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Serum selenium level and its relation with inflammatory profile in hemodialysis children

Nasrin Esfandiar[1], Mohammad Hassan Fallahkohan[2*], Masoumeh Mohkam[1], Seyed Mohammad Taghi Hosseini Tabatabaei[1], Reza Dalirani[1]

[1]Pediatric Nephrology Research Center, Faculty of Medicine, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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ABSTRACT

Introduction: Chronic kidney disease (CKD) is described by structural or functional defects staying for three months. End-stage kidney disease (ESKD) patients undergoing renal replacement therapy (RRT) face complications and increased susceptibility to infections due to their compromised immune system. In addition, malnutrition and chronic inflammatory conditions are prevalent in CKD patients. Selenium, an essential trace element, plays a crucial role as a cofactor in antioxidant enzymes like glutathione peroxidase (GPX), contributing to vascular endothelial function. Selenium deficiency in patients with ESKD may intensify oxidative stress, increase susceptibility to cardiovascular complications, and impact mortality rates. Despite the significance of selenium in this context, studies on its levels in children undergoing hemodialysis (HD) are limited.

Objectives: This study assessed serum selenium levels in children undergoing HD, compared with healthy children. Furthermore, we sought to establish correlations between selenium levels and inflammatory profiles in the HD group.

Patients and Methods: An observational cross-sectional study was conducted with 30 pediatric patients with ESKD undergoing HD (HD group) and 50 healthy children (control group) in Tehran, Iran. Blood samples were collected from both groups, and serum selenium levels along with inflammatory markers were analyzed. The inclusion criteria encompassed pediatric ESKD patients undergoing HD for at least six months without recent inflammation or infections. The exclusion criteria comprised active infections, immunodeficiency syndromes, and corticosteroid therapy. Statistical analyses were performed using SPSS statistics.

Results: Significant differences were observed in serum selenium levels between the HD and control groups ($P=0.039$). Correlation analysis disclosed a direct relationship among selenium levels and participant age ($r = 0.235$, $P=0.036$), with no significant difference between genders. Notably, significant correlations were found between selenium levels and erythrocyte sedimentation rate (ESR) and platelet-to-lymphocyte ratio (PLR). In contrast, no significant correlation between selenium levels and other inflammatory profiles was established.

Conclusion: This study underscores the importance of assessing serum selenium levels in pediatric ESKD patients undergoing HD. Understanding the interplay between selenium deficiency and inflammatory profiles can inform interventions aimed at improving outcomes and reducing complications in this vulnerable population. Further researches are necessary to explain these associations and to explore possible therapeutic interventions.

Implication for health policy/practice/research/medical education:
This study suggests that children with CKD undergoing HD may have lower selenium levels, which could potentially increase the risk of selenium deficiency, oxidative stress, cardiovascular events, and mortality rates. More research is needed to determine whether selenium supplementation can improve health outcomes in this population.

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*Corresponding author: Mohammad Hassan Fallahkohan,
Email: mfallahkohan@sbmu.ac.ir, kfallahkohan@yahoo.com

Original Article

Introduction

KDIGO (Kidney Disease: Improving Global Outcomes) has described chronic kidney disease (CKD) as the presence of structural or functional kidney abnormalities that persist for three months. Chronic kidney disease staging is based on either solely reduction of glomerular filtration rate (GFR) less than 60 mL/min per 1.73 m^2 for more than three months regardless of the presence of other markers; or in a higher GFR accompanying structural and functional abnormalities, including proteinuria, albuminuria and renal tubular disorders that are discovered in histology or imaging (1).

Patients with terminal CKD and end-stage kidney disease (ESKD) who undergo hemodialysis (HD) are prone to complications associated with advanced disease and dialysis (2). ESKD children on maintenance dialysis have decreased appetite and lower food intake than the normal population and strict restrictions on protein, potassium, and phosphorus diet intake; thus, they are at risk of malnutrition (3-7). Malnutrition in this setting is due to multiple factors that impact prognosis. These factors include reduced nutrient intake, endocrine and gastrointestinal abnormalities metabolic acidosis, chronic inflammatory state that cause increased energy expenditure, hypercatabolic state, muscle weakness and sarcopenia (8).

Patients with ESKD who are on long-term HD are considered immunodeficient and susceptible to infections. Consequently, chronic inflammatory condition is frequent. Several Studies have shown elevated levels of inflammatory cytokines such as C-reactive protein (CRP), interleukin 1β, 6, 8, tumor necrosis factor-alpha (TNF-α). Furthermore, low-serum albumin and higher ferritin levels are common features in terminal CKD and are related with more cardiovascular complications and mortality rate (9-16).

Selenium is an essential trace element that contributes as a cofactor in the form of selenocysteine amino acids in the enzyme glutathione peroxidase (GPX) which functions as an antioxidant in the setting of the vascular endothelium (17). Therefore, selenium deficiency may accompany progressive coronary artery disease, secondary to imbalances of Redox activities and oxidative damage, and cause dialysis patients to be vulnerable to oxidant stress and increase the risk of mortality (18-22). In severe forms of selenium deficiency, Keshan disease, nutritional cardiomyopathy, and neurological impairments may occur (23,24). The kidneys are responsible for the synthesis of GPX enzyme, and in the advanced stages of CKD, its plasma level diminishes (25-27).

Objectives

As far as, there are few studies conducted on plasma selenium level in children undergoing HD, Hence, we conducted a study to measure serum selenium level in children undergoing renal replacement therapy (RRT) compared with the normal population and to establish the association between serum selenium levels and the inflammatory profile in the mentioned group.

Patients and Methods

Study design

This study was an observational cross-sectional and case control study carried out with 30 pediatric ESKD patients on hemodialysis (HD group) and 50 healthy children (control group). All participants in this study consented and voluntarily participated and were collected from three major children's hospitals, Mofid Children's Hospital, Children's Medical Center, and Ali-Asghar Children's Super-Specialty Training Center in Tehran, Iran. All patients were attending maintenance HD sessions at the time of filling out the questionnaire for more than six months. Blood samples were collected just before the beginning of HD for analysis of serum selenium levels and inflammatory markers concentration, including complete blood count (CBC), erythrocyte sedimentation rate (ESR), serum CRP, albumin (Alb), and ferritin. Blood samples from otherwise healthy children were also obtained.

Inclusion criteria

Pediatric patients with ESKD who underwent HD for at least six months and who voluntarily signed the informed consent form were included. Patients had no chronic or acute inflammation or infections in the past 3 months.

Exclusion criteria

Patients with chronic and acute inflammation and infections, those using antibiotic therapy or supplements containing selenium, those with a history of active or prior cancers, those with inherited or acquired immunodeficiency syndrome, and those undergoing corticosteroid therapy were excluded.

Sample collection

We collected 5ml of venous blood sample for the measurement of Se in EDTA-containing tubes kept at 4 °C and centrifuged for plasma separation. The separated plasma was stored at -20 °C until being analyzed. The participants' serum selenium levels were determined using a PG-Instrument AA500 Atomic Absorption Spectrophotometer, featuring a graphite furnace atomizer (model AA500FG).

Statistical analysis

The data is statistically exhibited with mean and the standard deviations. The analysis was conducted using SPSS Statistics for Windows version 27. The study employed analysis of variance for comparing quantitative data. Pearson's correlation coefficient was utilized to define the association between sets of quantitative data. The chi-square test was utilized for comparing qualitative data while the Mann-Whitney U test served for the comparison of independent variables. The findings revealed a significant difference at $P<0.05$.

Results

In present study, the following variables including selenium and inflammatory markers (ESR, CRP, Alb, ferritin, neutrophil-to-lymphocyte ratio [NLR], and platelet-to-lymphocyte ratio [PLR]) were evaluated in two groups comprising 30 children undergoing maintenance hemodialysis (HD group) and 50 otherwise healthy children (control group). No significant difference in the demographic data was observed (Table 1).

Significant differences were observed in mean serum selenium levels between the HD group and the control group ($P=0.039$). The mean serum selenium level in the HD group was 79.8 µg/L (SD: ±10.2), whereas in the control group, it was 74.98 µg/L (SD: ± 9.6), with an overall mean of 76.8 µg/L (SD: ±10.2) (Table 2).

Notably, there was no significant disparity in selenium levels between two genders within total participants ($P=0.285$; Table 3).

Additionally, correlation analysis disclosed a direct relationship between serum selenium levels and participant's age (r= 0.235 and a p= 0.036; Figure 1).

Furthermore, significant correlations were observed between serum selenium levels and inflammatory markers. A significant correlation between selenium levels and ESR (r = -0.289, $P=0.028$) and PLR (r = -0.283, $P=0.029$) was established. However, no significant correlations were found between selenium levels and other inflammatory markers, including CRP, Alb, ferritin, and NLR (Table 4, Figure 2).

Discussion

The findings from previous studies confirm our observations regarding selenium deficiency being prevalent among dialysis patients, as indicated by several studies (28-30). Findings in our study reinforces that selenium deficiency is prevalent in both group; However, there was a significant disparity in serum selenium levels between dialysis patients and the control group ($P<0.039$). The study by Beligaswatta et al regarding peritoneal dialysis patients found a substantial proportion whom experienced selenium deficiency (40.1%), highlighting its association with low-nutritional consumption and heightened vulnerability to fatigue and inflammation (30). Moreover, the study by Tonelli et al showed significantly lower selenium and zinc levels in dialysis patients compared with healthy children or those with CKD under conservative management further favor the prevalence of micronutrient deficiencies in this population (31).

It is noteworthy that we found a linear regression relationship between serum selenium levels and participant's age. Moreover, our study also identified a significant correlation between serum selenium and the inflammatory marker ESR, further underlining the potential association between selenium status and

Table 1. Demographic data of the participants

	Count		Total	*P* value
	Male	Female		
Hemodialysis group	18	12	30	0.64
Control group	26	24	50	
Total	44	36	80	

Table 2. Distribution of mean serum selenium level in the hemodialysis (HD) and control group

	Mean Se (µg/L)	Mean ± SD	*P* value	95% CI of means
Hemodialysis group	79.8	79.8 ± 10.5	0.039	74.5-79.1
Control group	74.98	74.98 ± 9.6		
Total	76.8	76.8 ± 10.2		

Table 3. Correlation between serum selenium levels and gender

	Mean Se (µg/L)	Mean ± SD	95% CI of Mean	*P* value
Males	77.9	77.9 ± 9.6	80.8-74.98	0.258
Females	75.4	75.4 ±10.8	79.1-71.7	

Table 4. Association of serum selenium level and inflammatory profile in hemodialysis group

		ESR	CRP	Albumin	Ferritin	NLR	PLR
Selenium (µg/L)	Pearson's correlation	-0.289	0.046	0.079	0.016	-0.158	-0.283
	P value	0.028	0.721	0.553	0.900	0.225	0.029

inflammation in dialysis patients. While previous researches have suggested correlations between selenium and other inflammation markers such as serum albumin levels (32-34), our study did not find a significant association with CRP and serum albumin levels. However, it's plausible that a larger sample size might uncover correlations between selenium and other inflammation markers.

In addition, Yang et al provided additional insight into the clinical implications of selenium deficiency in dialysis patients ($P = 0.026$). Their longitudinal analysis shown that lower serum selenium levels were linked with a higher likelihood of hospitalization due to infectious diseases, emphasizing the importance of maintaining adequate selenium levels in this population (35).

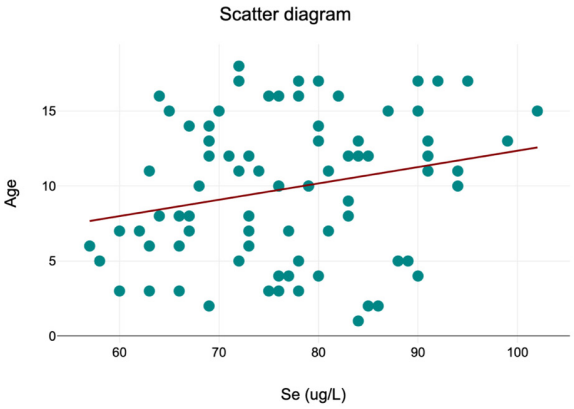

Figure 1. Correlation between serum selenium level and age ($r = 0.235$, $P = 0.036$)

Conclusion

This study highlighted the importance of assessing serum selenium levels in pediatric ESKD patients undergoing HD. Understanding the interplay between selenium deficiency and inflammatory profiles can inform interventions aimed at improving outcomes and reducing complications in this vulnerable population. Further researches are necessary to explain these associations and to explore possible therapeutic interventions.

Limitations of the study

One of the limitations of this study was the limited number of available patients who participated. It is recommended for further evaluation; data being

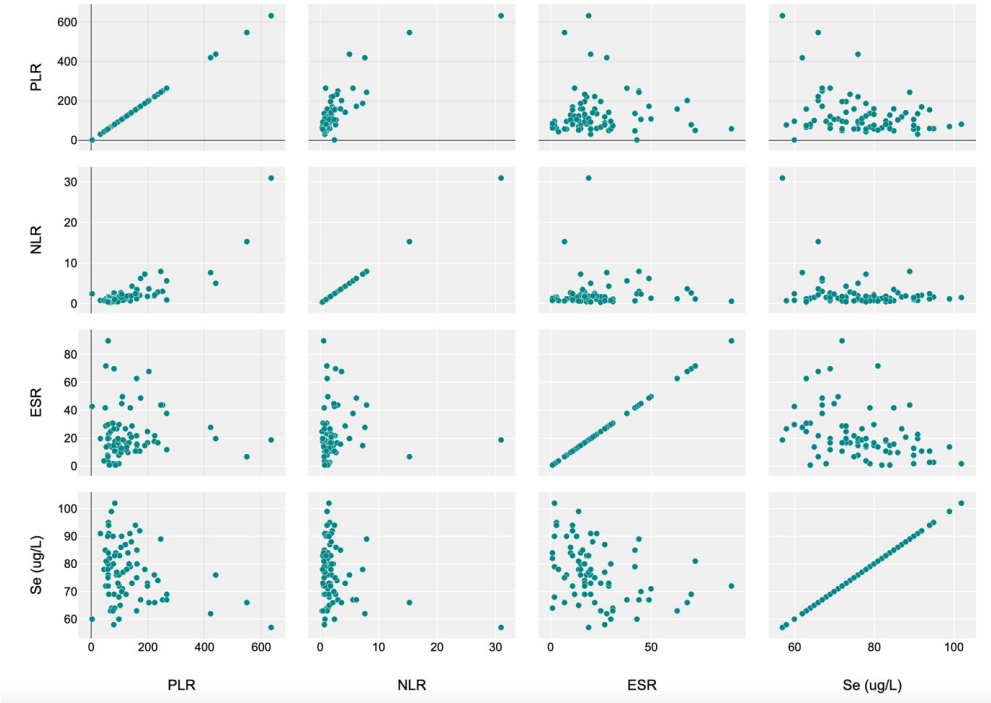

Figure 2. Correlation between serum selenium levels and the inflammatory profile.

collected from different centers elsewhere. The fundamental mechanisms and factors of selenium deficiency that may affect directly or indirectly and the interplay between them; were not the main objectives investigated in this study.

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Authors' contribution

Conceptualization: Mohammad Hassan Fallahkohan, Nasrin Esfandiar, Masoumeh Mohkam.
Data curation: Mohammad Hassan Fallahkohan.
Formal analysis: Mohammad Hassan Fallahkohan, Masoumeh Mohkam.
Investigation: Mohammad Hassan Fallahkohan, Nasrin Esfandiar.
Methodology: Seyed Mohammad Taghi Hosseini Tabatabaei, Reza Dalirani.
Project administration: Masoumeh Mohkam, Nasrin Esfandiar.
Resources: Seyed Mohammad Taghi Hosseini Tabatabaei, Mohammad Hassan Fallahkohan.
Supervision: Nasrin Esfandiar, Masoumeh Mohkam, Reza Dalirani.
Validation: Nasrin Esfandiar, Reza Dalirani, Mohammad Hassan Fallahkohan.
Visualization: Mohammad Hassan Fallahkohan.
Writing–original draft: Mohammad Hassan Fallahkohan.
Writing–review & editing: Nasrin Esfandiar.

Conflicts of interest

All authors declare that they have no conflicts of interest.

Ethical issues

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki and was approved by the Research Ethics Committees of the School of Medicine, Shahid Beheshti University of Medical Sciences (Ethical code#IR.SBMU.MSP.REC.1401.200). Informed consent was obtained from all participants. The study was conducted as a part of MD thesis of Mohammad Hassan Fallahkohan (Thesis #1401059) in Shahid Beheshti University of Medical Sciences. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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