Published online 2019 August 17.

**Research Article** 



# Serum Zinc Level in Recurrent Nephrotic Syndrome

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Received 2019 July 26; Accepted 2019 August 02.

### **Abstract**

**Background:** Based on the evidence, the correction of zinc deficiency in patients with nephrotic syndrome may improve the prognosis of these patients.

**Objectives:** So this study aimed to investigate the serum zinc level in children with nephrotic syndrome.

**Methods:** This cross-sectional study was conducted in 102 children with nephrotic syndrome. After obtaining informed consent, we collected data regarding age, gender, the severity of nephrotic syndrome (mild, moderate, and severe), and serum zinc level.

**Results:** The mean age of the patients was  $6.2\pm3.2$  years. The serum zinc level was normal in 12 patients (11.76%), lower than normal in 86 patients (84.31%), and higher than normal in 4 patients (3.92%). Also we observed that, the serum zinc level was significantly lower in patients with severe nephrotic syndrome (31.48  $\pm$  6.8) than in patients with moderate (59.12  $\pm$  5.4) and mild (78.82  $\pm$  4.1) nephrotic syndrome.

Conclusions: We can improve the nephrotic syndrome condition of children by correcting their serum zinc levels.

Keywords: Zinc Level, Recurrent Nephrotic Syndrome, Children

## 1. Background

Nephrotic syndrome is one of the most important chronic kidney diseases in children. Steroids are the drugs of choice for the treatment of nephrotic syndrome in children. In some cases, due to the chronicity of the disease and recurrent episodes, they are used for a long time, causing complications such as severe growth disorder, obesity, cataract, osteoporosis, bone aseptic necrosis, immune system weakness, hypersensitivity, psyche, and peptic ulcer, among other complications (1, 2).

Nephrotic syndrome can be seen in children in three forms of congenital, secondary, and idiopathic based on origin (3, 4). Diseases that initially affect the kidneys and interrupt the structure, glomerular function, or both in the absence of a systemic condition may lead to the early or idiopathic nephrotic syndrome in children. Childhood nephrotic syndrome is unexplained in more than 90% of the cases while 25% of nephrotic syndrome cases are unexplained in adults (5).

On the other hand, mild to moderate micronutrient deficiency is very common in developing countries, especially in nations with high growth rates. High levels of in-

fection in developing countries increase the importance of zinc deficiency. Zinc supplementation can reduce morbidity and mortality due to diarrhea and pneumonia and accelerate population growth in developing countries (6). The plasma level is usually normal in mild deficiency while it is less than 60  $\mu$ g/dL in moderate to severe cases. Based on the evidence, the zinc level can reduce many clinical disorders, such as cirrhosis, nephrotic syndrome, and renal failure (5, 7).

## 2. Objectives

Therefore, due to the important of serum zinc levels in prognosis of nephrotic syndrome, the current study aimed to investigate the serum zinc levels in children with nephrotic syndrome.

#### 3. Methods

## 3.1. Study Setting

A descriptive-analytical study was conducted on patients with nephrotic syndrome at the Pediatrics Clinic of Amir-Kabir hospital in Arak city, Iran.

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#### 3.2. Study Population

The study population included children with nephrotic syndrome aged 1 to 14 years from both genders who referred to Amir Kabir Hospital in Arak. A sample of 102 children with nephrotic syndrome was recruited.

#### 3.3. Measurement

Nephrotic syndrome in children was determined based on their medical history as diagnosed by pediatric nephrology specialists. The nephrotic syndrome severity was classified into the mild, moderate, and severe categories based on diagnostic criteria and response to treatment. The serum zinc levels were also evaluated in these patients to compare with the severity of nephrotic syndrome.

#### 3.4. Tools

A checklist was used to record the demographic and clinical characteristics including age, sex, serum zinc level, and the severity of nephrotic syndrome. The levels of zinc were determined in 2.5 cc of peripheral blood samples. As soon as possible after sampling, serum or plasma samples were centrifuged for up to 2 h in trace element-free tubes containing anticoagulant such as EDTA, until the measurement of zinc. The serum zinc concentrations were measured based on the 5-Br-PAPS method using a diagnostic kit (Biochemistry, Tehran, Iran) and expressed as mg/dL.

#### 3.5. Ethical Considerations

Before entering the study, all children and their parents were explained about the study and they gave their informed consent and in the case with the age of under 12 years of age, the patients are enrolled in the study. The study followed the statements of the Helsinki Declaration and it was approved by the Ethics Committee of the Research Council of the Arak University of Medical Sciences (ethical code 21-171-93).

## 3.6. Statistical Analysis

Data were analyzed by SPSS software. Descriptive statistics were used to express the frequency of variables. Fisher's exact test was used to evaluate the correlation between the severity of nephrotic syndrome and the serum zinc level. The P values of < 0.05 were considered significant.

#### 4. Results

The mean age of the children was  $2.6\pm2.3$  years. Moreover, 58 out of 102 (56.86%) children were male and 56 (43.14%) were female (Table 1). Based on severity, the nephrotic syndrome was severe in 23 (22.54%) children, moderate in 36 (36.23%) children, and mild in 43 (42.15%) children (Table 2).

Variables	Values
Age, mean $\pm$ SD	$6.2 \pm 3.2$
Gender	
Male	58 (56.8)
Female	44 (43.1)

ble 2. Frequency Distribution of Nephrotic Syndrome Severity		
Nephrotic Syndrome	Frequency (%)	
Severe	23 (22.5)	
Moderate	36 (35.3)	
Mild	43 (42.2)	

The serum zinc level was normal in 12 (11.76%) patients, lower than normal in 86 (84.3%) patients, and higher than normal in 4 (2.94%) patients (Table 3). The mean serum zinc level was 64.82 mg/dL. The serum zinc level was significantly lower in the group with severe nephrotic syndrome (48.8  $\pm$  6.8) than in the groups with moderate (59.12  $\pm$  5.4) and mild (78.22  $\pm$  4.1) nephrotic syndrome (P < 0.001) (Table 4)

able 3. Frequency Distribution of Serum zinc levels		
Serum Zinc Levels	Frequency (%)	
Normal	12 (11.7)	
Lower than normal	86 (84.3)	
Higher than normal	4 (3.9)	

able 4. Correlation Between Severity of Nephrotic Syndrome and Serum Zinc Leve		
Nephrotic Syndrome	Serum Zinc Levels	P Value
Severe	31.4	
Moderate	59.1	0.023
Mild	78.8	

#### 5. Discussion

In the present study, although the prevalence of nephrotic syndrome was more in male children rather than in female the difference was not significant. Most patients with nephrotic syndrome had low serum zinc levels. It was also found that the serum zinc level was significantly lower in patients with severe nephrotic syndrome than in patients with mild to moderate nephrotic syndrome. Serum zinc levels had a statistically significant association with the severity of nephrotic syndrome. However, different results have been observed in previous studies, which are further addressed.

A study by McBean et al. found that the serum zinc level was significantly lower in patients with nephrotic syndrome than in a control group (P < 0.001)(8), which is consistent with the results of our survey and indicates the important role of zinc level in patients with nephrotic syndrome. Moreover, a case-report study by Yang et al. in 2011 evaluated a newborn with transient short-term nephrotic syndrome. In this study, the serum zinc level was lower than normal while it was normal in the mother. Moreover, the serum level of zinc was very low in breast milking children (9). The results obtained from the mentioned study are different from our study results possibly due to differences in the methodology of the two studies. In another study, Abrams found that more urea excretion in healthy kidneys than unhealthy kidneys, could be a sign of decreased renal reabsorption. Zinc levels in the urine may also affect kidney damage and kidney stones. Therefore, the therapeutic use of zinc may have beneficial effects on kidney stone disease (10). In addition, a study by Gurgoze and Sari concluded that chronic hemodialysis may lead to abnormal serum levels of trace elements in children with chronic renal failure. The low levels of these trace elements, especially zinc, may be associated with prognosis and symptoms in children undergoing chronic hemodialysis (11). These results are consistent with the results of the current study. Based on the results of the current study and other studies in this area, it is crucial to pay attention to the serum zinc level in patients with nephrotic syndrome.

## 5.1. Conclusions

The mean serum zinc level was significantly lower in patients with severe rather than in those with mild to moderate nephrotic syndrome. The correlation between the zinc level and the nephrotic syndrome severity was significant, which may have implications for improving the prognosis of patients with nephrotic syndrome.

#### **Acknowledgments**

This study was performed in partial fulfillment of the requirements for Dr. Saba Norozi, at the School of Medicine, Arak University of Medical Sciences, Arak, Iran.

#### **Footnotes**

**Authors' Contribution:** All authors were equal in preparation and submission of manuscript.

**Conflict of Interests:** The authors declare no competing interests.

**Ethical Approval:** Before entering study, giving full explanations to all patients and their parents and obtaining informed consent from them, and in the case of the age of under 12 years of age, the patients are enrolled in the study and can be excluded at any time. The research team is required to observe all the provisions of the Helsinki statement and the ethics statements of the Arak University of Medical Sciences. This research project was approved by the Ethics Committee of the Research Council of Arak University of Medical Sciences with ethical code of 21-171-93.

**Funding/Support:** Our study was funded by Arak University of Medical Sciences.

#### References

- Uwaezuoke SN. Steroid-sensitive nephrotic syndrome in children: Triggers of relapse and evolving hypotheses on pathogenesis. *Ital J Pediatr*. 2015;41:19. doi: 10.1186/s13052-015-0123-9. [PubMed: 25888239]. [PubMed Central: PMC4379699].
- 2. Yousefichaijan P, Ahmad Goudarzi A, Rezagholizamenjany M, Kahbazi M, Rafeie M, Arjmand Shabestari A, et al. Efficacy of ascorbic acid supplementation in relief of symptoms due to febrile upper urinary tract infection in children, a clinical trial and hospital based study. *Arch Pediatr Infect Dis.* 2018;**6**(4). doi: 10.5812/pedinfect.57071.
- Alinejad S, Yousefichaijan P, Rezagholizamenjany M, Rafie Y, Kahbazi M, Arjmand A. Nephrotoxic effect of gentamicin and amikacin in neonates with infection. Nephro-Urol Mon. 2018;10(2). doi: 10.5812/numonthly.58580.
- 4. Yousefichaijan P, Rezagholizamenjany M, Safi F, Rafiei F, Arjmand A. Detection of extended-spectrum beta-lactamases in Escherichia coli isolates and it's correlation with vesicoureteral reflux nephropathy. *Arch Pediatr Infec Dis.* 2018;**6**(3). doi: 10.5812/pedinfect.12101.
- Yousefichaijan P, Rezagholizamenjany M, Rafiei F, Taherahmadi H, Rafiei M. The relationship between blood biomarkers level and the prognosis of nephrotic syndrome in the children. *Int J Pediatr*. 2016;4(9):3489-97.
- Moorani KN. Infections are common a cause of relapse in children with Nephrotic syndrome. Pak Paed J. 2011;35(4):213-9.
- Sherali AR, Moorani KN, Chishty SH, Khan SI. Zinc supplement in reduction of relapses in children with steroid sensitive nephrotic syndrome. *J Coll Physicians Surg Pak.* 2014;24(2):110-3. [PubMed: 24491005].

- McBean LD, Smith JJ, Berne BH, Halsted JA. Serum zinc and alpha2macroglobulin concentration in myocardial infarction, decubitus ulcer, multiple myeloma, prostatic carcinoma, Down's syndrome and nephrotic syndrome. Clin Chim Acta. 1974;50(1):43-51. doi: 10.1016/0009-8981(74)90076-x. [PubMed: 4273941].
- Yang WL, Hsu CK, Chao SC, Huang CY, Lee JYY. Transient zinc deficiency syndrome in a breast-fed infant due to decreased zinc in breast milk (type II hypozincemia of infancy): A case report and
- review of the literature. *Dermatologica Sinica*. 2012;**30**(2):66–70. doi: 10.1016/j.dsi.2011.09.013.
- Abrams S. Zinc deficiency and supplementation in children and adolescents. *Uptodate Wellesley*. 2007;15(3).
- Gurgoze MK, Sari MY. Results of medical treatment and metabolic risk factors in children with urolithiasis. *Pediatr Nephrol*. 2011;26(6):933-7. doi:10.1007/s00467-011-1803-3. [PubMed: 21340610].