quadriplegic CP showed a greater nutritional loss and the most affected ratio was height for age z-score.[20]

Evaluation of minerals status in these 90 children with CP showed a high proportion of them had low serum mineral levels particularly low serum calcium (table-2). Previous studies demonstrate our findings. For example, Hillesund et al[11] has reported low serum minerals and trace elements in children with CP. Whereas low ferritin was less common in our study, but low zinc was more common (table-2). Also, mean of copper was lower in our study (18.91 ± 6.3 μmol/L in our study versus 21.7 ± 4.2 μmol/L in Hillesund's study). Schoendorfer et al[21] investigated that children with CP had inadequate intakes of Ca, K, I, and Mn. Also, zinc deficiency was significant in orally fed and control group than PEG (percutaneous endoscopic gastrostomy) fed children. In one study by Asmah et al.,[9] 86.21% had copper concentration below normal physiologic range, and serum zinc levels were normal in only 20.1% of cases. Kalra et al[10] study also revealed that serum levels of iron, copper, magnesium are significantly less in children with CP.

What is new in our study is we found correlations between age and P level with $p = 0.03$. No correlation was found between minerals level and sex variant. Low Zn level had associations with higher GMFCS grades (grade 5) with $p = 0.04$. A significant association was found between severe malnutrition and the type of CP ($p = 0.002$). 91.7% of the children with severe malnutrition (grade 3 of Gomez) were spastic quadriplegic patients. Also, a significant association was found between the type of CP and wasting ($p = 0.013$) and also stunting ($p = 0.005$). 92.6% of the patients with severe wasting and 85.7% with severe stunting had spastic quadriplegic CP.

The differences in serum minerals level between our study and previous one are mostly due to feeding problems. Most of the children in our study are from families with low socioeconomic status, and 35 patients have been referred from disabled care centers. A high proportion of them (96%) had oral feeding despite oral motor dysfunction and this limited their food intake and only three patients had tube feeding. Also, most of them (n = 76) have not received any nutritional supplements. Therefore, they did not have sufficient mineral intakes. In addition, they did not have sufficient sunlight exposure due to severe disabilities and inability to walk. A review article by Penagini et al[22] noticed that biochemical deficiency of micronutrients is common in children with CP, indicating that dietary intakes of vitamins and minerals are often too low to balance needs in these population. Also, iron deficiency anemia is a frequent complication in neurologically impaired children due to the low iron intake. Thus, special attentions should be paid to these children's nutritional status, food intake, and route of feeding. As previous studies have shown, the enteral tube feeding is more effective and leads to weight gain and linear growth in severely disabled children with CP.[16]

CONCLUSION

Our study showed that children with CP had malnutrition and low anthropometric measurements that can influence their quality of life. Adequate nutritional support improves linear growth and weight gain, enhances the quality of life and health, and reduces the frequency of hospitalization. Therefore mineral deficiencies should be corrected considering the amount of supplement usage. More attentions should be paid to nutritional status and feeding problems in neurologically impaired children, including CP.

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