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Research Article
Impact of Iron Deficiency Anemia on Functional Abilities and Muscle Strength in Children with Spastic Cerebral Palsy

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Abstract

Background and Objective: The most common nutritional deficiency is iron deficiency that leads to anemia. The purpose of the study was to investigate the impact of iron deficiency anemia on functional abilities and muscle strength in children with spastic cerebral palsy. **Materials and Methods:** One hundred children with spastic CP from both gender ranging in age from 4-6 years participated in this study. They were selected from the Outpatient Clinic of Pediatrics, Faculty of Physical Therapy, Cairo University. The selected children were assigned into 2 groups of equal number i.e., 5 children in each group. Group A included 50 anemic spastic CP children and Group B included 50 non-anemic spastic CP children. All children were evaluated for hemoglobin, serum iron, functional abilities, hand grip strength and knee extensor strength. **Results:** The results showed statistically significant differences in all measured variables between both groups in favor of group B ($p<0.05$). Additionally, there were strong positive significant correlations between hemoglobin and motor skills and muscle strength as well as serum iron and all measured variables. **Conclusion:** Iron deficiency anemia had a negative impact on functional abilities and strength. Anemic children had a lower motor function scores and strength compared to non-anemic children.

Key words: Iron deficiency anemia, hemoglobin, motor functions, handgrip, knee extensors, spastic cerebral palsy

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Cerebral Palsy (CP) is a common childhood disability that defined as a non-progressive neuromotor disorder of central nervous system occurring in early life affecting tone, posture, balance and locomotion. Children with CP often exhibit feeding problems, multiple nutritional deficiencies with or without seizers[1,2]. Spastic CP is the common type that affects 75% of children with CP resulting from injury to motor center of cerebral cortex[3]. Children with spastic CP experience various motor and sensory impairments that affect daily activities such as; walking, reaching and grasping[4]. A number of factors have been associated with poor nutritional status and growth in children with CP including self-feeding difficulties, limited physical performance of mastication and swallowing due to oral motor dysfunction resulting in reduced dietary intake, prolonged feeding times and inadequate nutrient intake which contribute to iron deficiency[5-7].

Anemia is described as a condition in which the number of red blood cells or their oxygen-carrying capacity is insufficient to meet physiologic needs[8]. The incidence of anemia is considered to be high in children with CP due to lack of iron intake[9]. Anemia is associated with impairment in the ability to perform activity of daily living, weakness and fatigue[10-12]. Iron deficiency anemia (IDA) developed from depletion of iron stores and characterized by low serum iron <75 mg dL^{-1} and low hemoglobin level with increased red cell distribution width (RDW)[13]. It may affect muscle strength and motor functions including gross and fine motor function due to decreased oxygen transportation by hemoglobin (Hb) to the working muscle and increased building up of lactic acid leading to fatigue, weakness and declined physical performance[14-16].

No studies have been conducted to examine the possible effects of IDA on neurodevelopmental abilities and muscle performance in children with spastic CP. Therefore, this study aimed to investigate the impact of IDA on functional abilities and muscle strength in children with spastic CP.

MATERIALS AND METHODS

This study was conducted at the Faculty of Physical Therapy, Cairo University, during the period from September, 2017-October, 2018 to investigate the impact of iron deficiency anemia on functional abilities and muscle strength in children with spastic CP.

Subjects: One hundred children with spastic CP from both gender ranging in age from 4-6 years participated in this study. They were selected from the Outpatient Clinic of Pediatrics, Faculty of Physical Therapy, Cairo University.

Inclusion criteria: They were enrolled in this study if they had the following inclusion criteria, (a) Mild degree of spasticity (1 or 1+) according to the modified Ashworth scale[17], (b) Level II of the gross motor function classification system for cerebral palsy[18], (c) Microcytic hypochromic anemia with (Hb) level below 11.5 g dL^{-1} and serum iron level below 75 mg dL^{-1}, the non-anemic children had normal (Hb) level >11.5 g dL^{-1} and the serum iron above[13,19] 75 mg dL^{-1} and (d) Able to understand and follow verbal commands and instructions during the testing procedure.

Exclusion criteria: Children were excluded from the study if they had; (a) Visual, auditory defects or another type of anemia rather than iron deficiency anemia, (b) Systematic disease that cause anemia such as renal or hepatic failure as well as who received blood transfusion within 3 months before measuring the hematological indices and (c) Documented trauma in the previous 12 months in the muscle fibers or those taking medication that affect strength.

The children were equally divided into two groups with 50 children in each group. Group A included 50 anemic spastic CP children (25 hemiplegic CP and 25 diplegic CP children). Group B included 50 non-anemic spastic CP children (25 hemiplegic CP and 25 diplegic CP). The study was performed according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. It was approved by the Ethics Review Committee of the Faculty of Physical Therapy, Cairo University, Egypt (No.: P.T. REC/012/001850).

The purpose and procedures of the current study were explained to the parents of participating children and they signed a written informed consent approving their children participation in the study.

Procedures: Blood samples were taken from all children to analyze Hb and serum iron levels by laboratory tests using fully automated blood cell counter (sysmex-Xs 800i) and AU 480-chemistry auto-analyzer (Beckman Coulter Diagnostics-USA)[20].

Assessment of fine and gross motor functions: The PDMS-2 comprises 6 subtests that measure the inter-related

gross and fine motor abilities that develop early in life. Locomotion, stationary and grasping subtests were chosen to assess the functional abilities of the children in the present study. The children were evaluated from sitting position for grasping subtest which includes 26-item that measure the child's ability to use his or her hands. When administrating the gross motor subtests includes (stationary and locomotion) the children were evaluated from different positions according to the nature of tasks. Stationary subtest includes 30 items that measured the child's ability to sustain control of his or her body within its center of gravity and retain the equilibrium. Locomotion subtest included 89 items that measured the child's ability to move from one place to another. After administration of all items in each subtest, raw and standard score were calculated for each one[21].

Assessment of hand grip strength: Jamar hydraulic hand dynamometer is a reliable and valid tool used to measure the isometric muscle strength of hand grip for CP children[22,23]. Each child was positioned in the seating position with shoulder adducted, elbow flexed to 90° with the forearm and wrist in neutral position. The dynamometer was adjusted for hand size to maintain the accuracy of the measurement. Each child was asked to squeeze the dynamometer with maximum isometric effort, which is maintained for about 5 sec. Grip strength was carried out smoothly without any jerking motion. This procedure was repeated for 3 times with 30 sec rest between trials and the mean value of three trials was recorded for analysis[24].

Assessment of knee extensor strength: Lafayette manual muscle test system was used for measuring the isometric muscle strength of knee extensors in the present study. It was employed to measure the force in kilograms (kg) providing reliable and accurate muscle strength recordings[25]. Each child was evaluated from the sitting position at the edge of the evaluation chair with flexed hip and knee 90°. The leg was well stabilized and the strap resisted the isometric knee extension during the test. The child performed two sub-maximal contractions as a warm-up to ensure that the task was well understood and the stabilization was adequate followed by a 30 sec rest period. During testing, each child was instructed to maintain contraction of knee extensors for 10 sec and then the force of contraction was measured. This procedure was repeated for 3 times with 60 sec rest between trials. The mean of three trails was recorded and used for analysis[26].

Statistical analysis: All data were presented as descriptive statistics (mean value±standard deviation for parametric values and median and interquartile range (IQR) for non-parametric values). Independent t-test was conducted for comparison of the mean age, weight, height, BMI, Hb level, serum iron level and muscle strength between both groups. Mann-Whitney U-test was used for comparison of median values of PDMS-2 sub-tests scores between both groups. Spearman correlation coefficient was conducted to determine the relationship between hemoglobin and iron levels with PDMS-2 subtests scores while Pearson Correlation Coefficient was used to determine the relationship between hemoglobin and iron levels with muscle strength. The level of significance for all statistical tests was set at $p<0.05$. All statistical measures were performed through the statistical package for social studies (SPSS) version 19 for windows.

RESULTS

Demographic characteristics of the participants: As shown in Table 1, there were no statistically significant differences between both groups ($p>0.05$).

Comparison of PDMS-2 subtests scores between both groups: As presented in Table 2 there were statistically significant differences in the median values of PDMS-locomotion, stationary and grasping sub-tests scores between both groups in favor of Group B ($p = 0.0001$).

Table 1: Demographics and clinical characteristics of participants in both groups

	$\overline{X}$±SD			
Parameters	Group A (n = 50)	Group B (n = 50)	t-value	p-value
Age (years)	4.87±0.65	4.77±0.63	0.81	0.41
Weight (kg)	14.06±1.47	14.20±1.54	-0.46	0.64
Height (cm)	100.44±6.82	100.34±6.21	0.07	0.93
BMI (kg m^{-2})	14.08±2.21	14.21±2.01	-0.3	0.76
Hemoglobin (g dL^{-1})	10.60±0.46	12.00±0.47	-14.91	0.0001*
Iron (µg dL^{-1})	60.15±6.82	99.00±14.25	-17.37	0.0001*

$\overline{X}$: Mean, SD: Standard deviation, t-value: Independent t-test, p-value: Probability value, *p<0.05

Table 2: Comparison of the median values of PDMS-2 subtests scores between both groups

	Median (IQR)			
Parameters	Group A	Group B	z-value	p-value
Locomotion subtest (Standard score)	4 (3.75-5)	6 (5-10)	389.5	0.0001*
Stationary subtest (Standard score)	5 (3-5)	6.5 (5-9)	585.5	0.0001*
Grasping subtest (Standard score)	2 (1-3)	3 (2.75-7.25)	585.5	0.0001*

IQR: Interquartile range, z-value: Mann-Whitney U-test, p-value: Probability value, *p<0.05

Comparison of knee extensors strength and hand grip strength between both groups: Statistically significant differences were observed in the mean values of knee extensors and hand grip strength between both groups in favor of Group B (Table 3).

Correlations between hemoglobin and serum iron levels and the outcome measures in Group A: In Table 4, the Spearman correlation coefficient revealed that there were strong positive significant correlations between Hb and serum iron levels and the standard score of PDMS-2 subtests (p = 0.0001) in Group A. In addition, Pearson correlation coefficient also revealed that there were strong positive significant correlations between Hb and serum iron levels and muscle strength.

Correlations between hemoglobin and serum iron levels and the outcome measures in group B: In Table 5, the Spearman correlation coefficient revealed that there were strong positive significant correlations between hemoglobin and serum iron levels and the standard score of PDMS-2 sub-tests in Group B. While, Pearson correlation coefficient also exhibited strong positive significant correlations between hemoglobin and serum iron levels and muscle strength.

Table 3: Comparison of knee extensors strength and hand grip strength between both groups

	$\bar{X}\pm SD$			
	Group A	Group B	t-value	p-value
Extensor knee strength (kg)	3.86±1.46	5.85±1.94	-5.8	0.0001*
Hand grip strength (kg)	1.8±1	3.05±1.25	-5.52	0.0001*

$\bar{X}$: Mean, SD: Standard deviation, t-value: Independent t-test, p-value: Probability value, *p<0.05

DISCUSSION

The results of the current study revealed that there were significant differences in all measured variables between anemic and non-anemic spastic CP children regarding locomotion, stationary and grasping skills as well as knee extensors and hand grip strength. Furthermore, there were strong associations between Hb and serum iron levels with functional abilities and muscle strength in both groups.

The result of the current study comes in agreement with Pollitt *et al.*[27], who investigated the IDA in preschool children aged (3-5 years). They found significant differences between anemic and non-anemic children in the gross and fine motor scores. They also added that anemic children had lower score in the motor scales than non-anemic. The significant differences between both groups in all measured variables could be explained by the work of Stugiewicz *et al.*[28], who reported that IDA forced the muscles to depend on anaerobic metabolism due to two mechanisms. First, declined hemoglobin concentration and reduced myoglobin within cells as a result of iron stores depletion. This is related to diminished oxygen transport, oxygen diffusion, mitochondria within the exercising tissue and altered oxidative to glycolytic fiber ratio of exercising muscle. Second, excess production of lactic acid because of insufficient oxygen transported to the muscle tissues leading to reduced muscle strength and endurance[14].

The results of the present study indicated that there were significant differences between both groups in muscle performance including knee extensors strength and hand grip strength. These findings come in agreement with Dougherty *et al.*[29] who examined muscle strength in anemic children. They found that anemic children have a lower hand grip strength compared to non-anemic children. Furthermore,

Table 4: Correlations between hemoglobin and iron levels and the outcome measures in Group A

	Locomotion		Stationary		Grasping		Knee extensors strength		Hand grip strength	
Parameters	$r^{a)}$	p-value	$r^{a)}$	p-value	$r^{a)}$	p-value	$r^{b)}$	p-value	$r^{b)}$	p-value
Hb Level	0.73	0.0001*	0.95	0.0001*	0.96	0.0001*	0.89	0.0001*	0.92	0.0001*
Iron level	0.77	0.0001*	0.96	0.0001*	0.93	0.0001*	0.9	0.0001*	0.91	0.0001*

$r^{a)}$: Spearman correlation coefficient, $r^{b)}$: Person correlation coefficient, p-value: Probability value, *p<0.05

Table 5: Correlations between hemoglobin and iron levels and the outcome measures in group B

	Locomotion		Stationary		Grasping		Knee extensors strength		Hand grip strength	
Parameters	$r^{a)}$	p-value	$r^{a)}$	p-value	$r^{a)}$	p-value	$r^{b)}$	p-value	$r^{b)}$	p-value
Hb level	0.71	0.0001*	0.91	0.0001*	0.91	0.0001*	0.88	0.0001*	0.87	0.0001*
Iron level	0.6	0.0001*	0.85	0.0001*	0.93	0.0001*	0.92	0.0001*	0.95	0.0001*

$r^{a)}$: Spearman correlation coefficient, $r^{b)}$: Person correlation coefficient, p-value: Probability value, *p<0.05

Georgieff[30] and Algarin *et al.*[31] also demonstrated that IDA in preschool age has multiple effects on the brain growth process and hippocampal and cortical regions development as well as myelinogenesis, dendritogenesis and synaptogenesis. The impaired myelination of sensory and motor nerves fibers could result in slower conduction of impulses. Strong associations between Hb and serum iron levels with functional abilities and muscle strength observed in the current study come in agreement with Shafir *et al.*[15,32] who investigated the relationship between IDA and infant motor development. They found that there is a linear association between iron level and gross and fine motor abilities. They added that the children with IDA have poorer gross and fine motor PDMS-2 scores. Moreover, Cesari *et al.*[33] studied the relation between Hb level and skeletal muscle performance. They found that there is a positive association between IDA and reduced motor functions, reduced knee extensors and hand grip strength. McDonagh *et al.*[34] also reported that Hb has an effect on motor performance and muscle strength in anemic and non-anemic children. Within the same context, Ramesh *et al.*[35] and Beard[36] found that IDA results in decreased oxygen carrying capacity, reduced muscular strength and motor activities.

The results of the present study revealed positive relationship between Hb and serum iron levels and muscle strength. These findings come in agreement with Kocahan *et al.*[37] who examined the relation between serum iron and isokinetic muscle strength. They found that there was moderate positive relationship between serum iron and knee extensors strength.

The limitation of this study includes small sample size, which makes it difficult to make generalization of the results. Therefore, further study with a large sample size is necessary to generalize these findings. Future study is needed to investigate the effect of appropriate nutrition and iron supplementation on motor efficiency and quality of life in CP children.

CONCLUSION

It could be concluded that anemic spastic CP children have a lower motor functions score and decreased muscle strength compared to non-anemic CP children. Additionally, there were linear associations between Hb and serum iron levels with functional abilities and muscle strength in children with spastic CP.

SIGNIFICANCE STATEMENT

This study discovered the impact of iron deficiency anemia on functional abilities and muscle strength in children with spastic CP, which can be beneficial for the early identification of iron deficiency anemia in CP children to prevent its neurodevelopmental consequences and to help researchers to approach the critical areas that affect motor abilities and muscular strength in those children that many researchers were not able to explore. Thus, a new theory on the necessity of iron therapy may be arrived at.

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