Published Online: 2026 February 24 **Research Article**

# The Association Between Zinc Levels and Inflammatory Markers in Pediatric Urinary Tract Infections: A Cross-Sectional Study with New Insights

Samira Zakeri Shahvari [1], Maryam Esteghamati [2,*], Sara Sang Pahni [3]

[1] Department of Pediatrics, Reaserch Development Center of Children's Hospital, School of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
[2] Department of Pediatric Nephrology, Clinical Research Development Center of Children's Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
[3] School of Medicine, Hormozgan University of Medical Sciences, Iran, Bandar Abbas, Iran

[*] ***Corresponding Author:*** Department of Pediatrics, Reaserch Development Center of Children's Hospital, School of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. Email: maryamesteghamati@gmail.com

**Received:** 25 November, 2025; **Revised:** 7 January, 2026; **Accepted:** 12 February, 2026

## Abstract

**Background:** Zinc is an essential supplement in brain function and in inflammation, helps to regenerate damaged tissues, and regulates inflammatory cytokines. However, its relationship with diagnostic indicators such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) is controversial.

**Objectives:** Since there are no clear results regarding its relationship with procalcitonin (PCT), this study sought to investigate this relationship and the diagnostic value of zinc.

**Methods:** This cross-sectional study was conducted on 93 children with urinary tract infection (UTI) referred to Bandar Abbas Children's Hospital over a one-year period (2023 - 2024). Demographic data (age, sex), clinical findings (symptoms, fever, physical examination), and laboratory parameters including complete blood count with differential, CRP, ESR, serum creatinine (Cr), sodium (Na), potassium (K), zinc, and PCT levels were collected using a researcher-designed questionnaire. Statistical analyses were performed to assess correlations between serum zinc levels and inflammatory markers.

**Results:** The mean serum zinc level of the patients was 53.49 ± 8.95 µg/L, and the serum PCT level was 2.67 ± 0.67 ng/mL. Correlation tests showed that the relationship between zinc and PCT ($\rho = 0.064$, $P = 0.545$), zinc and CRP ($\rho = 0.192$, $P = 0.065$), and zinc and ESR ($\rho = -0.103$, $P = 0.325$) was not statistically significant. Also, comparison between different pathogens (*Escherichia coli* and *Klebsiella*) did not show significant differences in zinc and PCT levels ($P > 0.05$).

**Conclusions:** In children with UTIs, serum zinc levels did not show a significant correlation with inflammatory markers such as PCT, CRP, and ESR, and there were no notable differences based on the specific pathogen involved. These results indicate that zinc may have a minimal impact on acute inflammatory responses in pediatric UTIs. It is suggested that further research with larger sample sizes and long-term studies be conducted to better understand the possible clinical significance of zinc.

*Keywords:* Zinc, Procalcitonin, Urinary Tract Infections, Pediatrics

## 1. Background

Immune function and the activity of lymphocytes and regulatory cytokines depend on the function of minerals that play a role in the regulation and remodeling of cellular pathways (1). Zinc is one of the minerals whose deficiency in children results in increased production of the proinflammatory cytokines interleukin 6 (IL-6) and tumor necrosis factor (TNF)-α, both of which increase oxidative stress and tissue inflammation (2-4). Zinc supplementation has been shown to significantly improve clinical outcomes in children with pneumonia or influenza who experience clinical manifestations (5, 6). In addition, zinc has been



**How to Cite:** Zakeri Shahvari S, Esteghamati M, Sang Pahni S. The Association Between Zinc Levels and Inflammatory Markers in Pediatric Urinary Tract Infections: A Cross-Sectional Study with New Insights. Nephro-Urol Mon. 2026;18(1):e168445. doi: https://doi.org/10.5812/numonthly-168445

shown to play a role in inflammatory pathways in the gut and negatively affect the NF-κB and MAPK signaling pathways, which ultimately disrupt the regulatory activity of T helper cells (7, 8), thereby promoting a proinflammatory immune response. The role of zinc in the regulation of inflammation and tissue repair, as well as the regulation of proinflammatory pathways, has made it a suitable supplement for the pediatric population (7, 9, 10).

However, although zinc has been demonstrated to have beneficial effects in the regulation of external infections involving external agents, as in gastroenteritis (11), its role in other infectious conditions remains insufficiently elucidated, including infections such as urinary tract infection (UTI) in children

Urinary tract infections are one of the most prevalent bacterial infections in children and can be manifested with fever, irritability, dysuria, and changes in urinary pattern (12). The diagnosis is made with appropriate urinalysis for nitrates, leukocyte esterase, and white blood cell (WBC), as well as a urine culture (13, 14).

Also, inflammatory markers include elevated serum C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and procalcitonin (PCT) (15). Procalcitonin is elevated in bacterial infections and has significant value in differentiating bacterial from viral infections (16). Procalcitonin has also been cited as a biomarker with higher accuracy for diagnosis of systemic infections and renal parenchymal involvement (17). Given the importance of early diagnosis and prevention of complications with UTI in children, theorizing there could be a possible correlate between zinc and PCT levels may have value in the clinical setting. While zinc has been established for regulating natural killer cells and T cells, it has not been definitively shown to regulate these inflammatory markers.

## 2. Objectives

Zinc deficiency has been associated with increased susceptibility to various infections, including UTIs, in children. Although lower zinc levels have been observed in children with UTIs compared to healthy controls, few studies have addressed this issue (18). This study aimed to evaluate the association between serum zinc levels and inflammatory markers, particularly PCT, in children with UTI. We also compared the serum zinc levels across UTIs caused by different bacterial pathogens. Our study questions the efficacy of zinc in pediatric UTIs.

## 3. Methods

### 3.1. Study Design

This cross-sectional study was conducted to investigate the relationship between serum zinc and PCT levels in children with UTI at Bandar Abbas Children's Hospital in 2022 - 2023. This study was conducted under the supervision and ethics approval of Hormozgan University of Medical Sciences, and data were collected through a review of medical records and tests of patients aged 2 months to 14 years. This study was reported in accordance with the STROBE checklist (19). Written informed consent was obtained from the parents or legal guardians of all children before entering the study.

### 3.2. Participants

Our participants included all children aged 2 months to 14 years who were admitted to our center during the period and had a confirmed diagnosis of UTI (Table 1). The diagnosis of UTI was defined by the American Academy of Pediatrics (AAP) as a positive culture with a single organism at 50,000 colony-forming units per milliliter in a catheter specimen or 100,000 colony-forming units per milliliter (20).

### 3.3. Urinary Sampling

The urine sampling method included midstream urine collection and catheterization depending on the clinical conditions. In the midstream urine collection method, after placing the girls in the lithotomy position and washing the perineum with water, the initial and final part of the urine was discarded and about 200 cc of the midstream urine was collected. In the boys, after washing the glans and phallus with water, the collection was performed using the above method. In the catheterization method, after obtaining consent from the parents, a catheter number 6 or 8 was inserted into the bladder through the duct in a sterile manner and based on clinical standards, and about 15 cc of urine was collected.

### 3.4. Blood Tests

A blood sample was obtained for all patients including CBC diff, creatinine (Cr), sodium (Na), potassium (K), zinc, ESR, CRP, and PCT. The samples were taken on the first day of admission and transported to the center's laboratory in standard and defined test

**Table 1.** Inclusion and Exclusion Criteria

| Inclusion | Exclusion |
|---|---|
| **Children aged 2 months to 14 years; Definite UTI diagnosis: Presence of at least $10^5$ CFU of bacteria per mL of cultured urine, accompanied by clinical symptoms (as fever, restlessness, or urinary symptoms) or findings of pyuria (positive pyuria with > 5 WBCs per microscopic field). This criterion is consistent with the recommendations of the AAP (2011) and the studies. Complete laboratory data: Availability of serum test results including zinc levels (μg/dl), PCT (ng/mL), CRP (mg/L), and ESR (mm/hr).; Absence of underlying diseases: Absence of chronic renal failure, diabetes, immunodeficiency, or other chronic inflammatory diseases that may affect inflammatory markers.; No antibiotic treatment before sampling: Patients who have not received antibiotics for at least 48 hours before sampling to prevent its effect on markers.** | Zinc supplementation in the past month; Presence of concurrent infections: Presence of other systemic or local infections (such as pneumonia or meningitis) that may alter inflammatory markers; Antibiotic use before sampling: Patients who received antibiotics before sampling, due to the possibility of reducing inflammatory markers; Congenital or structural urinary anomalies: Presence of high-grade VUR, hydronephrosis, or anatomical renal anomalies that may alter the severity of UTI; Metabolic diseases or severe malnutrition: Conditions that independently affect zinc levels; Lack of consent or incomplete file: Lack of parental consent to participate in the study or incomplete patient demographic or clinical information. |

Abbreviations: UTI, urinary tract infection; CFU, colony-forming units; WBC, white blood cell; AAP, American Academy of Pediatrics; PCT, procalcitonin; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; VUR, vesicoureteral reflux.

tubes to be centrifuged and analyzed under standard conditions in the hospital's central laboratory.

### 3.5. Zinc

Serum zinc levels were measured using atomic absorption spectrophotometer (AAS), which was measured by taking a fasting morning blood sample. The unit of measurement was μg/dL and values less than 60 were considered zinc deficiency. To minimize pre-analytical error, particular attention was paid to preventing blood hemolysis, which can cause falsely increased zinc levels. Therefore, standard precautions were applied to prevent hemolysis in taking the sample and transporting the sample to the laboratory.

### 3.6. Procalcitonin

Procalcitonin levels were measured by the electrochemiluminescence method using the cobas kit from Roche; the unit of measurement was ng/dL. According to the criteria, PCT values less than 0.5 indicate non-infectious inflammation, values between 0.5 and 2 indicate possible infection, and values greater than 2 indicate sepsis. This method was selected due to its reported high sensitivity and specificity.

### 3.7. Data Collection

The primary data collection tool for the research was a researcher-made checklist developed using the variables stated in the proposal. The checklist consisted of demographic information (age and gender), clinical information (including symptoms, fever, examination results), and laboratory data (including CBC diff, CRP, ESR, Cr, Na, K, zinc, and PCT). To confirm the accuracy of the data, investigators examined the available data by directly reviewing the patient medical records, and, as appropriate, laboratory results were obtained from the hospital's central laboratory. The content validity of the checklist was reviewed and confirmed by the research team, which included a pediatric infectious disease specialist, statistician, and other supervisors. To assess instrument reliability, investigators recorded part of the data and independently compared the data again in parallel to assess the accuracy of the data recorded by the investigators.

### 3.8. Statistical Analysis

We used version 22 of the SPSS statistical software for statistical analysis. We assessed the normality of the continuous variables included in this study (body temperature, WBC, neutrophil percentage, platelet count, Cr, ESR, CRP, PCT) using the Kolmogorov-Smirnov test. The findings indicated that none of the continuous variables were normally distributed ($P < 0.05$).

As the data did not follow a normal distribution, we primarily used non-parametric statistical tests. Quantitative variables were reported as median and interquartile range (IQR), and categorical variables were reported in frequencies and percentages. We compared the two independent groups (*Escherichia coli* and *Klebsiella* species) using the Mann-Whitney U test, and for comparisons across more than two groups, we used the Kruskal-Wallis test. We evaluated the homogeneity of variances between the microbial groups using Levene's test and confirmed that the variances of the microbial groups were equal. We evaluated the relationships between serum zinc and inflammatory markers (PCT, CRP, and ESR) using the Spearman's rank correlation coefficient. A P-value of $< 0.05$ was considered to be statistically significant in all analyses. All eligible hospitalized children diagnosed with UTI during the study period were included, and the minimum required sample size with a precision of 0.05

and a confidence level of 95% with 10% data loss was set to 93 people based on a previous article (21).

## 4. Results

### 4.1. Participants

Sixty point twenty-two percent (60.22%) of the 93-person population in our study were boys, with a mean age of all children of 3.81 years (45.76 months) with a standard deviation of 3.22 years (38.62 months). All children were grouped into 2-year age groups, with the largest age distribution being between 2 and 4 years old (Table 2).

**Table 2.** Descriptive Indices of Clinical and Laboratory Variables of Patients

| Variants | Mean ± Standard Deviation |
|---|---|
| **Age (mon)** | 45.76 ± 38.62 |
| **Temperature (°C)** | 38.27 ± 0.36 |
| **WBC (cell/μL)** | 11629 ± 3203 |
| **Percentage of neutrophils (%)** | 69.58 ± 7.37 |
| **Platelets (number/μL)** | 244280 ± 53638 |
| **Cr (mg/dL)** | 0.59 ± 0.16 |
| **Zinc (μg/dL)** | 53.49 ± 8.95 |
| **ESR (mm/h)** | 21.17 ± 5.36 |
| **PCT (ng/mL)** | 2.67 ± 0.67 |

Abbreviations: WBC, white blood cell; Cr, creatinine; ESR, erythrocyte sedimentation rate; PCT, procalcitonin.

Most children with UTI had fever and laboratory evidence of active inflammation at the time of admission. High WBC counts, neutrophil percentage, and PCT levels confirm the typical pattern of immune response to bacterial infections. Erythrocyte sedimentation rate was also slightly elevated, consistent with acute inflammation. Creatinine levels remained within normal limits, indicating relatively stable function, but zinc excretion was within normal limits.

### 4.2. Serum Zinc Levels Showed No Significant Correlation with Inflammatory Parameters

All research variables (temperature, WBC, percentage of neutrophils, platelets, Cr, PCT, ESR, and zinc) had a non-normal distribution. Levene's Test showed that the distribution of variables between the two microbial groups *E. coli* and *Klebsiella* was equal. Zinc did not show a positive correlation with ESR level; its relationship with CRP was positive but statistically insignificant (Figure 1). Considering that PCT is a specific marker of microbial inflammation and related infections, zinc did not show a significant correlation.

### 4.3. Zinc and Procalcitonin Levels Did Not Change Between UTI Groups

Kruskal-Wallis test further demonstrated that the factor causing UTI does not enhance the changes in zinc levels. Zinc levels did not show a statistically significant difference between different microbial groups (P = 0.206). Considering that *E. coli* is the most important factor causing UTI, it was not associated with significant differences in serum zinc levels compared to *Klebsiella* (P = 0.199). Following zinc, PCT also did not show a significant correlation between different UTI factors.

Overall, serum zinc levels were not significantly correlated with inflammatory indices, and different UTI factors did not show a significant difference in zinc levels. Although there is no occupational relationship between zinc and PCT, both did not show a significant relationship with the factor causing UTI.

## 5. Discussion

Statistical analysis of the 93 children available to us showed that although patients with UTI had clear signs of inflammation at the time of admission, including high fever, increased WBC count, high percentage of neutrophils, and increased ESR and PCT levels, serum zinc levels remained within normal limits in most cases and did not show a significant relationship with inflammatory indices. The results of correlation tests showed that neither in the total sample nor in the microbial subgroups (*E. coli* and *Klebsiella*), was there a statistically significant relationship between zinc and PCT, nor was there a significant difference in serum zinc or CRP levels between the different microbial groups.

Zinc is an essential trace element that is important to the regulation of inflammation and the immune system (22). Deficiency in serum zinc is accompanied by increased inflammatory markers including ESR, CRP, and PCT (23). For instance, pregnant women with COVID-19 had zinc and the Zn/Cu ratio show a significant negative correlation with ESR, CRP, and PCT (r = - 0.243 for disease severity) (24, 25). In chronic inflammatory diseases such as psoriatic arthritis, a positive correlation was found in the Cu/Zn ratio with increased CRP and ESR, representing the imbalance of trace elements regarding inflammation (26).

Meta-analytic studies substantiate the impact of zinc supplementation to reduce CRP levels (3, 27), specifically

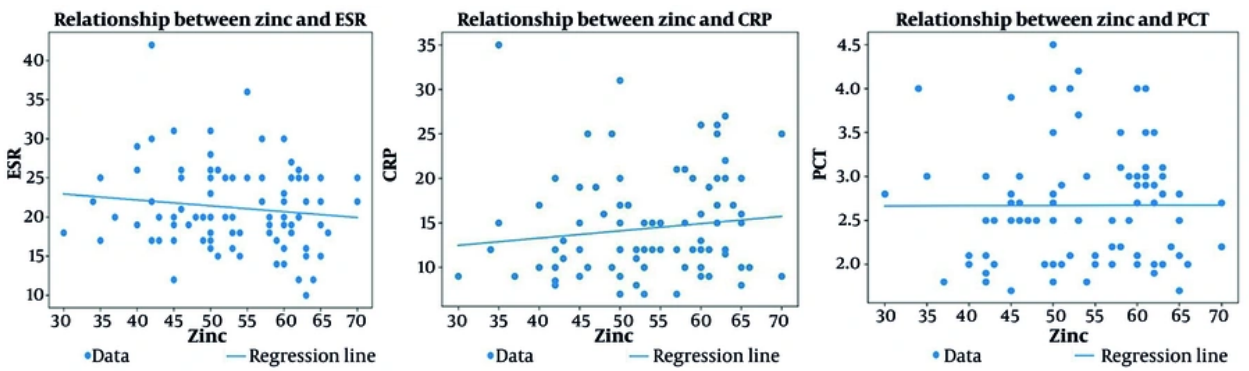


**Figure 1.** Scatter plot of zinc and PCT (down one), zinc and ESR (up and left), zinc and CRP (up and right) (Abbreviations: PCT, procalcitonin; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein)

in diabetic, cardiovascular patients, and the elderly, particularly with doses exceeding, but not limited to, 50 mg daily. In obese children, deficiency for zinc is associated with increased CRP and systemic inflammation (28), which heightens the incidence of metabolic disorders. Furthermore, in the context of perinatal depression, low zinc was associated with increased CRP, as well as signs and symptoms of physio-somatic, providing further evidence of the impact of zinc levels regarding mental health and inflammation. Conversely, our findings showed zinc did not show any significant associations with CRP and ESR. The mechanism of action of zinc is through inhibition of inflammatory pathways such as NF-κB and reduction of the production of proinflammatory cytokines such as IL-6 (9, 29). In infectious diseases, zinc can modulate PCT and reduce the severity of the inflammatory response, which was contradicted by our results (30). Overall, zinc supplementation has been proposed as a low-cost and effective strategy to reduce inflammatory markers in various conditions, although the optimal dose and duration require further investigation.

In infections caused by bacteria such as *Staphylococcus aureus* or *Streptococcus pneumoniae* (31), zinc supplementation can reduce the production of proinflammatory cytokines and modulate the severity of inflammation. In animal models, zinc has been shown to reduce the bacterial burden of *Mycobacterium tuberculosis* (TB) by increasing the production of reactive oxygen species (ROS) (32).

In infections caused by gram-negative bacteria such as Pseudomonas aeruginosa, zinc can induce a differential response by regulating the expression of antibiotic resistance genes (33). Our findings also indicate that there is no difference between UTI caused by *E. coli* versus *Klebsiella* species. This observation may be partially explained by the genetic and metabolic similarities of the two bacteria, which both depend on zinc for growth and proliferation and show similar responses to zinc changes. This finding is consistent with studies showing that Enterobacteriaceae have similar zinc uptake systems (34). Thus, while zinc generally has anti-inflammatory and antimicrobial effects in bacterial diseases, differences in the response to zinc are evident in different bacterial species (such as gram-positive versus gram-negative) (35), but in our study, the similarities between *E. coli* and *Klebsiella* led to similar responses. This indicates the importance of bacterial characteristics in the effects of zinc.

Zinc has been suggested to be associated with inflammatory responses and susceptibility to UTIs in some populations (36). In contrast, zinc deficiency has been reported to be associated with increased PCT levels, a marker of inflammation in UTI (18). These findings are in contrast to the results observed in the present pediatric cohort, which clearly demonstrated that the association between zinc and PCT and UTI is nonsignificant. In fact, unlike several other inflammatory conditions, serum zinc levels were not significantly reduced in children with UTI in our study, although this was not the case in all patients. In children, data are limited, but one study reported that PCT is increased in UTI caused by *E. coli* and

*Klebsiella pneumoniae* and that zinc can reduce inflammation, which was in contrast to our results.

In adults, zinc supplementation reduces the severity of UTI and PCT levels, especially in acute pyelonephritis (21). In pregnant women, low zinc is associated with elevated PCT and more severe UTI (17). Zinc modulates inflammation and PCT by inhibiting the NF-κB pathway and reducing proinflammatory cytokines such as IL-6 (1, 9). These effects were observed in a range of ages, from children to the elderly, but the severity of the response to zinc may vary depending on nutritional status and bacterial species. Therefore, zinc supplementation could be an effective strategy for managing UTIs and reducing PCT in different age groups, although further research in children is needed to confirm our results.

The findings of this study showed that serum zinc levels in children with UTI were not significantly different from common inflammatory markers, including PCT, CRP, and ESR. Overall, the present findings suggest that the relationship between zinc and inflammatory markers in hospitalized children with UTI is more complex than a simple linear relationship and likely requires investigation in settings with a larger sample size, longitudinal design, and simultaneous measurement of other micronutrients (such as copper and ferritin).

### 5.1. Limitations

The present study is limited by many factors, such as cross-sectional studies cannot establish a direct cause-and-effect relationship for serum zinc levels and PCT, an inflammatory marker in children with UTIs. Since we could not assess the effect of zinc and the inflammatory markers on the development of UTIs or after treatment, we are unable to illustrate how serum or zinc concentrations affect those inflammatory marker levels. Second, since serum zinc concentrations were measured as soon as the children were admitted to the hospital, this single measurement might not represent the participants' long-term serum zinc levels as they may be affected by their recent illness, dietary intake before their hospital admission, or the acute-phase response that occurred shortly after they became ill. Third, the current sample size was relatively small and was taken only from one tertiary referral center, thus limiting the generalizability of these findings to larger pediatric populations or outpatient settings. In addition, given the small number of patients with causative pathogens other than *E. coli*, our ability to perform subgroup analyses based on causative pathogens is limited.

### 5.2. Conclusions

This study points out a possible link between zinc levels and UTI s in children, but it does not establish a clear or independent therapeutic role for zinc in this context. Although zinc might play a part in immune regulation, its actual significance in UTIs seems to be restricted and varies by situation. Therefore, current evidence does not support the routine use of zinc supplements for treating pediatric UTIs. Further prospective and controlled research is needed to explore whether zinc deficiency affects the likelihood, severity, or recovery from these infections in children.

## Acknowledgements

The authors would like to thank the Department of Pediatrics at Hormozgan University of Medical Sciences for their assistance in this study and for their efforts in verifying the obtained results.

## Footnotes

**AI Use Disclosure:** The authors declare that no generative AI tools were used in the creation of this article.

**Authors' Contribution:** S. Z. S. contributed to the study design and protocol development, oversaw the clinical trial implementation, contributed to data interpretation and manuscript writing. M. E. managed participant recruitment and retention, performed statistical analysis, and drafted sections of the results and discussion. S. S. and M. E. conducted literature review, provided expertise in clinical methodology, assisted in data collection and quality assurance, and contributed to manuscript revisions. S. Z. S. supervised the overall project and ensured compliance with ethical standards; reviewed and approved the final manuscript.

**Conflict of Interests Statement:** The authors declare no conflict of interest.

**Data Availability:** The dataset presented in the study is available on request from the corresponding author during submission or after publication.

**Ethical Approval:** All procedures performed in this investigation involving human participant studies were under the ethical standards of the Institutional and National Research Committee and following the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The present study is a research project held under the supervision of the neurology department of Arak University Medical Sciences (IR.HUMS.REC.1402.461 ).

**Funding/Support:** The present study received no funding/support.

**Informed Consent:** Written informed consent was obtained from the participants.

## References


1. Gammoh NZ, Rink L. Zinc in Infection and Inflammation. *Nutrients*. 2017;**9**(6). [PubMed ID: 28629136]. [PubMed Central ID: PMC5490603]. https://doi.org/10.3390/nu9060624.
2. Yusuf S, Soenarto Y, Juffrie M, Lestariana W. The effect of zinc supplementation on pro-inflammatory cytokines (TNF-alpha, IL-1 AND IL-6) in mice with Escherichia coli LPS-induced diarrhea. *Iran J Microbiol*. 2019;**11**(5):412-8. [PubMed ID: 32148672]. [PubMed Central ID: PMC7049316].
3. Ceylan MN, Akdas S, Yazihan N. The Effects of Zinc Supplementation on C-Reactive Protein and Inflammatory Cytokines: A Meta-Analysis and Systematical Review. *J Interferon Cytokine Res*. 2021;**41**(3):81-101. [PubMed ID: 33750215]. https://doi.org/10.1089/jir.2020.0209.
4. Ustundag B, Yilmaz E, Dogan Y, Akarsu S, Canatan H, Halifeoglu I, et al. Levels of cytokines (IL-1beta, IL-2, IL-6, IL-8, TNF-alpha) and trace elements (Zn, Cu) in breast milk from mothers of preterm and term infants. *Mediators Inflamm*. 2005;**2005**(6):331-6. [PubMed ID: 16489252]. [PubMed Central ID: PMC1533895]. https://doi.org/10.1155/MI.2005.331.
5. Bose A, Coles CL, John H, Moses P, Raghupathy P; Gunavathi, et al. Efficacy of zinc in the treatment of severe pneumonia in hospitalized children <2 y old. *Am J Clin Nutr*. 2006;**83**(5):1089-96. quiz 1207. [PubMed ID: 16685051]. https://doi.org/10.1093/ajcn/83.5.1089.
6. Bhandari N, Bahl R, Taneja S, Strand T, Molbak K, Ulvik RJ, et al. Effect of routine zinc supplementation on pneumonia in children aged 6 months to 3 years: randomised controlled trial in an urban slum. *BMJ*. 2002;**324**(7350):1358. [PubMed ID: 12052800]. [PubMed Central ID: PMC115208]. https://doi.org/10.1136/bmj.324.7350.1358.
7. Jarosz M, Olbert M, Wyszogrodzka G, Mlyniec K, Librowski T. Antioxidant and anti-inflammatory effects of zinc. Zinc-dependent NF-kappaB signaling. *Inflammopharmacology*. 2017;**25**(1):11-24. [PubMed ID: 28083748]. [PubMed Central ID: PMC5306179]. https://doi.org/10.1007/s10787-017-0309-4.
8. Tang M, Yuan D, Liao P. Berberine improves intestinal barrier function and reduces inflammation, immunosuppression, and oxidative stress by regulating the NF-kappaB/MAPK signaling pathway in deoxynivalenol-challenged piglets. *Environ Pollut*. 2021;**289**:117865. [PubMed ID: 34358871]. https://doi.org/10.1016/j.envpol.2021.117865.
9. Shen H, Oesterling E, Stromberg A, Toborek M, MacDonald R, Hennig B. Zinc deficiency induces vascular pro-inflammatory parameters associated with NF-kappaB and PPAR signaling. *J Am Coll Nutr*. 2008;**27**(5):577-87. [PubMed ID: 18845708]. https://doi.org/10.1080/07315724.2008.10719741.
10. Chen Y, Cai J, Liu D, Liu S, Lei D, Zheng L, et al. Zinc-based metal organic framework with antibacterial and anti-inflammatory properties for promoting wound healing. *Regen Biomater*. 2022;**9**:rbac019. [PubMed ID: 35493287]. [PubMed Central ID: PMC9046580]. https://doi.org/10.1093/rb/rbac019.
11. Salvatore S, Hauser B, Devreker T, Vieira MC, Luini C, Arrigo S, et al. Probiotics and zinc in acute infectious gastroenteritis in children: are they effective? *Nutrition*. 2007;**23**(6):498-506. [PubMed ID: 17499972]. https://doi.org/10.1016/j.nut.2007.03.008.
12. Brandstrom P, Hansson S. Urinary Tract Infection in Children. *Pediatr Clin North Am*. 2022;**69**(6):1099-114. [PubMed ID: 36880924]. https://doi.org/10.1016/j.pcl.2022.07.003.
13. Pineiro Perez R, Cilleruelo Ortega MJ, Ares Alvarez J, Baquero-Artigao F, Silva Rico JC, Velasco Zuniga R, et al. Recommendations on the diagnosis and treatment of urinary tract infection. *Ann Pediatr*. 2019;**90**(6):4000-9. https://doi.org/10.1016/j.anpede.2019.02.002.
14. Desai DJ, Gilbert B, McBride CA. Paediatric urinary tract infections: Diagnosis and treatment. *Aust Fam Physician*. 2016;**45**(8):558-63. [PubMed ID: 27610444].
15. Shaikh KJ, Osio VA, Leeflang MM, Shaikh N. Procalcitonin, C-reactive protein, and erythrocyte sedimentation rate for the diagnosis of acute pyelonephritis in children. *Cochrane Database Syst Rev*. 2020;**9**(9). CD009185. [PubMed ID: 32911567]. [PubMed Central ID: PMC8479592]. https://doi.org/10.1002/14651858.CD009185.pub3.
16. Ayazi P, Mahyar A, Daneshi MM, Jahani Hashemi H, Pirouzi M, Esmailzadehha N. Diagnostic Accuracy of the Quantitative C-Reactive Protein, Erythrocyte Sedimentation Rate and White Blood Cell Count in Urinary Tract Infections among Infants and Children. *Malays J Med Sci*. 2013;**20**(5):40-6. [PubMed ID: 24643248]. [PubMed Central ID: PMC3957355].
17. Hu L, Shi Q, Shi M, Liu R, Wang C. Diagnostic Value of PCT and CRP for Detecting Serious Bacterial Infections in Patients With Fever of Unknown Origin: A Systematic Review and Meta-analysis. *Appl Immunohistochem Mol Morphol*. 2017;**25**(8):e61-9. [PubMed ID: 28885233]. https://doi.org/10.1097/PAI.0000000000000552.
18. Zabihi F, Mostafavi M, Esmaeili M, Issapour Cheshani M. Investigating the Effect of Zinc Deficiency on the Risk of Urinary Tract Infection in Children. *J Pediatr Perspect*. 2020;**8**(9):11959-66. https://doi.org/10.22038/ijp.2020.47133.3819.
19. Adams AD, Benner RS, Riggs TW, Chescheir NC. Use of the STROBE Checklist to Evaluate the Reporting Quality of Observational Research in Obstetrics. *Obstet Gynecol*. 2018;**132**(2):507-12. [PubMed ID: 29995749]. https://doi.org/10.1097/AOG.0000000000002689.
20. Newman TB. The new American Academy of Pediatrics urinary tract infection guideline. *Pediatrics*. 2011;**128**(3):572-5. [PubMed ID: 21873698]. https://doi.org/10.1542/peds.2011-1818.
21. Yousefichaijan P, Naziri M, Taherahmadi H, Kahbazi M, Tabaei A. Zinc Supplementation in Treatment of Children With Urinary Tract Infection. *Iran J Kidney Dis*. 2016;**10**(4):213-6. [PubMed ID: 27514768].
22. Bonaventura P, Benedetti G, Albarede F, Miossec P. Zinc and its role in immunity and inflammation. *Autoimmun Rev*. 2015;**14**(4):277-85. [PubMed ID: 25462582]. https://doi.org/10.1016/j.autrev.2014.11.008.
23. Bao B, Prasad AS, Beck FW, Fitzgerald JT, Snell D, Bao GW, et al. Zinc decreases C-reactive protein, lipid peroxidation, and inflammatory cytokines in elderly subjects: a potential implication of zinc as an

atheroprotective agent. *Am J Clin Nutr*. 2010;**91**(6):1634-41. [PubMed ID: 20427734]. [PubMed Central ID: PMC2869512]. https://doi.org/10.3945/ajcn.2009.28836.

24. Ivanova ID, Pal A, Simonelli I, Atanasova B, Ventriglia M, Rongioletti M, et al. Evaluation of zinc, copper, and Cu:Zn ratio in serum, and their implications in the course of COVID-19. *J Trace Elem Med Biol*. 2022;**71**:126944. [PubMed ID: 35168023]. [PubMed Central ID: PMC8820953]. https://doi.org/10.1016/j.jtemb.2022.126944.
25. Anuk AT, Polat N, Akdas S, Erol SA, Tanacan A, Biriken D, et al. The Relation Between Trace Element Status (Zinc, Copper, Magnesium) and Clinical Outcomes in COVID-19 Infection During Pregnancy. *Biol Trace Elem Res*. 2021;**199**(10):3608-17. [PubMed ID: 33236293]. [PubMed Central ID: PMC7685187]. https://doi.org/10.1007/s12011-020-02496-y.
26. Grober U, Tsiami S, Chillon TS, Rousis E, Kisters K, Karmeli S, et al. Trace Element Deficiency in Axial Spondyloarthritis and Psoriatic Arthritis in Relation to Markers of Inflammation and Remission. *Int J Mol Sci*. 2025;**26**(10). [PubMed ID: 40430066]. [PubMed Central ID: PMC12112114]. https://doi.org/10.3390/ijms26104924.
27. Faghfouri AH, Baradaran B, Khabbazi A, Khaje Bishak Y, Zarezadeh M, Tavakoli-Rouzbehani OM, et al. Profiling inflammatory cytokines following zinc supplementation: a systematic review and meta-analysis of controlled trials. *Br J Nutr*. 2021;**126**(10):1441-50. [PubMed ID: 33468279]. https://doi.org/10.1017/S0007114521000192.
28. Zou Y, Zhang R, Huang L, Zhao D, Su D, Meng J, et al. Serum levels of vitamin D, retinol, zinc, and CRP in relation to obesity among children and adolescents. *Eur J Med Res*. 2022;**27**(1):51. [PubMed ID: 35379317]. [PubMed Central ID: PMC8977183]. https://doi.org/10.1186/s40001-022-00670-7.
29. Bao B, Prasad AS, Beck FW, Snell D, Suneja A, Sarkar FH, et al. Zinc supplementation decreases oxidative stress, incidence of infection, and generation of inflammatory cytokines in sickle cell disease patients. *Transl Res*. 2008;**152**(2):67-80. [PubMed ID: 18674741]. https://doi.org/10.1016/j.trsl.2008.06.001.
30. Bao S, Liu MJ, Lee B, Besecker B, Lai JP, Guttridge DC, et al. Zinc modulates the innate immune response in vivo to polymicrobial sepsis through regulation of NF-kappaB. *Am J Physiol Lung Cell Mol Physiol*. 2010;**298**(6):L744-54. [PubMed ID: 20207754]. [PubMed Central ID: PMC2886607]. https://doi.org/10.1152/ajplung.00368.2009.
31. Slupsky CM, Cheypesh A, Chao DV, Fu H, Rankin KN, Marrie TJ, et al. Streptococcus pneumoniae and Staphylococcus aureus pneumonia induce distinct metabolic responses. *J Proteome Res*. 2009;**8**(6):3029-36. [PubMed ID: 19368345]. https://doi.org/10.1021/pr900103y.
32. Dow A, Sule P, O'Donnell TJ, Burger A, Mattila JT, Antonio B, et al. Zinc limitation triggers anticipatory adaptations in Mycobacterium tuberculosis. *PLoS Pathog*. 2021;**17**(5). e1009570. [PubMed ID: 33989345]. [PubMed Central ID: PMC8121289]. https://doi.org/10.1371/journal.ppat.1009570.
33. Lei L, Chen J, Liao W, Liu P. Determining the Different Mechanisms Used by Pseudomonas Species to Cope With Minimal Inhibitory Concentrations of Zinc via Comparative Transcriptomic Analyses. *Front Microbiol*. 2020;**11**:573857. [PubMed ID: 33343517]. [PubMed Central ID: PMC7744410]. https://doi.org/10.3389/fmicb.2020.573857.
34. Porcheron G, Garenaux A, Proulx J, Sabri M, Dozois CM. Iron, copper, zinc, and manganese transport and regulation in pathogenic Enterobacteria: correlations between strains, site of infection and the relative importance of the different metal transport systems for virulence. *Front Cell Infect Microbiol*. 2013;**3**:90. [PubMed ID: 24367764]. [PubMed Central ID: PMC3852070]. https://doi.org/10.3389/fcimb.2013.00090.
35. Rihacek M, Kosaristanova L, Fialova T, Kuthanova M, Eichmeier A, Hakalova E, et al. Zinc effects on bacteria: insights from Escherichia coli by multi-omics approach. *mSystems*. 2023;**8**(6). e0073323. [PubMed ID: 37905937]. [PubMed Central ID: PMC10734530]. https://doi.org/10.1128/msystems.00733-23.
36. Gao P, Liang W, Li H, Guan L, Zhao Q, Li D. Effects of vitamins A, C, and D and zinc on urinary tract infections. *Qual Assur Saf Crop Foods*. 2023;**15**(3). https://doi.org/10.15586/qas.v15i3.1292.