PREVALENCE OF ZINC DEFICIENCY AND OXIDATIVE STRESS IN PEDIATRIC KIDNEY TRANSPLANTATION RECIPIENTS

Pimolpan Wiriyakunnan[*], Orn-uma Y. Sroijit[**], Chantida Subun[*], Adisorn Lumpaopong[*]

[*]Division of Pediatric Nephrology, Department of Pediatrics, Phramongkutklao Hospital, Bangkok, Thailand
****Faculty of Medical Technology, Rangsit University, Pathum Thani, Thailand**

Abstract

Background: Zinc (Zn) is a cofactor of essential enzymes involved in the antioxidant defense system. Increased oxidative stress affects the function of the transplanted kidney.

Objectives: We aimed to determine the prevalence of Zn deficiency and evaluate the relationship between Zn deficiency and oxidative stress. Additionally, we investigated the associated oxidative stress factors among pediatric kidney transplant recipients.

Methods: In this cross-sectional descriptive study, we enrolled children (1 to 21 years of age) who underwent kidney transplantation and were actively followed up at Phramongkutklao Hospital, Bangkok, Thailand, between December 2022 and May 2023. Patients' characteristics were reviewed; blood samples were collected for serum zinc (Zn) level, superoxide dismutase (SOD), malondialdehyde (MDA), lipid profile, hemoglobin A1C, fasting blood sugar, and serum creatinine.

Results: Twenty-four patients were included in the study. No differences in baseline characteristics between the two groups were observed. Zn deficiency was identified in eight patients. The prevalence of Zn deficiency in pediatric kidney transplant recipients was 33.33% (95% CI: 15.6%-55.3%). The median Zn level in the patients with and without Zn deficiency was 67 (49-72) and 83 (74-111) mcg/dL, respectively. The median percentage of Zn intake per dietary reference intake (DRI) in Zn-deficient patients was 88.57 (47.56-115.8) compared with 97.5 (62.89-120.6) in the non-Zn-deficient group. However, these were not statistically significant. One patient (1/1, 100%) who had a history of chronic allograft rejection revealed a significantly high SOD level in red blood cells (RBC) (p=0.026). Six patients with dyslipidemia (6/6, 100%), on the other hand, exhibited low SOD level in RBC (p=0.034).

Conclusion: We could not demonstrate an association between Zn deficiency and SOD or MDA levels. Regarding a role in pediatric kidney transplantation, Zn supplementation may benefit patients with low Zn intake.

Keywords: Zinc deficiency, kidney transplantation, oxidative stress, children

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Correspondence to:
Lumpaopong A, Division of Pediatric Nephrology, Department of Pediatrics, Phramongkutklao Hospital, Bangkok 10400, Thailand
Email:adisornuic@yahoo.com

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Introduction

Oxidative stress arises from an imbalance between free radicals and the antioxidant system, destroying deoxyribonucleic acid (DNA), proteins, and lipids. In patients who have undergone kidney transplantation, oxidative stress gradually decreases in the long term compared to before kidney transplantation. Oxidative stress occurs due to surgery and immunosuppressive drugs, particularly Cyclosporine A.[1] Furthermore, the immunosuppressive drugs may induce metabolic syndrome, decreasing antioxidants. Meanwhile, oxidative stress can lead to metabolic syndrome, resulting in atherosclerosis. Increased oxidative stress affects the functioning of transplanted kidneys from the early stages, leading to chronic allograft nephropathy (CAN) in the long term.[2,3] However, due to their short half-life, oxidative stress cannot be measured directly by measuring oxygen-free radicals. Thus, it has to be estimated from antioxidants or products of lipid, protein, or DNA destruction due to oxidative stress.[4] Additionally, previous studies found that administering antioxidants helps to reduce oxidative stress in kidney transplant patients.[5]

Zinc (Zn) is a trace element found in poultry, meat, eggs, and seafood, and is well-absorbed in the small intestines. It is essential for the body as it is a crucial part of several enzymes aiding in protein synthesis and controlling gene expression, which is vital for processes related to growth, reproduction, nervous system function, and importantly, it is a key component of superoxide dismutase (SOD), which is an antioxidant that reduces oxidative stress. When the inflammatory cytokines decrease, the risk of abnormal blood vessel formation and cell death also decreases; as a result, this also lowers the risk of cardiovascular diseases.[4-16]

The prevalence of zinc deficiency in Thai children was more than 57%.[16] Children with chronic kidney disease (CKD) are also at risk of Zn deficiency, although this condition is expected to improve after kidney transplantation.[15]

In the Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guideline for nutrition in CKD 2020 update, there is no recommendation to supplement Zn in adults with normal kidney function.[17] However, Zn supplementation in pediatric patients with kidney diseases is recommended in the KDOQI clinical practice guideline for nutrition in children with CKD 2008 update.[18] Nevertheless, there are still no recommendations regarding Zn supplementation in pediatric patients who have undergone kidney transplantation, and there have been no studies on Zn in pediatric kidney transplantation in Thailand.

Therefore, we aimed to determine the prevalence of Zn deficiency and evaluate the relationship between Zn deficiency and oxidative stress. We also determined associated oxidative stress factors among pediatric kidney transplant recipients.

Methods

Study design and subjects

In this cross-sectional descriptive study, we enrolled children aged 1 to 21 who underwent kidney transplantation and were actively followed up at Phramongkutklao Hospital in Bangkok, Thailand, between December 2022 and May 2023. The Institutional Review Board of the Royal Thai Army Medical Department approved the study, with approval number IRBRTA 825/2566.

To fulfill inclusion criteria, the patient must have a stable glomerular filtration rate (GFR), i.e., less than 20% change in the past 3 months. We excluded the patients who were admitted to the hospital due to bacterial, viral, or fungal infections within 1 month; those who received any supplements of beta-carotene, lutein, lycopene, selenium, vitamin A/C/E, L-arginine, glutathione, or coenzyme Q10 within 2 months. Patients who were diagnosed with cancer, allograft rejection, or recurrent disease within 3 months, those who received blood transfusions within three months, and those who refused to participate were also excluded. The patient and their parents were informed through verbal explanation and written documentation. Informed consent was obtained and documented through a signed consent form.

Data collection

We collected data from patients' medical records by researchers, including demographic information (age, gender, weight, height, and blood pressure), underlying conditions such as chronic kidney disease and comorbidities, pre-transplant kidney replacement therapy (KRT) modality and duration, donor information, medications, drug levels, and history of kidney allograft rejection. Blood samplings were scheduled alongside the patient's regular appointment. Before the appointment, the patients and their parents were asked to record two sets of a 3-day food diary (2 weekdays and 1 weekend per week) using paper-based forms and had to fast for 8 hours before blood sampling. We used the INMUCAL-Nutrients version 4.0 program to calculate Zn intake and the percentage of Zn intake relative to the Dietary Reference Intake (DRI). Blood samplings were performed by medical technologists and were obtained for serum Zn level, superoxide dismutase (SOD), malondialdehyde (MDA), total cholesterol, triglyceride, high-density lipoprotein (HDL), low-density lipoprotein (LDL), hemoglobin A1C (HbA1C), fasting blood sugar (FBS), serum creatinine; and urine for urine protein-to-creatinine ratio (UPCR). Immediately after collection, blood samples were placed in 2°C-8°C ice-packed containers and promptly transported for analysis.

Serum Zn level was measured by flame atomic absorption spectroscopy (FAAS). The suggested lower cutoffs, corresponding to the 2.5th percentile, are 74 mcg/dL in fasting men and 70 mcg/dL in fasting women.[19] Zn deficiency was identified when serum zinc levels were below these lower cutoffs.

MDA is a product of polyunsaturated fat peroxidation. It was measured as a thiobarbiturate derivative in the supernatant following an incubation of erythrocytes in hydrogen peroxide. MDA reacted with thiobarbituric acid and produced a pink pigment with a maximum absorption at 532 nm. The value of each sample was expressed as micromoles per liter (μmol/L). [20]

SOD is a metalloenzyme responsible for the dismutation of two superoxide radicals ($O_2^{\cdot-}$) by incorporating two hydrogen ions (H^+) to form hydrogen peroxide (H_2O_2) and oxygen (O_2).[21] The basis for an assay of SOD activity is the inhibition of the reduction of nitroblue tetrazolium (NBT) by superoxide radicals, generated by the illumination of riboflavin in the presence of oxygen and an electron donor, methionine. A chloroform-ethanol extract was prepared from the hemolysate, and the supernatant obtained was used for the assay. The solution was illuminated for 10 minutes, and the absorbance was read at 560 nm. Controls with and without NBT were included in the assay. One unit of SOD activity was defined as producing 50% inhibition of NBT reduction. Values were expressed as units of enzyme activity/g hemoglobin. [22]

Statistical analysis

Statistical analyses were performed using StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC. Mean, standard deviation, and median were used to describe continuous data and frequencies where appropriate, and percentages to describe categorical variables. For comparisons between two groups, the Independent Sample t-test was used for continuous variables, and Fisher's exact test was used for categorical variables. All analyses were performed at a 95% confidence interval (CI), with a two-sided *p*-value of less than 0.05 considered statistically significant.

Results

Baseline characteristics

Twenty-four patients who received kidney transplantation were enrolled in the study. Clinical and biochemical characteristics of the patients are summarized in **Table 1**. Sixteen recipients (66.7%) were male. Median age of the recipients at transplantation was 16.71 (10.42, 19.83) years. Median body mass index (BMI) was 21.62 (14.79, 35.78) kg/m^2. Most of them had a normal nutritional status (62.5%). The most common diagnosis of primary kidney disease in our patients was congenital anomalies of the kidney and urinary tract (CAKUT) (33.33%). Most recipients received peritoneal dialysis (87.5%)

for KRT before kidney transplantation—the median duration of KRT before kidney transplantation was 33.5 (10, 101) months. Most transplanted allografts were obtained from deceased donors (83.33%). The median follow-up duration was 50 (7, 117) months. Most recipients had a GFR of 60-89 ml/min/1.73 m^2 (41.67%). The prevalences of hypertension, dyslipidemia, and diabetes mellitus were 95.83%, 75%, and 8.33%, respectively. All of the patients received oral prednisolone and two other immunosuppressive drugs. In patients who received Tacrolimus, Tacrolimus's median coefficient of variation was 20.23 (6.8, 51.3) %. Regarding kidney allograft rejection, 25% of the patients had a history of acute rejection, and 4.2% had chronic rejection. CAN was diagnosed in 16.67% of the patients.

Table 1. Baseline and clinical characteristics of recipients

Characteristics	
Sex, n (%)	
Male	16 (66.67)
Age (years)	
Mean ± SD	16.24 ± 2.74
Median (min, max)	16.71 (10.42, 19.83)
BMI (kg/m²)	
Mean ± SD	21.20 ± 6.05
Median (min, max)	21.62 (14.79, 35.78)
Nutritional status, n (%)	
Thinness	1 (4.17)
Normal	15 (62.5)
Overweight	3 (12.5)
Obesity	5 (20.83)
End-stage kidney disease leading to transplantation, n (%)	
Congenital anomalies of the kidney and urinary tract	8 (33.33)
Chronic glomerulonephritis	4 (16.7)
Cystic kidney disease	2 (8.33)
Reflux nephropathy	2 (8.33)
Hereditary nephropathy	1 (4.17)
Thrombotic microangiopathy	1 (4.17)
Unknown	6 (25)
Mode of renal replacement therapy before kidney transplantation, n (%)	
Peritoneal dialysis	21 (87.5)
Hemodialysis	3 (12.5)

Table 1. Baseline and clinical characteristics of recipients (Cont.)

Characteristics	
Duration of renal replacement therapy before kidney transplantation (months)	
Mean ± SD	39.38 ± 24.35
Median [min, max]	33.5 (10, 101)
Type of kidney transplantation, n (%)	
Deceased donor	20 (83.33)
Living donor	4 (16.67)
Duration after kidney transplantation (months)	
Mean ± SD	33.5 (10, 101)
Median [min, max]	
Type of kidney transplantation, n (%)	
Deceased donor	20 (83.33)
Living donor	4 (16.67)
Duration after kidney transplantation (months)	
Mean ± SD	54.83 ± 29.88
Median [min, max]	50 (7, 117)
Glomerular filtration rate (ml/min/1.73m^2), n (%)	
≥ 90	6 (25)
60-89	10 (41.67)
45-59	4 (16.67)
30-44	2 (8.33)
15-29	2 (8.33)
<15	0 (0)
Coexistent diseases relating to cardiovascular status, n (%)	
Hypertension	23 (95.83)
Hyperlipidemia	18 (75)
Diabetes mellitus	2 (8.33)
Immunosuppressive drugs, n (%)	
Mycophenolate mofetil	22 (91.67)
Tacrolimus	20 (83.33)
Cyclosporine A	1 (4.17)
mTOR inhibitor	4 (16.67)
Azathioprine	1 (4.17)
Prednisolone	24 (100)
Coefficient of variation of Tacrolimus (%)	
Mean ± SD	23.35 ± 10.57
Median [min, max]	20.23 (6.8, 51.3)

Table 1. Baseline and clinical characteristics of recipients (Cont.)

Characteristics	
History of rejection, n (%)	
Acute rejection	6 (25)
Chronic rejection	1 (4.2)
Chronic allograft nephropathy, n (%)	4 (16.67)

Prevalence and characteristics of Zn deficiency patients

Among 24 kidney transplantation recipients, eight Zn-deficient patients were identified, which accounted for 33.33% (95% CI: 15.6% - 55.3%). The median Zn level in the Zn deficiency group was 67 (49-72) mcg/dL, while the median Zn levelin the Zn non-deficiency group was 83 (74-111) mcg/dL (p<0.001). There were no significant differences regarding baseline characteristics of the patients, such as age, sex, BMI, nutritional status, type of transplantation, and post-kidney transplant duration, between the two groups. The median GFR of the patients in the Zn deficiency group was 65.5 (23-90) ml/min/1.73m^2, whereas the median GFR of the non-Zn deficiency group was 75 (40-149) ml/min/1.73m^2 (p= 0.245). The median Zn intake per DRI was 88.57 (47.56-115.8) % and 97.5 (62.89-120.6) % in Zn-deficient and non-Zn-deficient patients, respectively (p= 0.298). There were no significant differences in MDA levels in plasma and red blood cells (RBC); and SOD levels in RBC between the two groups. The data are summarized in **Table 2**.

Associated factors of oxidative stress and antioxidants in the recipient are shown in **Table 3**. MDA represents oxidative stress via lipid peroxidation. SOD represents one of the antioxidant enzymes. One patient (100%) with a history of chronic allograft rejection had significantly high SOD in RBC (p = 0.026). All of the patients with dyslipidemia had low SOD in RBC (p=0.034). On the other hand, all patients with diabetes mellitus (DM) had normal MDA in plasma (p=0.011). The levels of zinc, nutritional status, concomitant hypertension, GFR, cyclosporin A use, history of acute rejection, and CAN showed no statistically significant effect on plasma MDA, MDA in RBC, and SOD in RBC.

Table 2. A characteristic comparison between the zinc-deficient and the non-zinc-deficient group

	Zn deficiency. (n=8)	**Non-Zn deficiency (n=16)**	***p*-value**
Zn level (mcg/dL)			< 0.001*
Median [min-max]	67 (49-72)	83 (74-111)	
Age			0.270
Median [min-max]	17.63 (12.17-19.5)	16.33 (10.42-19.83)	
Sex, n (%)			0.221
Male	4 (25)	12 (75)	
Female	4 (50)	4 (50)	
BMI			0.058
Median [min-max]	17.35 (14.79-30.1)	21.99 (15.6-35.780	
Nutritional status, n (%)			0.494
Thinness	1 (100)	0	
Normal	5 (33.33)	10 (66.67)	

Table 2. A characteristic comparison between the zinc-deficient and the non-zinc-deficient group

	Zn deficiency. (n=8)	Non-Zn deficiency (n=16)	*p*-value
Overweight	1 (33.33)	2 (66.67)	
Obesity	1 (20)	4 (80)	
Type of kidney transplantation, n (%)			0.699
Deceased	7 (35)	13 (65)	
Living	1 (25)	3 (75)	
Post-kidney transplantation duration			0.312
Median [min-max]	59 [8-117]	48.5 [7-105]	
Glomerular filtration rate (ml/min/1.73m^2)			0.245
Median [min-max]	65.5 (23-90)	75 (40-149)	
Serum albumin (g/dL)			0.951
Median [min-max]	4.56(3.87-4.85)	4.56(3.87-4.85)	
Zn intake (mg/day)			0.066
Median [min-max]	6.04 (4.28-8.28)	7.76 (4.52-10.18)	
Percent of Zn intake per dietary reference intakes (%)			0.298
Median [min-max]	88.57 (47.56-115.8)	97.5 (62.89-120.6)	
MDA in plasma (umol/L)			1.000
Median [min-max]	1.44 (1.17-1.78)	1.46 (0.71-1.92)	
MDA in RBC (nmol/gHb)			0.581
Median [min-max]	814 (538-1157)	769 (516-1446)	
SOD in RBC (U/gHb)			0.668
Median [min-max]	2473.5 (1606-4787)	2186.5 (1104-4137)	

Discussion

There have been publications on serum zinc status in various patient groups, such as a normal pediatric population and patients with chronic kidney disease (CKD), both with and without kidney transplant rejection. However, very little is known about the prevalence of zinc deficiency and oxidative stress status in pediatric kidney transplantation recipients. Previous studies have shown that oxidative stress can affect the transplanted kidney from the early stages, leading to the development of chronic allograft nephropathy (CAN) in the long term.[2,3] This study provides novel data on the prevalence of zinc deficiency and its association with oxidative stress and antioxidant status in pediatric kidney transplantation recipients in Thailand.

The prevalence of zinc deficiency in this study was 33.33%. Escobedo-Monge et al. found that 40.5% of children with non-dialyzed chronic kidney disease (CKD) had Zn deficiency.[23] Thurlow et al. reported a 57% Zn deficiency prevalence in school-age children in Northeast Thailand.[24] These differences may be attributed to population characteristics, underlying kidney conditions, dietary patterns, and regional nutritional status variations.

In this study, there was no significant difference regarding baseline characteristics between patients with and without Zn deficiency, which differed from previous literature. Thurlow et al. identified being male as a significant risk factor for low serum Zn due to their higher lean body mass and growth rate.[24] Hotz et al. demonstrated

Table 3. Associated factors for oxidative stress and antioxidant

	MDA in plasma (umol/L)			MDA in RBC (nmol/gHb)			SOD in RBC (U/gHb)			
	0.54-1.32 (Normal) n = 6	**>1.32 (High) n = 18**	***p*-value**	**400-900 (Normal) n = 17**	**>900 (High) n = 7**	***p*-value**	**<2400 (Low) n = 13**	**2400-3700 (Normal) n = 8**	**>3700 (High) n = 3**	***p*-value**
Zn status, n (%)			0.317			0.751				0.409
Deficiency	1 (12.5)	7 (87.5)		6 (75)	2 (25)		4 (50)	2 (25)	2 (25)	
No deficiency	5 (31.25)	11 (68.8)		11 (66.75)	5 (31.3)		9 (56.25)	6 (37.5)	1 (6.25)	
Nutritional status, n (%)			0.549			0.310				0.10
Thinness	0 (0)	1 (100)		1 (100)	0 (0)		0 (0)	0 (0)	1 (100)	
Normal	3 (20)	12 (80)		9 (60)	6 (40)		7 (46.67)	6 (40)	2 (13.33)	
Overweight/obesity	3 (37.5)	5 (62.5)		7 (87.5)	1 (12.5)		6 (75)	2 (25)	0 (0)	
Glomerular filtration rate (ml/min/1.73m^2), n (%)			0.183			0.187				0.615
≥ 90	1 (16.67)	5 (83.33)		5 (83.33)	1 (16.67)		2 (33.33)	3 (50)	1 (16.67)	
60-89	5 (50)	5 (50)		8 (80)	2 (20)		8 (80)	1 (10)	1 (10)	
45-59	0 (0)	4 (100)		1 (25)	3 (75)		1 (25)	2 (50)	1 (25)	
30-44	0 (0)	2 (100)		2 (100)	0 (0)		1 (50)	1 (50)	0 (0)	
15-29	0 (0)	2 (100)		1 (50)	1 (50)		1 (50)	1 (50)	0 (0)	
<15	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	
Cyclosporin A use, n (%)			0.555			0.512				0.4
No	16 (26.08)	17 (73.91)		16 (69.57)	7 (30.43)		13 (56.52)	7 (30.43)	3 (13.05)	
Yes	0 (0)	1 (100)		1 (100)	0 (0)		0 (0)	1 (100)	0 (0)	

Table 3. Associated factors for oxidative stress and antioxidant (Cont.)

	MDA in plasma (umol/L)			MDA in RBC (nmol/gHb)			SOD in RBC (U/gHb)			
	0.54-1.32 (Normal) n = 6	**>1.32 (High) n = 18**	***p*-value**	**400-900 (Normal) n = 17**	**>900 (High) n = 7**	***p*-value**	**<2400 (Low) n = 13**	**2400-3700 (Normal) n = 8**	**>3700 (High) n = 3**	***p*-value**
History of acute rejection, n (%)			0.586			0.070				0.6
No	4 (22.22)	14 (77.78)		11 (61.11)	7 (28.89)		9 (50)	7 (38.89)	2 (11.11)	
Yes	2 (33.33)	4 (66.67)		6 (100)	0 (0)		4 (66.67)	1 (16.67)	1 (16.67)	
History of chronic rejection, n (%)			0.555			0.5				0.026*
No	6 (26.09)	17 (73.91)		16 (69.57)	7 (30.43)		13 (56.52)	8 (34.78)	2 (8.7)	
Yes	0 (0)	1 (100)		1 (100)	0 (0)		0 (0)	0 (0)	1 (100)	
Chronic allograft nephropathy, n (%)			1.000			0.841				0.416
No	5 (25)	15 (75)		14 (70)	6 (30)		12 (60)	6 (30)	2 (10)	
Yes	1 (25)	3 (75)		3 (75)	1 (25)		1 (25)	2 (50)	1 (25)	
Dyslipidemia, n (%)			0.102			0.437				0.034*
No	3 (16.67)	15 (83.33)		12 (66.67)	6 (33.33)		7 (38.89)	8 (44.44)	3 (16.67)	
Yes	3 (50)	3 (50)		5 (83.33)	1 (16.67)		6 (100)	0 (0)	0 (0)	
Hypertension, n (%)			0.555			0.111				0.40
No	0 (0)	1 (100)		0 (0)	1 (100)		0 (0)	1 (100)	0 (0)	
Yes	6 (26.09)	17 (73.91)		17 (73.91)	6 (26.09)		13 (56.52)	7 (30.43)	3 (13.05)	
Diabetic mellitus, n (%)			0.011*			0.343				0.40
No	4 (18.18)	18 (81.82)		15 (68.18)	7 (31.82)		11 (50)	8 (36.36)	3 (13.64)	
Yes	2 (100)	0 (0)		2 (100)	0 (0)		2 (100)	0 (0)	0 (0)	

that low dietary Zn intake and malnutrition were risk factors of zinc deficiency.[25]

Regarding oxidative stress, no statistically significant differences were observed in the levels of MDA in plasma, MDA in red blood cells (RBCs), and SOD in RBCs between Zn-deficient and non-deficient groups. However, it is noteworthy that a higher percentage of elevated MDA levels was observed in the Zn-deficient group (87.5%) compared to the non-deficient group (68.8%). Although not statistically significant, this pattern suggests a potential trend that warrants further investigation in a larger cohort. Previous literature supports a link between Zn status and oxidative stress. For example, Jain et al. reported that serum Zn level was associated with a high level of MDA in children with protein-energy malnutrition.[26] A systematic review and meta-analysis, which included 10 randomized controlled trials, suggested that Zn supplementation would significantly decrease MDA in the adult population.[27] Apart from MDA, there are many other markers of oxidative stress such as lipid hydroperoxide (LPO), protein carbonylation and protein nitration (3-nitrotyrosines), advanced glycation end products (AGE), advanced oxidation protein products (AOPP), and 8-hydroxydeoxyguanosine (8-OHdG).[28] Therefore, this study might not report some patients with protein or DNA oxidation. Kocatürk et al. found that the activity of Cu/Zn-SOD before Zn treatment in patients with Zn deficiency and growth retardation group was higher than the controls. With Zn treatment, Cu/Zn-SOD appeared to approach normal values.[29] Coudray et al. found that SOD activity in Zn-deficient dialysis patients was decreased compared with control; and the study also showed concomitant decrease in SOD activity which paralleled their Zn levels.[30] In our current study, we could not demonstrate the association between Zn deficiency and SOD; this may be because SOD functions as a molecular switch that activates the endoplasmic reticulum stress response, which plays an important role in cellular homeostasis under Zn-deficient conditions.[31]

Cristol et al. reported that adult kidney transplant recipients with dyslipidemia had significantly increased MDA and decreased SOD. In addition, oxidative stress increased in recipients with chronic rejection, which suggested that oxidative stress may participate in the development and/or progression of vascular lesions observed in these patients.[32] Similar to our study, patients who had a history of chronic rejection had significantly high SOD in RBC, meanwhile, dyslipidemic patients had low SOD in RBC.

Yepes-Calderón et al. found that plasma MDA concentration in adult kidney transplant recipients was inversely and independently associated with a long-term risk of new-onset diabetes after transplantation (NODAT).[33] In our study, patients with DM had normal MDA in plasma. However, given that only two recipients with DM, this could have happened by chance.

The strength of this study is that it is the first investigation into Zn deficiency and oxidative stress, specifically in pediatric kidney transplant recipients in Thailand. However, several limitations should be acknowledged. The small sample size limits the generalizability and statistical power of the study. The absence of multivariable analyses means that potential confounding factors could not be accounted for. Furthermore, conducting the study at a single center may restrict the applicability of results to broader populations. Future multicenter studies with larger sample sizes and more comprehensive biomarker assessments are warranted.

Conclusion

The prevalence of Zn deficiency is one-third of pediatric kidney transplant recipients. We did not find an association between Zn deficiency and SOD or MDA levels. Patients with a history of chronic rejection had significantly high antioxidant response, while dyslipidemic patients showed low antioxidant levels. Regarding a role in pediatric kidney transplantation, Zn supplementation may benefit patients with low Zn intake.

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References

1. Nafar M, Sahraei Z, Salamzadeh J, Samavat S, Vaziri ND. Oxidative stress in kidney transplantation: causes, consequences, and potential treatment. Iran J Kidney Dis 2011; 5: 357-72.
2. Tabriziani H, Lipkowitz MS, Vuong N. Chronic kidney disease, kidney transplantation and oxidative stress: a new look to successful kidney transplantation. Clin Kidney J 2018; 11: 130-5.
3. Nankivell BJ, Chapman JR. Chronic allograft nephropathy: current concepts and future directions. Transplantation. 2006; 81: 643-54.
4. Tejchman K, Kotfis K, Sienko J. Biomarkers and mechanisms of oxidative stress—last 20 Years of Research with an emphasis on kidney damage and renal transplantation. Int J Mol Sci. 2021; 22: 8010.
5. Blackhall ML, Coombes JS, Fassett R. The relationship between antioxidant supplements and oxidative stress in renal transplant recipients: a review. ASAIO J. 2004; 50: 451-7.
6. Swaminathan S, Singh M. Trace elements, toxic metals, and metalloids in kidney disease. In: Nutritional Management of Renal Disease. 2nd ed. London: Academic Press; 2022. p. 467-88.
7. Hennig B, Meerarani P, Ramadass P, Toborek M, Malecki A, Slim R, et al. Zinc nutrition and apoptosis of vascular endothelial cells: implications in atherosclerosis. Nutrition 1999; 15: 744-8.
8. Beattie JH, Kwun IS. Is zinc deficiency a risk factor for atherosclerosis? Br J Nutr 2004; 91: 177-81.
9. Little PJ, Bhattacharya R, Moreyra AE, Korichneva IL. Zinc and cardiovascular disease. Nutrition. 2010; 26: 1050-7.
10. Prasad AS. Zinc is an antioxidant and anti-inflammatory agent: its role in human health. Front Nutr 2014; 1: 14.
11. Choi S, Liu X, Pan Z. Zinc deficiency and cellular oxidative stress: prognostic implications in cardiovascular diseases. Acta Pharmacol Sin 2018; 39: 1120-32.
12. Knez M, Glibetic M. Zinc as a biomarker of cardiovascular health. Front Nutr 2021; 8: 87217.
13. Begum F, Me HM, Christov M. The role of zinc in cardiovascular disease. Cardiol Rev 2022; 30: 100-8.
14. Shen T, Zhao Q, Luo Y, Wang T. Investigating the role of zinc in atherosclerosis: a review. Biomolecules 2022; 12: 1358.
15. Paun S, Tudosie M, Petris R, Macovei R. The effects of zinc on the human body, including on renal failure and renal transplantation. J Med Life 2012; 5(Spec Issue): 137-41.
16. Changbamrung S, Mo-Suwan L, Polrat B. Zinc: Dietary Reference Intake for Thais 2020. Bangkok: Nutrition Department, Ministry of Public Health; 2020. p. 319-29.
17. Ikizler TA, Burrowes JD, Byham-Gray LD, Campbell KL, Carrero JJ, Chan W, et al. KDOQI clinical practice guideline for nutrition in CKD: 2020 update. Am J Kidney Dis 2020; 76(3 Suppl 1): S1-107.
18. Kidney Disease Outcomes Quality Initiative. KDOQI clinical practice guideline for nutrition in children with CKD: 2008 update. Executive summary. Am J Kidney Dis 2009; 53(3 Suppl 2): S11-104.
19. Ross AC, Caballero B, Cousins RJ, Tucker KL. Modern Nutrition in Health and Disease. 12th ed. Burlington: Jones & Bartlett Learning; 2020.
20. Esterbauer H, Cheeseman KH. Determination of aldehydic lipid peroxidation products: malonaldehyde and 4-hydroxynonenal. Methods Enzymol 1990; 186: 407-21.
21. Saxena A, Lakshmi J, Bhattacharjya R, Singh PK, Mishra B, Tiwari A. The role of antioxidant enzymes in diatoms and their therapeutic role. In: Marine Antioxidants. London: Academic Press; 2023. p. 89-118.
22. Beauchamp C, Fridovich I. Superoxide dismutase: improved assays and an assay applicable to acrylamide gels. Anal Biochem 1971; 44: 276-87.
23. Escobedo-Monge MF, Ayala-Macedo G, Sakihara G, Peralta S, Almaraz-Gómez A, Barrado E, et al. Effects of zinc supplementation on nutritional status in children with chronic kidney disease: a randomized trial. Nutrients 2019; 11: 2671.

24. Thurlow RA, Winichagoon P, Pongcharoen T, Gowachirapant S, Boonpraderm A, Manger MS, et al. Risk of zinc, iodine and other micronutrient deficiencies among school children in Northeast Thailand. Eur J Clin Nutr 2006; 60: 623-32.
25. Hotz C, Peerson JM, Brown KH. Suggested lower cutoffs of serum zinc concentrations for assessing zinc status: reanalysis of the second National Health and Nutrition Examination Survey data (1976–1980). Am J Clin Nutr 2003; 78: 756-64.
26. Jain A, Varma M, Agrawal BK, Jadhav AA. Serum zinc and malondialdehyde concentrations and their relation to total antioxidant capacity in protein energy malnutrition. J Nutr Sci Vitaminol (Tokyo) 2008; 54: 392-5.
27. Mousavi SM, Hajishafiee M, Clark CC, Nascimento IJ, Milajerdi A, Amini MR, et al. Clinical effectiveness of zinc supplementation on the biomarkers of oxidative stress: a systematic review and meta-analysis of randomized controlled trials. Pharmacol Res 2020; 161: 105166.
28. Daenen K, Andries A, Mekahli D, Van Schepdael A, Jouret F, Bammens B. Oxidative stress in chronic kidney disease. Pediatr Nephrol 2019; 34: 975-91.
29. Kocatürk PA, Kavas GÖ, Erdeve Ö, Siklar Z. Superoxide dismutase activity and zinc and copper concentrations in growth retardation. Biol Trace Elem Res 2004; 102: 51-9.
30. Coudray C, Richard MJ, Laporte F, Faure P, Roussel AM, Favier A. Superoxide dismutase activity and zinc status: a study in animals and man. J Nutr Med 1992; 3: 13-26.
31. Homma K, Fujisawa T, Tsuburaya N, Yamaguchi N, Kadowaki H, Takeda K, et al. SOD1 as a molecular switch for initiating the homeostatic ER stress response under zinc deficiency. Mol Cell 2013; 52: 75-86.
32. Cristol JP, Vela C, Maggi MF, Descomps B, Mourad G. Oxidative stress and lipid abnormalities in renal transplant recipients with or without chronic rejection. Transplantation 1998; 65: 1322-8.
33. Yepes-Calderón M, Sotomayor CG, Gomes-Neto AW, Gans RO, Berger SP, Rimbach G, et al. Plasma malondialdehyde and risk of new-onset diabetes after transplantation in renal transplant recipients: a prospective cohort study. J Clin Med 2019; 8: 453.