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ORIGINAL ARTICLE

Serum selenium level among critically ill child in Aswan university hospital

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ABSTRACT

Background: Selenium plays important role in the protection against lipid peroxidation; mediating inflammatory response. This study aimed to assess the effects of changes in plasma selenium on critically ill children. **Material and Methods:** A cross-sectional study that was conducted on 40 critically ill children admitted to the pediatric intensive care unit in Aswan university hospital**.** All children were subjected to full history taking, clinical examination and laboratory investigations including (CBC, CRP, Blood culture, and plasma selenium, estimated on 5 days after admission. **Results:** median age was 27 months, 55% of cases were males. 15% had a history of pre-natal complication, 17.5% had a history of post-natal complication and 20% were developmentally-delayed. 30 % of cases had respiratory disorders, 20% had gastrointestinal disorders, and 15% had neurological disorders**.** 15% of cases were positive for Streptococcus pneumoniae, 5% positive for Staph aureus, 2.5% positive for E. Coli and, 2.5% positive for Pseudomonas Aeruginosa. 30% had pneumonic patches in chest X-ray. Median of selenium level was 0.52 µmol/L with range between 0.13 and 1.50. low selenium level was more among children with post-natal complication, p value =0.031**. Conclusion:** low plasma selenium among critically ill children admitted to intensive care unit.

Keywords: selenium, critically ill, children, intensive care

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INTRODUCTION

Micronutrients include inorganic trace elements and organic vitamins, all of which are essential in maintaining the body's homeostasis. They function as co-factors for many significant metabolic enzymes, power the body's defense against oxidative stress and regulate gene transcription. Most micronutrients circulate in association with carrier proteins; acute inflammation and the body's response to physiologic stress reduce micronutrient level. That's why; critically ill patients are at danger of micronutrient deficiency [(1).]

Selenium plays an important role in the protection against lipid peroxidation mediating the inflammatory response, aiding thyroid hormone metabolism and in regulating T cell activity, Biological properties of selenium are attained by 25 selenoproteins, where the most known are

selenoprotein P, the glutathione peroxidases, thioredoxin reductases and iodothyronine deiodinases [2].

Systemic inflammation is known to decrease serum selenium levels, most probable as a consequence of tissue redistribution rather than real deficiency. Assessment of selenium status in critically ill children, therefore, has to take into account both the nutritional status and the degree of inflammation. An inverse correlation between CRP and serum selenium is only accurate in well-nourished children, while the correlation between nutritional status and serum selenium is best assessed in the lack of severe inflammation [3].

An examination of children enrolled in the Critical Illness Stress Induced Immune Suppression (CRISIS) prevention trial also revealed that depressed serum selenium levels are commonly to occur in chronically ill children and those suffering from infection or sepsis [4]. Low serum selenium or an increased fraction of reduced GSHpx has also been associated with increased incidence of multi-organ failure in children admitted to the PICU [5]. Vice versa, an increase in serum selenium during critical illness has been associated with decreased ventilator dependence, ICU length of stay, and even mortality [6].

This study aimed to assess the effects of changes in plasma selenium on critically ill children

MATERIAL AND METHODS

A cross-sectional study was conducted on 40 critically ill children admitted to the pediatric intensive care unit (PICU) in Aswan university hospital**.** All children included in this study were subjected to full history taking, clinical examination, and laboratory investigations including CBC, CRP, Blood culture, and plasma selenium, all were estimated on 5 days after admission.

Sample collection

Venous blood sample (7 cc) was withdrawn from all subjects of the study under complete aseptic technique. First part of the sample (2 cc) was collected in EDTA tubes for CBC assessment. Second part (5 cc) was collected in sterile plastic tubes, centrifuged and serum was collected and frozen at – 80 C for assessment of CRP and plasma selenium level.

Plasma selenium was prospectively measured in children. Selenium level was estimated on day 5 of stay in PICU [7]

Normal blood serum selenium level was 0.35 - 1 μmol/L (30 to 75 ug/L).

Statistics

All statistics were performed using SPSS version 23. Continuous data Were presented as mean ± standard deviation and range and qualitative variables were expressed as percentages also bivariate analysis: Tests of significances were carried out. P value of <0.05 was defined as statistically significant.

Ethical consideration

Verbal & written consent was obtained from all patients before getting them involved in the study. The steps of the study, the aim of the study, the potential benefit and hazards, all will be discussed with the patient's parents and also the patient or the patient's parents will be informed by the result of research. Confidentiality of all data were ensured**.** The patients have the right to withdraw from the study at any time without giving any reason.

RESULTS

The present study were conducted at Pediatrics department, Aswan University Hospital among children admitted to PICU from the period of August 2019 to January 2020 and included 40 patients.

Demographic characteristics of the studied children (table 1) showed that their median age were 27 months, 32.5% of them were less than one year, 45.0% were from 1 to 5 years and 22.5% of

them were from 6 to 12 years. 55% were males and 45% were female. 15% of the studied children had a history of pre-natal complication in the form of maternal eclampsia, pre-eclampsia, maternal diabetes and maternal pyrexia during pregnancy. 17.5% of studied children had a history of post-natal complication in the form of admission to NICU for complication of prematurity. 20% have a history of delayed development.

Final diagnosis of the studied children (fig 1) showed that 30 % of our cases had respiratory disorders (pneumonia, bronchiolitis, respiratory distress), 20% had gastrointestinal disorders (gastroenteritis and dehydration), 15% had neurological disorders (coma , brain tumor, CNS infection, status epilepticus and epilepsy), 12.5% had cardiovascular disorders (rheumatic fever, CHD, infectious endocarditis, status asthmaticus and Fallot teratology), 10% had diabetes ketoacidosis, 10% had toxicology disorders (anaphylactic shock, scorpion sting, ingestion of toxic dose of paracetamol), and 5% had surgery complication (post ventricular peritoneal shunt).

Table (2) showed investigations of the studied children. Regarding blood culture, 15 % of children positive for Streptococcus pneumoniae, 5% positive for Staph aureus, 2.5 % positive for E. Coli and, 2.5 % positive for Pseudomonas Aeruginosa. 30 % of children have pneumonic patches in chest X-ray and 7.5% have Pneumonic patches with cardiac problem in their chest X-ray.

Table (3) showed laboratory parameters of the studied children. The median of hemoglobin level was 10.75 g/dl with range between 6.8 and 14.00 g/dl, median total leucocytic count was 15 x 1000/ CC ranged between 5.0 and 29.0 x 1000/ CC , median platelets count was 172 x 1000/ CC and ranged from 55.0 to 489 x 1000/ CC. Median of CRP level was 24.0 with range between 3.0 and 88.0. Median of selenium level was 0.52 µmol/L with range between 0.13 and 1.50.

Table (4) showed factors associated with low serum level of selenium among studied children admitted to PICU. low selenium level was more among children with post-natal complication than normal children (85.7 % compared to 42.4% respectively, and p value =0.031), among children with involved chest X-ray than children with free chest X-ray (80.0 % compared to 32.0% respectively, and p value =0.008). No statistically significant difference in children with low selenium level regarding sex, natal history, vaccination status, and development, p value > 0.05.

DISCUSSION

Micronutrients refer to a group of organic vitamins and inorganic trace elements, all of which play a wide range of essential functions in maintaining the body's homeostasis. Critically ill patients are at risk of developing micronutrient deficiency [(1)]. Selenium plays an essential role in the protection against lipid peroxidation, in regulating T cell activity, mediating the inflammatory response and aiding thyroid hormone metabolism [(2)]. The present cross- sectional study conducted in the period from August 2019 to January 2020 on critically ill children aged from one month up to 18 years, to assess the effects of changes in plasma selenium on critically ill children.

In Our Study, 40 critically ill children admitted to the PICU of Aswan university hospital and with their mean age was 27 months, which is close to **Iglesias et al.** [(3)] **and Leite et al.** [(6)], as the median age in their study was 34 months. On the other hand, this disagree with **Lee et al.** [(8)] **and Broman et al.** [(9)] study as they had median age in their study was 61.4 ± 14.9 years and 57 years respectively. This difference may be due to different inclusion and exclusion criteria between the different studies.

In the present study we have 55 % males and 45% females, this is in line with a study by **Iglesias et al.** [(3)] **and Broman et al.** [(9)] as they had more males than females in their study as 61% and 60% were male children and 39 % and were female children, respectively. While **Roudi et al.** [(9)] study had equal percentage of male and femle (50% of each for both study).

In our study, patients with chest problems represented the majority of cases (30%), followed by those with gastrointestinal tract conditions (20%), neurological (15%), cardiovascular (12.5%), Endocrine (10%), Toxicology (10%) and surgery (5%). Which agree with **Negm et al.** [10], as the patients in their study with chest problems represented most cases (44.0%`), followed by those with central nervous system (16.0%), and then cardiac and gastrointestinal tract conditions (12%). In addition, **Iglesias et al.** [3] **study** revealed most of their cases diagnosed with respiratory problems (73%) followed by cardiovascular then miscellaneous causes (22.1%). This is in contrast with **Choi et al.** [11], as their patients had infectious complications from multiple traumas as the majority of cases in their study, Also our study disagree with **Roudi et al. [12],** as the majority of cases in their study were diagnosed with severe oxidative stress and inflammation following major gastrointestinal surgeries. This difference may be due to the different inclusion and exclusion criteria between the studies.

We found the Median of CRP level in our cases was 24.0 mg/L with range between (3.0 and 88.0). Which agree with **Costa et al.** [13] **and Iglesias et al.** [3] , as in their study the median of CRP level was 23 mg/L. and 49.3 mg/L, respectively. On the other hand, this disagreed with **Broman et al.** [14], as CRP level in their study was 1.003 mg/L with range (0.994 -1.009), this may be due to that most of their patients had staying >5 days and improved clinically which was lowered their CRP with treatment.

We found no statistically significant difference between CRP level and low selenium level. Which agree with **Oguzhan et al.** [15], as they found that CRP did not show any correlation with serum selenium level in addition,a study done by **Ghashut et al.** [16] stated that patient with low plasma selenium that has concentrations of CRP within normal limits can be susceptible to deficiency. This same author showed that plasma concentrations of selenium are associated with CRP level changes. On the other hand, **Sakr et al.** [17] found that the minimum plasma selenium concentration was inversely correlated to the maximum serum CRP.

Serum selenium level among studied children was 1.8 ug/l. This is inconsistent with **Heidemann et al.** [4] and **Dylewski et al.** [18] as they reported significant selenium deficiency in critically ill patients. **Sakr et al.** [17] showed a consistent decrease in plasma selenium concentrations during the PICU stay in all their cases, compared to for PICU controls. **Ruocco et al.** [19] found that all their patients were presented with plasmas selenium level concentrations below normal with statistically significant difference lower in critically ill children compared to control group, which also in agreement with other multiple studies such as **Jang et al.** [20] and **Mertns et al.** [21].

On the other hand, the result disagrees with **Negm et al.** [10], as they found that there was no difference in selenium level between critically ill children and controls. In addition to the findings of **Heyland et al.** [22] randomized, blinded trial conducted in North American patients; they had reported normal plasma selenium concentration, which was observed in European and South American patients. Therefore, they concluded that racial factors may affect selenium level.

We found that children with low selenium level had no statistically significant correlation with CBC indices (Hb, WBC, and PLTS) than children with normal selenium level, which agree with **Kupka et al.** [23] findings as they stated that they didn't support a role for selenium in the maintenance of hemoglobin concentrations and in the prevention of anemia. On the other hand, this disagreed with **Semba et al.** [24] and **Nhien et al.** [25] studies that stated the biochemical selenium deficiency in the etiology of anemia. In addition, this contrasts with **Lettow et al.** [26], as they found among adults from Malawi with pulmonary tuberculosis, selenium concentrations were inversely related to hemoglobin concentrations. In addition, Laboratory studies done by **Rotruck**

et al. [27] showed that selenium, as part of glutathione peroxidases, protects against hemolysis of erythrocytes and thus may be relevant to hemoglobin levels.

Our study found that low selenium level was more among children with post-natal complication than normal children. Which is in line with **Wilson et al.** [28], as they found that inadequate micronutrient and selenium intake may result in poor fetal growth and development as well as poor pregnancy outcome. Moreover, **Mariath et al.**[29] found that decreased serum selenium have been associated with pregnancy complications. **Yang et al.** [30] indicated that both low and high levels of cord serum selenium had adverse effects on neonatal neurodevelopment. In addition, **Polanska et al.** [31] had found a supportive experimental evidence indicating a significant role of Se in brain and behavior development.

CONCLUSION

The results of our study suggest that low concentrations of plasma selenium may be representative of systemic inflammation. The indication for supplementation may be low plasma selenium concentrations in those patients, although this does not necessarily mean that all low plasma selenium patients should be supplemented. While there are no records of harmful effects of selenium supplementation in critically ill patients for a limited period, it should be considered that high concentrations of selenium compounds are toxic, and that sodium selenite may also serve as an oxidant molecule.

It is worth mentioning, before concluding, that there are some limitations to this research do exist. Restricted sample size and confinement of our study to patients in Aswan University Hospital are of the major constraints in our study, hence our results need to be validated by further studies including larger sample size and multi-regional cooperation.

However, our results illustrate the importance of low plasma selenium correlated with the magnitude of the inflammatory response in children admitted to the PICU. When interpreting plasma concentrations as an index of selenium status in patients with systemic inflammation as well as in the selenium supplementation decision, this relationship should be considered.

REFERENCES

1. Dao, Anez-Bustillos, Puder, Bennet S Cho , Zhilling Li ,Kathleen M Gura (2017). Assessment of Micronutrient Status in Critically Ill Children: Challenges and Opportunities. Nutrients, 9(11), 1185
2. Rayman (2012). Selenium and human health. Lancet 379, 1256–68.
3. Iglesias, Leite, Paes, de Oliveira& Sarni (2014). Low plasma selenium concentrations in critically ill children: the interaction effect between inflammation and selenium deficiency. Critical care, 18(3), R101.
4. Heidemann S, Holubkov R, Meert KL, Sabrina M , Dean JM, Berger J, Bell M,Anand K J S, Zimmerman J, Christopher J L, Harrison NR, Willson DF, Nicholson C, Carcillo J (2013). Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Collaborative Pediatric Critical Care Research Network (CPCCRN). Baseline serum concentrations of zinc, selenium, and prolactin in critically Ill children. Pediatr Crit Care Med.;14:202-6 .
5. Broman, M; Lindfors, M; Norberg, Å; Hebert, C; Rooyackers, Wernerman, Fläring (2017). Low serum selenium is associated with the severity of organ failure in critically ill children. Clin. Nutr.

6. Leite, Nogueira, de Oliveira Iglesias, de Oliveira, Sarni (2015). Increased plasma selenium is associated with better outcomes in children with systemic inflammation. Nutrition , 31, 485–90.
7. Cuparigova, F. and Stafilov, T., (2011). Determination of Selenium in Human Blood Serum by Electrothermal Atomic Absorption Spectrometry. *Chemical Sciences Journal*, 2.
8. Lee, Dikiy A, Kim and Gladyshev (2019). Functions and evolution of selenoprotein methionine sulfoxide reductases. Biochim. Bio-phys. Acta 1790, 1471–7..
9. Broman, LM, Bernardson, A, Bursell, K, Wernerman, J, Fläring, U & Tjäder, I (2020). Serum selenium in critically ill patients: Profile and supplementation in a depleted region. Acta Anaesthesiologica Scandinavica, 64(6), 803-9.
10. Negm FF, Soliman DR, Ahmed ES & Elmasry RA (2016). Assessment of serum zinc, selenium, and prolactin concentrations in critically ill children. Pediatric health, medicine and therapeutics, 7, 17
11. Choi SB, Jung YT & Lee JG (2019). Association of Initial Low Serum Selenium Level with Infectious Complications and 30-Day Mortality in Multiple Trauma Patients. Nutrients, 11(8), 1844
12. Roudi F, Khademi G, Ranjbar G, Rafatpanah H, Esmaily H & Nematy M (2020). Effects of High-Dose Selenium Supplementation on Oxidative Stress and Inflammatory Markers in Critically Ill Children After Gastrointestinal Surgery: A Randomized Clinical Trial. Iranian Journal of Pediatrics, 30(4).
13. Costa NA, Gut AL, Pimentel JA, Cozzolino SM, Azevedo PS, Fernandes AA, Polegato BF, Tanni SE, Gaiolla RD, Leonardo Antonio Mamede Zornoff, Sergio Alberto Rupp de Paiva & Minicucci MF (2014). Erythrocyte selenium concentration predicts intensive care unit and hospital mortality in patients with septic shock: a prospective observational study. Crit Care ; 18: R92
14. Broman M , Lindfors M, Hebert C, Rooyackers O, Wernerman J, Flaring U (2018). Low concentration of serum selenium is associated with the severity of multiple organ failure in critically ill children. Clin Nutr.; 37(4):1399-405.
15. Oguzhan D, Osman Baspinar, Derya Koser (2016). Nutritional risk, Micronutrient status and clinical outcomes: A Prospective observational study in an infectious disease clinic , Nutrients:8(124): 2-14.
16. Ghashut RA, McMillan DC, Kinsella J, Vasilaki AT,Talwar D, Duncan A (2016). The effect of the systemic inflammatory response on plasma zinc and selenium adjusted for albumin. Clinical Nutrition 35:381-7.
17. Sakr Y, Reinhart K, Bloos F, Marx G, Russwurm S, Bauer M & Brunkhorst F (2007). Time course and relationship between plasma selenium concentrations, systemic inflammatory response, sepsis, and multiorgan failure. British journal of anaesthesia, 98(6), 775-84.
18. Dylewski ML, Bender JC, Smith AM, Prelack K, Lydon M, Weber JM, Sheridan RL (2010). The selenium status of pediatric patients with burn injuries.J Trauma. Sep; 69(3):584-8; discussion 588.
19. Ruocco, Pacheco Cechinatti, Barbosa F & Navarro AM (2018). Zinc and selenium status in critically ill patients according to severity stratification. Nutrition, 45, 85–9.
20. Jang JY, Shim H, Lee SH, Lee JG (2014). Serum selenium and zinc levels in critically ill surgical patients. J Crit Care 29, 317.e5–317.e8.

21. Mertns K, Lowes DA, Webster NR , Talib J, Hall L,Davies MJ, Beattie JH,Galley HF. (2015). Low zinc and selenium concentrations in sepsis are associated with oxidative damage and inflammation. Br J Anaesth 114, 990–9.
22. Heyland D, Muscedere J, Wischmeyer PE, Cook D, Jones G, Albert M, Elke G, Berger MM (2013). Canadian Critical Care Trials Group. A randomized trial of glutamine and antioxidants in critically ill patients.N Engl J Med. Apr 18; 368(16):1489-97
23. Kupka, Ferdinand Mugusi, Said Aboud, Ellen Hertzmark, Donna Spiegelman, Wafaie W Fawzi (2009). Effect of Selenium Supplements on Hemoglobin Concentration and Morbidity among HIV-1–Infected Tanzanian Women Clin Infect Dis. Author manuscript; available in PMC 2010 May 15. Published in final edited form as: Clin Infect Dis. 15; 48(10): 1475–8
24. Semba RD, Ferrucci L, Cappola AR, Ricks MO, Ray AL, Xue QL, Guralnik JM, Fried LP (2006). Low Serum Selenium Is Associated with Anemia Among Older Women Living in the Community: the Women's Health and Aging Studies I and II. Biol Trace Elem Res. 112(2):97-107.
25. Nhien N, Khan NC, Yabutani T, Ninh NX, Kassu A, Huong BT, Do TT, Motonaka J, Ota F (2006). Serum levels of trace elements and iron-deficiency anemia in adult Vietnamese. Biol Trace Elem Res.Summer;111(1-3):1-9.
26. van Lettow M, West CE, van der Meer JW, Wieringa FT, Semba RD (2005). Low plasma selenium concentrations, high plasma human immunodeficiency virus load and high interleukin-6 concentrations are risk factors associated with anemia in adults presenting with pulmonary tuberculosis in Zomba district, Malawi. Eur J Clin Nutr; 59(4):526-32.
27. Rotruck JT, Pope AL, Ganther HE, Hoekstra WG (1972). Prevention of oxidative damage to rat erythrocytes by dietary selenium. J Nutr. ; 102(5):689-96.
28. Wilson RL, Bianco-Miotto T, Leemaqz SY, Grzeskowiak LE, Dekker GA, Roberts CT (2018). Early pregnancy maternal trace mineral status and the association with adverse pregnancy outcome in a cohort of Australian women. J Trace Elem Med Biol.;46:103–9.
29. Mariath AB, Bergamaschi DP, Rondó PH, Ana C D'A Tanaka, Patrícia de Fragas Hinnig, Abbade JF, Diniz SG (2011). The possible role of selenium status in adverse pregnancy outcomes. Br J Nutr.;105:1418–28.
30. Yang X, Yu X, Fu H, Li L, Ren T (2013). Different levels of prenatal zinc and selenium had different effects on neonatal neurobehavioral development. Neurotoxicology;37:35–9.
31. Polanska K, Krol, A, Sobala W, Gromadzinska J, Brodzka R, Calamandrei G, Chiarotti F, Wasowicz W& Hanke W (2016). Selenium status during pregnancy and child psychomotor development—Polish Mother and Child Cohort study. Pediatr Res 79, 863–9 .

Table 1: Demographic data of the critically ill children admitted to PICU.

Variables	Frequency (n=40)	Percent (%)
Age		
1 month -<1year	13	32.5
1-5 year	18	45.0
6-12 year	9	22.5
Median (Range)	27 months (2 month-12 year)	
Gender		
Male	22	55.0
Female	18	45.0
Pre-natal history		
Normal	34	85.0
Complication	6	15.0
Post-natal history		
Normal	33	82.5
Complication	7	17.5
Development		
Normal	32	80.0
Delayed	8	20.0

Table 2: Investigation of the critically ill children admitted to PICU.

Variables	**Frequency (n=40)**	**Percent (%)**
Blood culture		
No growth	30	75.0
Streptococcus pneumoniae	6	15.0
Staph aureus	2	5.0
E. Coli	1	2.5
Pseudomonas Aeruginosa	1	2.5

Chest x ray		
Free	25	62.5
Pneumonic patches	12	30.0
Pneumonic patches and cardiac problem	3	7.5

Table (3): Laboratory parameters of children admitted to PICU.

Laboratory parameters	**Median (range)**
Blood picture	
HB g/dl	10.75 (6.8-14.0)
WBC x 1000/ CC	15.0 (5.0-29.0)
PLT x 1000/ CC	172.0 (55.0-489.0)
CRP	24.0 (3.0-88.0)
Selenium on admission µmol/L	0.52 (0.13-1.50)

Data is expressed as a Median (range)

Table (4): Factors associated with low serum level of selenium among studied children admitted to PICU.

Variables	**level of selenium**		**P value***
	Normal (n=20)	**Low (n=20)**	
Sex			
Male	12 (54.5)	10 (45.5)	0.521
Female	8 (44.4)	10 (55.6)	
Natal history			
Normal	19 (55.9)	15 (44.1)	0.071
Complication	1 (16.7)	5 (83.3)	
Post-natal history			
Normal	19 (57.6)	14 (42.4)	**0.031**
Complication	1 (14.3)	6 (85.7)	
Vaccination			

Complete	15 (53.6)	13 (46.4)	0.491
up to date/ not vaccinated	5 (41.7)	7 (58.3)	
Development			
Normal	18 (56.2)	14 (43.8)	0.232
Delayed	2 (25.0)	6 (75.0)	
Chest X-Ray			
Free	17 (68.0)	8 (32.0)	**0.008**
Involved	3 (20.0)	12 (80.0)	
Laboratory parameters			
CBC			
HB	11.35 (6.8-13.0)	10.15 (7.1-14.0)	0.122
WBC	14.0 (6-29)	15.0 (5-27)	0.675
PLT	168.0 (85-378)	198.0 (55-489)	0.525
CRP	24.00 (3-64)	24.00 (4-88)	0.678

*Chi square test, Fisher Exact Test

Figure (1): Diagnostic groups of critically ill children admitted to PICU**.**