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Methodology

Assessment of some micronutrients serum levels in children with severe acute malnutrition with and without cerebral palsy- A follow up case control study

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SUMMARY

Objective: Zinc, copper and selenium are essential for normal development and function of the central nervous system. This study aimed at assessment of serum levels of zinc, copper and selenium in children with severe acute malnutrition (SAM) with & without cerebral palsy both before and after nutritional rehabilitation.
Methods: A prospective case control study involved 2 groups (Group I); included160 children with SAM of both sex, aged 6–59 months, this group was subdivided into 2equal subgroups; subgroup A: SAM without cerebral palsy, subgroup B: SAM with cerebral palsy. Group II (control group) included 96 apparently healthy children matching age and sex with the first group. Both groups were subjected to a detailed history including nutritional history. Anthropometric measurements were recorded and laboratory assessment for serum levels of (copper, zinc, & selenium) before and after nutritional rehabilitation were performed for all children.
Results: Group I (A&B) showed a significant decrease in anthropometric measurements, serum zinc, serum selenium but normal copper level before nutritional rehabilitation in comparison to

Abbreviations: SAM: severe acute malnutrition, CP: cerebral palsy; WAZ: weight for age Z score, HAZ: height for age Z score; WHZ: weight for height Z score, MUAC: mid upper arm circumference.

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control. After nutritional rehabilitation, all cases of the group I showed a significant improvement of the three parameters except for (45%) of cerebral palsy cases, experienced a resistant low selenium.

Conclusion: Nutritional rehabilitation significantly improved micronutrients' serum level in SAM children with and without cerebral palsy. Selenium supplementation is advised for children with cerebral palsy in order to reach normal values with observation of effect on neurological state.

Table of contents

This article is dealing with severe acute malnutrition in children, analyzing mainly micronutrients in these patients with and without CP before and after nutritional rehabilitation.

What's known on this subject

Micronutrients such as zinc, iodine, iron, copper, and selenium are essential for the nervous system to develop and function normally. Hence, their deficiency is a critical issue and impairs cognitive, motor, and socioemotional abilities.

What this paper adds

Evaluation of micronutrients before and after nutritional rehabilitation of malnourished. Malnourished children have lower Zinc, Selenium and normal Copper. Deficiencies improved with nutritional rehabilitation, but Selenium was still deficient in high percentage of CP children.

1. Introduction

About 20 million children around the world suffer severe acute malnutrition (SAM) that accounts for 54% of mortality in that group [1] and is identified by a very low weight for height (below −3 Z scores of the median WHO growth standards), visible severe wasting and/or presence of nutritional edema [2].

Cerebral palsy(CP) describes a group of permanent disorders of the development of movement and posture. CP causes activity limitation, that are attributed to non-progressive disturbances occurring in the developing fetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, behavior, epilepsy, and by secondary musculoskeletal problems [3]. It is responsible for most of the motor disabilities in about 2.1 per 1000 live births [4] as it affects muscle tone, strength and coordination leading to skeletal and joint impairment and possibly deformities [5].

Children with CP suffer from poor nutritional status that may be attributed to difficulties with feeding due to excessive spillage, gastro-esophageal reflux, delayed gastric emptying and oral motor dysfunction [6].

Micronutrients such as zinc, iodine, iron, copper, and selenium are essential for the nervous system to develop and function normally. Hence, their deficiency is a critical issue that impairs cognitive, motor, and socioemotional abilities [7] and is of a special concern for cerebral palsy children [8].

Zinc is an essential mineral [9] with deficiency in children causes growth retardation, delayed sexual maturation, heightened infection susceptibility, and diarrhea. While over consumption of zinc causes ataxia, lethargy, and copper deficiency [10].

Copper is vital for the normal development of the human body since the beginning of the fetal life [11]. Its deficiency could cause a wide variety of neurological problems including myelopathy, peripheral neuropathy, and optic neuropathy [12].

Selenium may impact cognitive function by protecting the brain from oxidative damage [13]. and its deficiency is usually associated with cognitive and motor disabilities [14,15]. Due to the vivacious role of copper, zinc and selenium in central nervous system metabolism [16] we aimed in this study at assessment of serum levels of zinc, copper and selenium in children suffering from SAM with & without cerebral palsy both before and after nutritional rehabilitation in comparison to apparently healthy children.

2. Patients and methods

A prospective nonrandomized case control study that was carried out over the period from January 2017 to October 2017 in the pediatric nutrition rehabilitation unit and outpatient clinic of Children and Maternity Minia University Hospital in Egypt, which is considered as the main referral hospital for the governorate. The study was approved by the local Ethical Committee of the Faculty of Medicine and a written consent was taken from each care giver after explanation of the study purpose. The study included 2 groups; a case group (Group I) of 160 children with severe acute malnutrition (SAM), that was diagnosed by the presence of severe wasting [weight for height (WHZ) <-3.0 SD and/or the presence of nutritional edema [17]. Their age ranged from 6 to 59 months and they were divided into 2 equal subgroups (80 children each). Group IA: included malnourished children without cerebral palsy, group IB: included malnourished children with cerebral palsy, according to neurological and topographical cerebral palsy classification [3].

A control group (Group II) of 96 apparently healthy well-nourished children matching age and sex with the case group and were recruited consecutively from outpatient clinic of the same hospital as they came with their parents during routine follow up of their growth or consultation for an acute illness.

Children having neurological disorders like inflammatory brain disease, degenerative brain disease, intracranial space occupying lesion, encephalopathy, and children with a chronic medical disorder (chronic liver disease, kidney disease, congenital heart disease, diabetes mellitus) also, children with extreme WHZ, height for age z scores (HAZ) or weight for height z scores (WHZ) were excluded from the study.

3. Clinical data collection

All children were subjected to a detailed general history taking (including; name, age, sex, residence, socioeconomic standard, mode of delivery, and maturity at the time of birth) with emphasis on the nutritional history, birth weight, type of cerebral palsy, seizure type, and complications of the malnutrition. Anthropometrics were recorded for all included children as weight, height/length, and mid-upper arm circumference, in reference to the WHO growth charts [18]. Vital data (such as respiratory rate, heart rate, blood pressure and temperature), full body examination (chest, heart, and abdomen), and laboratory assessment of micronutrients' serum levels (copper, zinc, & selenium) before and after nutritional rehabilitation were performed for all children.

All cases of group I were treated at hospital according to the WHO standard protocol [19], and complications were managed. Patients were discharged from the hospital when their anthropometric measurements met the discharging criteria as; looking well and alert, restoring normal appetite, resolved edema, and absent medical complications [20].

After discharge from hospital the studied children were followed-up for 3 months with recording of their anthropometric measurements, other nutritional parameters, vital signs and examination for any complications. The follow-up schedule was weekly for the first 2 weeks following the hospital discharge and monthly thereafter until weight-for-height/length achieved the ≥−2 Z-score, mid-upper-arm circumference reached ≥125 mm, and no reported edema for at least 2 weeks [20].

3.1. Sample collection and laboratory methods

Blood samples were collected under complete sterile conditions from all studied children. Two ml of venous blood was withdrawn from each child, transferred into plain tubes and kept in upright position until clotted. Clotted blood was centrifuged at 3000 rpm for 15 min. The separated serum was then transferred into aliquots and stored at −20 °C till required for assessment of serum level of zinc, copper, and selenium which were performed for both the controls and the cases using a flame spectrophotometer. Final values of zinc and copper were expressed in microgram per deciliter (μg/dl). Serum level of selenium was expressed in Nano gram per deciliter (ng/dl).

4. Statistical methods

The data were analyzed using SPSS (statistical program for social science, version 13.0). Continuous variables were presented as a mean ± standard deviation (SD), and categorical variables were presented as a frequency and percentage. P-value < 0.05 considered significant. One-way ANOVA for quantitative data and by chi-square for qualitative data. The Chi-square(X^2) was used to compare more than one proportion.

5. Results

The demographic data (age, sex, residence, maternal mode of delivery, maturity and socioeconomic level) showed statistically insignificant differences between all groups (Table 1).

Seventy percent of children with SAM are related to rural areas and are of low socio-economic standard in contrast to only 30% lived in urban areas are of moderate to high socio-economic standards.

Regarding the cerebral palsy cases, 45% were quadriplegic, 30% were diplegic, and 25% were choreoathetotic.75% of them had seizures while 25% were seizures free. Feeding difficulties experienced in 60% of cases.

Table 1
Demographic data of studied malnourished children (group I) without CP(groupA) and with CP (group B) in comparison to control (group II).

Demographic data	Group I (n = 160)		Group II (n = 96)	P-value
	Group A n = 80	Group B n = 80		
Age (months)				
Range	6–36	6–43	7–38	0.3
Mean ± SD	14.7 ± 7.8	19.1 ± 11.2	16.1 ± 8.8	
Sex				
Male	32 (40%)	40 (50%)	42 (43.8%)	0.8
Female	48 (60%)	40 (50%)	54(56.2%)	
Residence				
Rural	56 (70%)	56 (70%)	66 (68.8%)	0.9
Urban	24 (30%)	24 (30%)	30 (31.2%)	
Maternal delivery				
Normal	44 (55%)	52 (65%)	54 (56.2%)	0.7
CS	36 (45%)	28 (35%)	42 (43.8%)	
Maturity				
Full term	60 (75%)	60 (75%)	66 (68.8%)	0.8
Preterm	20 (25%)	20(25%)	30 (31.2%)	
Socioeconomic level				
Low	56 (70%)	56 (70%)	66 (68.8%)	0.9
Moderate	24 (30%)	24 (30%)	30 (31.2%)	

SD: standard deviation, CS: caesarian section, P value calculated by one-way ANOVA for quantitative data and by chi-square for qualitative data.
* p value < 0.05 considered significant.

The 2 subgroups of group I had significantly low anthropometric measurements (Weight for age, length/height for age, weight for length/height & mid upper arm circumference Z score) before nutritional rehabilitation compared to the control group (Table 2).

Multiple co-morbidities were detected in malnourished children without cerebral palsy, the most frequent one was gastroenteritis in 45% of cases followed by dehydration 40% and the least was pneumonia with a percentage of 15%., meanwhile 45% of group IB (malnourished children with cerebral palsy) had gastroenteritis, 30% had dehydration and 25% had pneumonia.

Mean serum zinc and selenium were significantly lower in group I (A &B) before nutritional rehabilitation than the control group (P-value< 0.0001) with deficient zinc in 70% of neurologically normal malnourished and 90% in cerebral palsy malnourished children. Meanwhile, selenium level was deficient in 65% of neurologically normal and in 100% of cerebral palsy children with SAM. Mean serum copper level was within normal reference range in all children but differences between groups were documented as serum copper was significantly lower in cerebral palsy SAM compared to the control group and to neurologically normal SAM (P-value <0.05) (Table 3).

A significant rise regarding anthropometric measurements at admission was experienced by all cases in group I (cerebral palsy and neurologically normal children) after nutritional rehabilitation (P-value = 0.0001) (Table 4).

Also, a significant rise was detected in the mean serum levels of zinc, copper and selenium(P < 0.0001) in comparison to at admission levels. But Zinc level is still deficient in 15% of neurologically normal and 20% of cerebral palsy. Meanwhile, selenium was deficient in 45% of cerebral palsy but normalized in 100% of neurologically normal children after nutritional rehabilitation (Table 5).

Table 2
Anthropometric measurements of studied children with severe acute malnutrition before nutritional rehabilitation (group I) in comparison to control (group II).

Z score	Group I (n = 160)		Group II (n = 96)	P-value
	Group A n = 80	Group B n = 80		
WAZ				
Below −3 SD	80 (100%)	68(85%)	0 (0%)	0.0001*
−3 to −2 SD	0 (0%)	12 (15%)	0 (0%)	
−1 to 0 SD	0 (0%)	0 (0%)	24 (25%)	
0 to 1 SD	0 (0%)	0 (0%)	36 (37.5%)	
1 to 2 SD	0 (0%)	0 (0%)	36 (37.5%)	
HAZ				
Below −3 SD	80 (100%)	80 (100%)	0 (0%)	0.0001*
−1 to 0 SD	0 (0%)	0 (0%)	42 (43.8%)	
0 to 1 SD	0 (0%)	0 (0%)	48 (50%)	
1 to 2 SD	0 (0%)	0 (0%)	6 (6.2%)	
WHZ				
Below −3 SD	72 (90%)	80 (100%)	0 (0%)	0.0001*
−3 to −2 SD	0(0%)	0 (0%)	0 (0%)	
−2 to −1 SD	0 (0%)	0 (0%)	18 (18.8%)	
−1 to 0 SD	0(0%)	0 (0%)	12 (12.5%)	
0 to 1 SD	0(0%)	0 (0%)	18(18.8%)	
1 to 2 SD	0 (0%)	0 (0%)	18 (18.8%)	
Above 3 SD	0 (0%)	0 (0%)	30 (31.2%)	
MUAC				
Below −3 SD	80 (100%)	80 (100%)	0 (0%)	0.0001*
−1 to 0 SD	0 (0%)	0 (0%)	18 (18.8%)	
0 to 1 SD	0 (0%)	0 (0%)	60 (62.5%)	
1 to 2 SD	0 (0%)	0 (0%)	18 (18.8%)	

P value calculated by chi-square test.
WAZ: Weight for age, HAZ: Height for age, WHZ: Weight for Height, MUAC: Mid upper arm circumference, SD: standard deviation.
* P-value < 0.05 considered significant and calculated by chi-square test.

Table 3
Mean zinc, copper and selenium levels in malnourished children before nutritional rehabilitation (group I) in comparison to control (group II).

	Group I (n = 160)		Group II (n = 96)	P value		
	Group A (n = 80)	Group B (n = 80)		P1 IA v IB	P2 IA v II	P3 IB v II
Zinc (μg/dl)						
Range	55–83	48–79	68–100	0.01*	0.0001*	0.0001*
Mean ± SD	65.3 ± 7.3	58.4 ± 7.5	81.8 ± 9.8			
Normal %	30%	10%	100%			
Deficient %	70%	90%	0%			
Copper(μg/dl)						
Range	85–220	81–222	92–230	0.01*	0.6	0.05
Mean ± SD	157.6 ± 40.8	128.3 ± 33.1	152.5 ± 38.1			
Normal %	100%	100%	100%			
Selenium(ng/dl)						
Range	28–80	29–59	52–77	0.009*	0.003*	0.0001*
Mean ± SD	51.6 ± 12.7	43.3 ± 7.8	61.7 ± 6.9			
Normal %	35%	0%	75%			
Deficient %	65%	100%	25%			

P value calculated by one-way ANOVA.
* p value < 0.05 considered significant.

Table 4
Comparison between anthropometric measurements before and after nutritional rehabilitation in cases of SAM with (group A) and without CP (group B).

Z score	Group A Neurologically normal SAM			Group B SAM with CP		
	Nutritional rehabilitation		P value	Nutritional rehabilitation		P value
	Before	After		Before	After	
WAZ						
Below −3 SD	80 (100%)	0 (0%)	0.0001*	68(85%)	0 (0%)	0.0001*
−3 to −2 SD	0(0%)	0(0%)		12 (15%)	0 (0%)	
−2 to −1 SD	0 (0%)	12(15%)		0 (0%)	24(30%)	
−1 to 0 SD	0 (0%)	48 (60%)		0 (0%)	48 (60%)	
0 to 1 SD	0 (0%)	20 (25%)		0 (0%)	8 (10%)	
HAZ						
Below −3 SD	80 (100%)	0 (0%)	0.0001*	80 (100%)	0 (0%)	0.0001*
−2 to −1 SD	0 (0%)	40 (50%)		0 (0%)	40 (50%)	
−1 to 0 SD	0 (0%)	40 (50%)		0 (0%)	32 (40%)	
0 to 1 SD	0 (0%)	0 (0%)		0 (0%)	8 (10%)	
WHZ						
Below −3 SD	72 (90%)	0 (0%)	0.0001*	80 (100%)	0 (0%)	0.0001*
−3 to −2 SD	8 (10%)	4 (5%)		0 (0%)	0 (0%)	
−2 to −1 SD	0 (0%)	28 (35%)		0 (0%)	60 (75%)	
−1 to 0 SD	0(0%)	24 (30%)		0 (0%)	8(10%)	
0 to 1 SD	0(0%)	20 (25%)		0 (0%)	12 (15%)	
1 to 2 SD	0 (0%)	4 (5%)				
MUAC				80 (100%)	0 (0%)	
Below −3 SD	80 (100%)	0 (0%)	0.0001*	0 (0%)	12 (15%)	0.0001*
−2 to −1 SD	0 (0%)	28 (35%)		0 (0%)	60 (75%)	
−1 to 0 SD	0 (0%)	52 (65%)		0 (0%)	8 (10%)	

P value calculated by Mc Nemar's test.
* p value < 0.05 considered significant.

6. Discussion

Globally, child malnutrition is a public health problem with major consequences for survival, damaging cognitive and physical development of children [21]. SAM reported to affect 19 million children worldwide in 2013 and an estimated 2.9 million children under five were admitted globally for

Table 5
A comparison between mean levels of zinc, copper and selenium before and after nutritional rehabilitation in severely malnourished children.

	Neurologically normal SAM			SAM with CP		
	Nutritional rehabilitation		P-value	Nutritional rehabilitation		P-value
	Before	After		Before	After	
Zinc (μg/dl)						
Range	55–83	85–185	0.0001*	48–79	52–250	0.0001*
Mean ± SD	65.3 ± 7.3	132.6 ± 30.8		58.4 ± 7.5	131 ± 61.1	
Normal %	30%	85%		10%	80%	
Deficient %	70%	15%		90%	20%	
Copper (μg/dl)						
Range	85–220	116–260	0.0001*	81–222	122–250	0.0001*
Mean ± SD	157.6 ± 40.8	193.4 ± 45		128.3 ± 33.1	162.5 ± 34	
Normal %	100%	100%		100%	100%	
Selenium(ng/dl)						
Range	28–80	35–109	0.0001*	29–59	45–92	0.0001*
Mean ± SD	51.6 ± 12.7	69.4 ± 16.9		43.3 ± 7.8	64.8 ± 15.7	
Normal %	35%	80%		0%	55%	
Deficient %	65%	20%		100%	45%	

P value calculated by paired sample t-test.
* p value < 0.05 considered significant.

treatment of SAM [22]. Patients with SAM often have multiple nutritional deficiencies, anemia, multiple comorbidities and accounts for the most cases of child mortality worldwide [23].

This study indicated that the incidence of SAM was related to the type of the community and the socio-economic status. This was owed to the more spread of poverty and under nutrition in the rural communities. Similarly, Ezzati et al., and Yang et al., reported that maternal and child under nutrition are highly prevalent in low and middle-income countries, resulting in substantial increases in mortality and overall disease burden [24,25].

Moreover, Khatab et al., agreed with this study as they reported that many children living in some provinces in the Nile Delta and Upper Egypt were having malnutrition. They also reported that the survival, health, nutrition, cognition and education of these children were strongly dependent on the income and the level of education of their caregivers and finally concluded that under nutrition causes an intergenerational transmission of disadvantage and a perpetuation of the poverty cycle [26].

Regarding WHO criteria for diagnosis of SAM [27] at the time of hospital admission, 85% of malnourished children with cerebral palsy (Group B) were severely underweight but 100% were considered as severely wasted. On the other hand (100%) of malnourished children without cerebral palsy (Group A) were severely underweight, and 90% of were severely wasted.

This is consistent with the conclusion of Del Giudice et al., who stated that the feeding difficulties encountered in children with severe neuromotor disabilities sabotage the enough caloric intake required for their energy needs resulting in a crippled linear growth and a serious risk of malnutrition [28].

According to current study, the most common comorbidities detected in group A and B were gastroenteritis, dehydration, and pneumonia. Our finding are in line with Kerac et al. [29], WHO [17], and Chisti et al. [30], who reported that SAM was frequently associated with dehydration and pneumonia.

After nutritional rehabilitation, anthropometric measurements improved significantly for group I compared to at admission measurements (P-value <0.0001). In harmony with our results were; Dulloo [31], Stettler and Iotova [32], Public Health Foundation of India [33], and Kerac et al. [34], they reported a significant improvement in anthropometric measurements at the time of hospital discharge compared to that obtained at the time of hospital admission.

The serum levels of micronutrients (Zinc, Copper, Selenium) were assessed at the time of hospital admission for all studied children and showed a tendency to be significantly lower in group I (malnourished children with and without cerebral palsy) than the control group. After nutritional rehabilitation at the time of discharge from the nutritional rehabilitation program, mean serum micronutrients levels improved significantly but Selenium level remained deficient in (45%) of CP and Zinc level is still deficient in 15% of neurologically normal and 20% of cerebral palsy cases.

Black [35], Thakur et al. [36], Ugwuja et al. [37], and Henderson [38] reported similar results regarding serum zinc level. On the contrary, Hals et al. [39], and Hillesund et al. [40] reported similar zinc levels in malnourished CP children and controls. While, Asmah et al. [41], reported significantly higher selenium concentrations in cases with CP than controls despite the fact that the majority of included subjects (97%) exhibited selenium deficiencies. Meanwhile, mean copper concentration was significantly lower in cases than in control.

Our results demonstrated a range of nutritional imbalances with most cerebral palsy children displaying particular deficiencies in selenium and zinc below their physiological concentrations. In these nutritional handicapped patients, sometimes it is difficult to improve the levels of serum Selenium even with administration of natural food or trace element supplements so, continuous monitoring of the levels of serum Selenium is recommended for these nutritional handicapped patients [42].

7. Conclusions

Children suffering CP develop more severe malnutrition as the neuromotor impairment cripple their sufficient caloric intake. Malnourished children with cerebral palsy have significantly reduced serum zinc, copper and selenium than non-neurologically impaired malnourished children. Nutritional rehabilitation significantly improved the serum level of micronutrients in severely acute malnourished children with and without cerebral palsy but children with CP may need selenium and zinc as an adjuvant micronutrient supplementation to obviate complications that may arise from such nutritional insufficiencies.

Ethics approval and consent to participate

The study was approved from the local ethical committee of the Faculty of Medicine.

Consent for publication

Not applicable.

Availability of data and material

Please contact author for data requests.

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Authors' contributions

- Prof Mohamed and Dr. Gihan designed the study, analyzed the data and wrote and revised the draft of manuscript.
- Dr Doaa and Dr Samir has analyzed data and revised the manuscript.
- Dr Nagwa made the chemical analysis of samples and revised the manuscript.

- Eman has collected the data and samples and wrote the methodology.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conflict of Interest

The other authors have no conflicts of interest to disclose.

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