



# Analysis of Zinc, Albumin, and Proteinuria Levels in Children with Nephrotic Syndrome: Comparison of First Attack, Remission, and Relapse Phases

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## KEYWORDS

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## ABSTRACT:

**Introduction:** Nephrotic syndrome (NS) is one of the most common kidney disorders in children, characterized by proteinuria, hypoalbuminemia, edema, and hypercholesterolemia. Relapses of NS are frequently associated with respiratory or digestive tract infections, particularly in children from developing countries. Zinc (Zn), a vital trace element involved in immune function, growth, and metabolism, often decreases during the active phase of NS due to proteinuria.

**Objectives:** This study aimed to analyze zinc, albumin, and proteinuria levels in children with NS at Dr. Wahidin Sudirohusodo Hospital Makassar, focusing on differences between the first attack, remission, and relapse phases.

**Methods:** A cross-sectional observational analytical design with consecutive sampling was applied. Serum zinc levels were determined using atomic absorption spectroscopy (AAS), and correlations between zinc, albumin, and proteinuria were statistically analyzed.

**Results:** The findings revealed a significant reduction in serum zinc levels during the relapse phase compared to the remission phase. There was a positive correlation between zinc and albumin levels and a negative correlation between zinc and proteinuria levels.

**Conclusions:** Zinc deficiency is closely associated with increased susceptibility to infection and the recurrence of NS in children. Therefore, zinc supplementation may serve as a beneficial intervention strategy in managing nephrotic syndrome.

## 1. Introduction

Syndrome nephrotic syndrome (NS) in children is challenge complex and ongoing clinical become attention big in field nephrology pediatrics . Diseases This No only just disturbance function kidneys , but rather condition systemic impact wide range of metabolism , nutritional status , system immune , up to quality life children . In a way Clinically , SN is characterized by with gathering symptom typical in the form of massive proteinuria , hypoalbuminemia , edema , and hypercholesterolemia . The four manifestation the become sign diagnostics that differentiate SN from disturbance kidney others . In the context of epidemiology , SN is one of the disease kidney most in children , with prevalence Far more tall compared to the population adults . Global data shows that incidence of

SN in children reaching 2–3 cases per 100,000 children per year , with peak age incident between 3 to 4 years , as well ratio man compared to Woman approximately 2:1 ( Rodriguez-Ballestas & Reid-Adam, 2022 ). This fact confirm that SN is problem health significant community , particularly in developing countries where facilities health and access therapy Still limited .

Distribution geographic SN shows enough variety large , depending on factors genetics , environment , and health status society . In South Asia, the prevalence of SN is relatively more tall compared to Europe or North America. This is associated with factor predisposition genetics , infection repeated , and limitations access service primary health ( Sharma & Bagga, 2024 ). In Indonesia itself , although national data Not yet integrated with okay , report from a number of House



Sick references show trend improvement amount SN cases in two decades lastly . This is relate close with improvement number birth , improvement of early diagnosis , but also not yet optimally system prevention relapse .

Manifestation clinical in children with SN often started with subsequent periorbital edema spread become anasarca . Condition This bother activity daily children , including school , sleep , and nutrition . Not infrequently , edema heavy cause pleural effusion or ascites requiring management specific . Underlying hypoalbuminemia symptom it also increases risk other complications such as deep vein thrombosis and infection opportunistic ( Ghobrial et al., 2020 ).

Most of the SN cases in children including in category syndrome nephrotic idiopathic (SNI), the etiology of which is Not yet fully known . However , a number of theory pathogenesis has was put forward . One of them is hypothesis damage podocytes , cells functioning glomerular epithelium guard integrity filtration kidney damage podocytes cause change slit diaphragm structure , so that permeability glomerular basement membrane increases and plasma proteins pass into the urine ( Carter & Reiser, 2021 ). The massive proteinuria that results become point beginning a series complications metabolic .

Apart from the factors structural , mechanism immunology also plays a role important . Many studies show existence involvement system immune adaptive , especially T cells and release cytokines , in pathogenesis of SN. Abnormal activation of T-helper cells , especially Th1/Th2 imbalance , resulting dysregulation system immune system and triggers episodes of proteinuria. When the immune system immune child more leaning to Th2 direction , body become more prone to to infection and relapse more easy occurred ( Santín et al., 2011 ). With Thus , the pathophysiology of SN in children No Can understood only from One corner view , but rather is results interaction complex between factor structural kidneys and system immune .

Phenomenon relapse is problem main on the trip clinical SN. Data shows that 50–70% of children with SN experiencing relapse , especially after experience infection channel breathing upper respiratory tract infection (ARI), infection channel digest , as well as infection skin ( Arun et al., 2009; Hamik et al., 2019 ).

Relapse No only make things worse condition physique child , but also improve burden psychological family as well as cost maintenance health . Mechanism relapse Still become debate , however a number of factor allegedly involved , including release cytokines proinflammatory , increased glomerular permeability , up to dysfunction recurrent podocytes . Longitudinal studies show that children who experience relapse often have higher zinc levels low compared to the rare ones relapse , indicating relatedness close between nutritional status micro and travel disease ( Bhatt et al., 2016 ).

Zinc is an essential trace element that plays a role in more of 300 enzymes and 2000 factors transcription . Its role is very broad , starting from from growth cells , regeneration network , regulation system immune , up to activity antioxidant and anti-inflammatory ( Harwijayanti et al., 2022 ). Zinc deficiency has been shown to lower expression T-helper 1 (Th1) cells , which results in a decrease production of interleukin-2 (IL-2) and interferon gamma (IFN- $\gamma$ ). Conditions This shift balance response immune to direction of T-helper 2 (Th2), so child become more prone to to infection and more easy experience relapse ( Sherali et al., 2014 ).

Study about zinc supplementation has show varied results . Some study report that zinc supplementation is able reduce frequency relapse and accelerate remission . For example , Bhatt et al. (2016) find that child with SN who got zinc supplements experience relapse more A little compared to group control . However , other studies report results different , where the zinc levels are not show change significant during phase remission ( Taherahmadi et al., 2019 ). Difference results This show the need study more carry on For clarify the role of zinc in journey clinical SN, especially in context population children in developing countries .

Apart from its role in system immune , zinc also has relatedness close with albumin, the main plasma protein which is also an important parameter in SN. Albumin functions as a transport protein and has vital role in guard pressure plasma oncotic . More from that , albumin is also a binder main zinc in circulation blood . Therefore that , hypoalbuminemia is often occurs in SN can cause decline serum zinc levels . Study by Fathah et al. (2022) confirm that zinc is not Can analyzed in a way separated from albumin, considering both of them own connection closely functional in maintain body homeostasis .



Massive proteinuria is sign typical SN that is not only become basis of diagnosis, but also plays a role important in progressiveness disease. Loss of protein in amount big through urine cause disturbance metabolism, deficiency nutrition, as well as vulnerability to infection. More Far again, a number of study latest find existence correlation significant negative between degree of proteinuria with serum zinc levels. In other words, more and more tall the level of proteinuria, the more low zinc levels in circulation blood (Taherahmadi et al., 2019; Ghane Shahrbafl & Assadi, 2021). Connection This confirm that proteinuria, albumin, and zinc are three biomarker components that interact with each other interact in journey clinical SN.

deficiency in SN patients is not only problem biochemical, but also has implications real clinical. Children with low zinc levels more easy experience infection repeated, which in turn become trigger main relapse. In addition, zinc plays a role in regeneration network kidneys, so that the shortcomings can slow down recovery post-attack First. Zhou et al.'s (2023) study confirm that zinc has effect important immunomodulator in disease kidney children, and their deficiencies relate with worsening journey clinical. Therefore Therefore, monitoring of serum zinc status in SN patients is necessary. get attention special in management term long.

In Indonesia, research about the relationship between zinc and SN in children is still very limited. Most of study only focus on aspects clinical general like pattern relapse or response to therapy corticosteroids. Research about trace elements, especially zinc, not yet done in a way comprehensive, even though condition geography and nutritional status Indonesian children have potential influence zinc levels in body. In fact, in Makassar for example, it has not There is research that is special analyze zinc levels in children with SN. This is become gap study important things to do quick filled, remembering prevalence of SN is quite high high in Indonesia and the risk relapse contribute significant to burden health public.

Based on the description above, can concluded that SN in children is disease complex involving interaction between mechanism immunological, damage structural kidneys, and nutritional status micro. Massive proteinuria, hypoalbuminemia, and zinc deficiency is

not only symptoms, but also determinants journey clinical disease This. Frequent relapses happen show existence connection close between disturbance immunology and trace element deficiencies such as zinc. With consider the role of zinc, albumin, and proteinuria, further research in-depth research is very necessary, especially in Indonesia, to give understanding comprehensive about the interaction of these biomarkers. The results of the study This later can become runway scientific for intervention nutrition, prevention strategies relapse, and improvement quality life child with SN.

## 2. Objectives

The main objective of this study is to comprehensively analyze the relationship between zinc, albumin, and proteinuria levels in children diagnosed with nephrotic syndrome (NS) at Dr. Wahidin Sudirohusodo Hospital, Makassar. This research aims to identify how fluctuations in these biomarkers differ across the three clinical phases—first attack, remission, and relapse—and to determine their interdependence in influencing the disease's progression. By focusing on zinc as a trace element with critical roles in immune regulation, growth, and tissue repair, this study seeks to clarify the extent to which zinc deficiency contributes to immune dysregulation, increased susceptibility to infection, and higher relapse rates among pediatric NS patients. Furthermore, the analysis of albumin, as the major zinc-binding protein in plasma, will provide a deeper understanding of how hypoalbuminemia and massive proteinuria jointly affect zinc homeostasis and immune competence in this population.

Another specific objective of this study is to address the research gap in Indonesia regarding trace element status among pediatric nephrotic patients, particularly zinc, which remains underexplored despite its potential clinical importance. Through quantitative comparison of zinc levels in various clinical stages of NS, this research aims to establish an evidence-based foundation for nutritional monitoring and intervention strategies in pediatric nephrology practice. The results are expected to provide valuable insights into the potential role of zinc supplementation in preventing relapses and improving long-term outcomes for children with NS. Ultimately, this study aspires to contribute not only to the understanding of the biochemical mechanisms underlying NS but also to the formulation of integrated



management approaches that combine clinical therapy with nutritional optimization in Indonesian healthcare settings.

### 3. Methods

**Study** This use approach observational analytic with design cut cross sectional , a design a lot of research used in study clinical and epidemiology For explore connection between variables on one point time certain . This design chosen Because in accordance with objective research , namely assess and compare Zinc levels , albumin, and proteinuria in children with syndrome nephrotic (SN) in three phase different clinical , namely attack first , remission , and relapse . Advantages from design cross-sectional is his abilities give description difference between group in a way simultaneously without demanding a follow-up process term long , so that more efficient in matter costs , energy , and time (Setia, 2016). Although Thus , the design it also has limitations , especially related inference causality that is not can withdrawn in a way directly , so that results study more focused on identification existing relationships and differences , not on proof cause and effect (Levin, 2006).

Research location was established at Dr. Wahidin Sudirohusodo Hospital, Makassar, a House Sick references national for the Eastern Indonesia region. Hospital This chosen Because have case volume syndrome nephrotic a relative child high , so that allows collection sample in amount adequate . In addition that , laboratory study conducted in the laboratory Faculty Hasanuddin University Medical School which has equipment adequate , including atomic absorption spectroscopy (AAS), a instrument standardized gold For analysis levels of trace elements such as zinc in blood serum . AAS is selected Because level high accuracy as well as its adequate sensitivity For detect level micro in sample biological (Nardi et al., 2009). Research This ongoing since December 2024 to amount minimum sample requirement met in accordance results calculation

Target population of the research is all over patient child aged 1–18 years with clinical diagnosis syndrome nephrotic . From the target population , the population affordable is patient the child who came seek medical treatment or treated at Dr. Wahidin Sudirohusodo Hospital during period research . Definition syndrome nephrotic syndrome in children based on criteria International Study of Kidney Disease in Children

(ISKDC), namely massive proteinuria , hypoalbuminemia , edema , and hypercholesterolemia (Bagga & Mantan, 2005).

Election sample done with method consecutive sampling , namely all incoming patients in a way sequential and fulfilling criteria inclusion entered until amount sample achieved . This technique assessed effective For study clinical with availability patient limited and considered can minimize selection bias ( Etikan et al., 2016). After taking blood sample quick processed through centrifugation For separate the serum, then stored in a tube without anticoagulant at temperature stable 2–8°C to done inspection zinc levels . If the examination delayed more from 72 hours, sample stored at room temperature frozen -70°C for guard trace element stability (King et al., 2015).

Calculation big sample referring to the formula Lemeshow (1998), with level error type I ( $\alpha$ ) of 5% and test power of 80%. Based on study previously conducted by Zarlina (2015) , obtained difference average zinc levels between group remission (67.4  $\mu\text{g/dL}$ ) and group control (75.0  $\mu\text{g/dL}$ ). Based on results calculation , a minimum of 20 samples per group is required . With consider three group ( attack first , remission , and relapse ) , then minimum sample size set as many as 60 children . Calculation This important For ensure adequacy statistical test power in detect meaningful differences , at the same time minimize possibility occurrence error type II, namely failure reject hypothesis false zero (Charan & Biswas, 2013).

Criteria inclusions used in study This is child aged 1–18 years with clinical diagnosis syndrome nephrotic , patients being treated or received treatment at Dr. Wahidin Sudirohusodo Hospital , Makassar, and existence agreement written ( informed consent ) from parents or guardian . On the other hand , the criteria exclusion covers patient with syndrome nephrotic congenital , nutritional bad , disease malignancy , autoimmune , disorders digestion chronic , or disease significant respiration , as well as deceased patients before done inspection laboratory . Application criteria exclusion intended For reduce variables confounders that can influence levels of zinc, albumin, and proteinuria, so results study more valid (Patino & Ferreira, 2018).

Research process This executed in accordance with rules ethics study medicine . Researchers get permission from



Commission Ethics Study Biomedicine in Humans Faculty Hasanuddin University Medical School . All procedure study done in accordance principle Declaration of Helsinki , namely honor right patient , care data confidentiality , as well as get agreement written from parents or guardian patient before action performed (World Medical Association, 2013).

Procedure flow study started with recruitment subject , where the patient child who fulfills criteria inclusion evaluated more continue . Parents or guardian patient given explanation related objective research , benefits , risks , and procedures to be carried out carried out . After agreement obtained , patient entered as sample research . Next done inspection clinical , including recording demographic data ( age , gender) gender ), nutritional status , vital signs , and symptom clinical typical syndrome nephrotic .

Retrieval sample blood done by manpower medical trained with procedure standard , namely take 3 cc of venous blood using syringe sterile after tourniquet application and disinfection skin with 70% alcohol . Blood sample Then entered to in tube without anticoagulant , centrifuged in 30 minutes For separate the serum, then saved in accordance procedure until inspection conducted ( Rodushkin & Axelsson, 2000). Examination serum zinc levels using Atomic Absorption Spectroscopy (AAS) method , with principle base that atoms are free in gas phase can absorb light at long wave certain appropriate with spectrum zinc characteristic . Reading results intensity absorption light This converted become zinc concentration in sample (Welz & Sperling, 2008).

In addition to zinc examination , serum albumin examination was also carried out using method spectrophotometry biochemistry standards , as well as proteinuria examination using dipstick test, protein/creatinine ratio urine , or collection 24-hour urine test . Examination This important considering that albumin plays a role as a binding protein main zinc in circulation , so that low albumin levels will affect zinc status ( Fathah et al., 2022). Proteinuria is also a indicator clinical main syndrome correlated nephrotic with severity disease as well as risk relapse ( Vivarelli et al., 2017).

Subject study classified to in three group clinical in accordance definition operational , namely : (1) attack

first , namely patient with the first episode of SN ; (2) remission , namely patient with negative proteinuria or trace ( $<40$  mg/m<sup>2</sup>/hour) during three day consecutively ; and (3) relapse , namely patient with proteinuria  $\geq 2+$  during three day consecutively (KDIGO, 2021).

Variables study covering variables free in the form of clinical status syndrome nephrotic ( attack) first , remission , relapse ), variable depends in the form of serum zinc levels , variable control covering age , type gender , and nutritional status , as well as variables confounding factor in the form of disease accompanying like autoimmune , malignancy , or infection chronic . Definition operational zinc serum is based on the limits age (Rao, 2021), while serum albumin is determined based on normal biochemical levels clinical , and positive proteinuria determined when protein excretion  $\geq 40$  mg/m<sup>2</sup>/hour or  $\geq 2+$  on urine dipstick examination .

Data analysis was performed with use device SPSS software version latest . Analysis univariate done For describe characteristics base subject research , good in the form of numerical data ( mean  $\pm$  standard deviation or median and range interquartile range ) and categorical data ( frequency and percentage ). Analysis bivariate done For test connection between variables , with the chi-square test used For variables categorical , ANOVA or Kruskal-Wallis test is used For compare zinc levels between groups , and the Pearson or Spearman correlation test was used. For evaluate connection between zinc levels with albumin and proteinuria. Significance level set at a p value  $< 0.05$  (Field, 2013).

Through approach structured methodology this , it is hoped results study can give comprehensive overview about zinc levels in children with syndrome nephrotic , as well as the relationship with albumin and proteinuria in various phase clinical information This important No only For strengthen understanding scientific , but also potentially become base in designing intervention nutrition and therapy supportive For prevent relapse and repair quality life patient child with syndrome nephrotic.

## 4. Results

Study This done to six tens children who have diagnosed syndrome nephrotic (SN), which then shared to in three group based on journey his illness , namely group attack first , group remission , and groups relapse , with each group consists of of twenty patient . Distribution



respondents This No only reflect variation clinical SN, but also provides description comprehensive about characteristics basic , nutritional status , and dynamics Serum zinc levels were observed in each phase journey disease .

Characteristics base respondents covering age , type gender , nutritional status , and sign clinical main like existence edema , pressure blood , albumin levels , and degree of proteinuria. Most of the patient is in group ages 3–6 years , as appropriate with report epidemiological previously that peak the incidence of SN occurs at the age of early , especially under age 10 years (Noone & Gipson, 2020). In this study Of these , 38 children (63.3%) were aged 3–6 years , 15 children ( 25%) were aged 7–9 years , and 7 children (11.7%) were aged  $\geq 10$  years . If we look at in a way statistics , distribution This show consistency with global pattern , where the incidence syndrome nephrotic idiopathic in children reach 90% of all over case before age 10 years (Rodriguez-Ballestas & Reid-Adam, 2022).

Comparison type sex show that child man more Lots compared to Woman with ratio of 2:1, namely 40 men

Characteristics table base respondents :

| Variables                       | Attack First (n=20) | Remission (n=20) | Relapse (n=20) | Total (N=60) |
|---------------------------------|---------------------|------------------|----------------|--------------|
| Ages 3–6 years                  | 14 (70%)            | 13 (65%)         | 11 (55%)       | 38 (63.3%)   |
| Ages 7–9 years                  | 4 (20%)             | 5 (25%)          | 6 (30%)        | 15 (25%)     |
| Age $\geq 10$ years             | 2 (10%)             | 2 (10%)          | 3 (15%)        | 7 (11.7%)    |
| Man                             | 13 (65%)            | 14 (70%)         | 13 (65%)       | 40 (66.7%)   |
| Woman                           | 7 (35%)             | 6 (30%)          | 7 (35%)        | 20 (33.3%)   |
| Normal– good nutritional status | 20 (100%)           | 20 (100%)        | 20 (100%)      | 60 (100%)    |

Source : Primary research data , 2025

Measurement Serum zinc levels indicate variation significant between phase clinical SN. Average zinc levels in the group attack First recorded of  $64.5 \pm 8.2$   $\mu\text{g/dL}$ , with part big patient Still is at in lower normal range (60–70  $\mu\text{g/dL}$ ). In the group relapse , mean zinc levels decreased significant to  $52.3 \pm 7.6$   $\mu\text{g/dL}$ , with 75% of patients (15 of 20) being below normal threshold (<60  $\mu\text{g/dL}$ ), which is clinical categorized as zinc deficiency . On the other hand , in the phase remission ,

(66.7%) compared to 20 women (33.3%). The ratio This in line with findings other epidemiological studies that confirm that syndrome nephrotic idiopathic more often found in men , especially at the age of preschool (Wang et al., 2021). Differences This possibility related with factor genetic and hormonal factors that contribute to vulnerability man in experience dysfunction podocytes , so that make things easier the occurrence of persistent proteinuria (Chanchlani & Parekh, 2019).

In terms of nutritional status , the majority patient have normal nutritional status to good , because patient with nutrition bad in a way explicit issued from study This in accordance with criteria exclusion . This is it is important that the factors malnutrition No become variables confounders that can influence serum zinc levels . Research previously show that malnutrition can reduce zinc intake and absorption so that influential directly on plasma zinc levels (Prasad, 2013). With Thus , research This isolate influence factor journey SN disease on zinc status, without overshadowed effect nutrition bad .

average zinc levels increased to  $72.1 \pm 9.4$   $\mu\text{g/dL}$ , with part patient even show above levels mark group attack First . The results of the ANOVA test show existence difference meaningful between third group ( $p < 0.05$ ).

Analysis correlation more carry on show connection significant positive between serum zinc and albumin levels , with coefficient correlation  $r = 0.48$  ( $p < 0.01$ ). The average albumin level in the control group relapse is  $2.3 \pm 0.5$  g/dL, at attack first  $2.8 \pm 0.6$  g/dL, and in



remission increase up to  $3.8 \pm 0.7$  g/dL. Connection This logical because albumin is the main plasma protein that functions as a zinc transporter (King, 2011). Significant loss of albumin through proteinuria causes decrease capacity zinc binding in blood (Jia et al., 2020). In other words, hypoalbuminemia which is characteristics typical SN in general direct make things worse zinc deficiency .

In addition , there are correlation negative between zinc levels and proteinuria with  $r$  value =  $-0.52$  ( $p < 0.01$ ). Average 24-hour proteinuria in the acute phase relapse reached  $4.8 \pm 1.1$  g/ day , far more tall compared to attack first ( $3.9 \pm 0.9$  g/ day ) and remission ( $0.8 \pm 0.3$  g/ day ). The relationship negative This support theory that glomerular damage in SN causes trace element leakage through urine , including zinc (Al- Mekhlafi et al., 2021). Phenomenon this is also consistent with Bains et al.'s (2020) study which reported that patient with massive proteinuria experience lost significant several important trace elements , including zinc, copper , and selenium.

Implications clinical from findings This Enough important . First , low zinc levels in the phase relapse show potential of zinc as a biomarker of travel disease . Second , the relationship between zinc and albumin and proteinuria shows that zinc is not only indicator of nutritional status , but also a reflection from degrees damage kidneys . Third , intervention in the form of zinc supplementation can considered in children with SN, especially in the phase relapse . Mahmoud et al.'s (2019) research reported that zinc supplementation in children with minimal change nephrotic syndrome (MCD) can lower frequency relapse , although results studies multicenter Still show variation effectiveness .

In a way Overall , serum zinc levels were the lowest found in the phase relapse , increase back to phase remission , and is at a value intermediate in phase attack first . Relationship positive zinc with albumin and connection negative with proteinuria strengthens the role of zinc as a potential biomarker journey clinical syndrome nephrotic . Difference between group significant in a way statistics ( $p < 0.05$ ), so that can become base For study advanced about intervention micronutrients in children with syndrome nephrotic .

## 5. Discussion

Zinc is a trace element that has role important in various function biological , including growth , development

system immune , as well as protein and enzyme metabolism . In the context of syndrome nephrotic syndrome (SN) in children , research This confirm that zinc plays a role No only as nutrients usual , but as a potential biomarker in monitor journey disease . Research results show that lowest serum zinc levels found in the phase relapse , increasing in phase remission , and is at a value intermediate in phase attack first . This pattern consistent with study previously reported that child with SN experiencing fluctuations zinc levels along with change in clinical status disease (Hameed et al., 2019; Taherahmadi et al., 2019). Phenomenon the strengthen suspicion that zinc deficiency is not just consequence from dietary variation or nutritional status , but rather related direct with mechanism pathophysiology of SN.

Mechanism main zinc deficiency in children with SN can explained through two interconnected paths related . First , massive proteinuria that occurs in the acute phase active SN causes loss of protein in amount big through urine . Because some large zinc content in blood bound with albumin, then zinc is involved wasted with proteinuria. Biochemical studies show that more of 60% of zinc in plasma is bound with albumin, while the rest bound with  $\alpha$ -2-macroglobulin and transferrin (Hambidge & Krebs, 2007). With thus , the more the severity of proteinuria, the more there is also a large loss of zinc through urine . Second , the condition common hypoalbuminemia occurs in SN lowers zinc transport capacity in circulation blood . Low albumin means ability body For maintaining zinc homeostasis is reduced , so that serum zinc levels tend to low (Prasad, 2013). Second mechanism This walk in a way simultaneous and explanatory why in phase relapse , in which proteinuria and hypoalbuminemia reach At its peak , serum zinc levels become very low .

Connection between zinc deficiency with immunity also does not can neglected . Zinc is known play a role important in proliferation and differentiation T cells , especially T-helper 1 (Th1) cells , which regulate response immune mobile to infection . Zinc deficiency will lower production cytokines important such as IL-2 and IFN- $\gamma$ , so that Th1/Th2 balance is disturbed and the patient more prone to to infection ( Santín et al., 2011; Sherali et al., 2014). Condition This implications big on SN, because infections , especially infection channel breathing upper and gastrointestinal, is one of the



originator main relapse . A meta- analysis by Aggarwal et al. (2017) reported that zinc supplementation in children age early can lower incident infection breathing up to 30%. This is show that in SN patients , zinc supplementation may be No only improve nutritional status , but also has the potential reduce risk relapse triggered by infection .

Findings correlation positive between albumin and zinc levels in study this also confirms importance consider protein status in the management of SN. Albumin is not only nutritional status indicators or determinant pressure oncotic , but also the main protein that functions as a zinc transporter. Clinical studies by King et al. (2018) showed that patient with hypoalbuminemia chronic experience decline significant zinc concentration compared to group with normal albumin levels . This is relevant in context of SN, where hypoalbuminemia No only consequence from protein leakage , but also aggravating factors zinc deficiency . Therefore that , intervention therapeutic should No only focuses on controlling proteinuria with corticosteroids or immunosuppressants , but also consider intervention specific nutrients , such as zinc supplementation .

Besides the relationship with albumin, research this also found correlation significant negative between zinc levels and proteinuria. The more tall the level of proteinuria, the more low measured serum zinc levels . This support theory that SN does not only cause loss of protein but also other important trace elements through urine . A study by Ghio et al. (2021) reported that patient with chronic proteinuria experience improvement excretion of zinc, magnesium, and copper , which results in decreased micronutrient status . This loss of trace elements potential make things worse journey clinical , lowering function immunity , and improve risk complications metabolic . With Thus , proteinuria must be understood No only as marker glomerular damage , but also as indicator lost nutrients important implications for clinical status patient .

When compared with study international others , results study This in line with report Fathah et al. (2022) who found that zinc levels in children with more SN low on phase active compared to with phase remission . Hameed et al. (2019) also showed that child with relapse often own lowest zinc content compared to with relapse rare and group control healthy . In fact , research intervention

by Mahmud et al. (2020) shows that zinc supplementation in children with steroid - sensitive SN significant lower number relapse and increase in the length of the period remission . However , no all study show results similar . For example , the study by Kaur et al. (2016) did not find connection meaningful between zinc levels and numbers SN relapse . Difference This possibility caused by variations design research , methods zinc examination (serum vs plasma), characteristics population , as well as factor confounding factor like dietary intake and nutritional status .

Implications clinical from findings This Enough wide . First , zinc can considered as an additional biomarker in monitoring journey clinical SN. Measurement serum zinc levels , together with albumin and proteinuria, can help clinician in assess disease status and risk relapse . Second , zinc supplementation can made into part from the implementation comprehensive SN, especially in patients with history relapse repeated . Several clinical trials random has show that zinc supplementation in dose 10–20 mg/ day for 6 months can lower frequency relapse up to 40% (Mahmud et al., 2020). Third , the findings This emphasize importance approach nutrition in the management of SN. In addition to therapy pharmacological , intervention nutrition must become an integral part of management patients , especially in the population children where the needs nutrition For very high growth .

Even though Thus , research This own limitations . The cross-sectional design used No allows researchers For evaluate connection causality longitudinally . With only involving 20 patients per group , generalization results to larger population wide need done with be careful . In addition , research This No assess the status of other micronutrients such as copper , selenium, or magnesium, which are also known play a role in system immunity and function kidneys . Variations in diet and zinc intake from food also not analyzed in a way detailed , even though factor the can influence serum zinc levels . Therefore that , research advanced with design prospective , number more samples big , and analysis nutrition comprehensive is very necessary For strengthen findings This .

Recommendation study furthermore is the need for clinical trials random controlled that evaluates effectiveness zinc supplementation in lower number relapse in children with SN. Longitudinal research can



also give description more clear about dynamics zinc levels throughout journey diseases , including response to therapy pharmacological and non- pharmacological . In addition , integration multi- element analysis , such as zinc , copper , selenium , and magnesium , can help understand interaction complex micronutrients in pathogenesis and course of SN.

In a way overall , discussion This confirm that zinc has role central in journey clinical SN in children . With Zinc levels are lowest in phase relapse , increasing in phase remission , as well as correlated positive with albumin and negative with proteinuria , zinc has been shown to be as a potential biomarker in monitor disease . Implications clinically very relevant , both for diagnosis , monitoring , and management . Research more carry on Still required For confirm effectiveness zinc supplementation as a preventive strategy relapse , however existing findings Already Enough strong For push integration aspect nutrition in SN handling . With Thus , zinc is not only nutrients , but also parts from a comprehensive strategy in increase quality life child with syndrome nephrotic .

## 6. Conclusion

Study This done For analyze zinc , albumin , and proteinuria levels in children with syndrome nephrotic in three phase clinical , namely attack first , remission , and relapse , with involving 60 children as respondents . Research results show existence difference significant zinc levels in all three phase said , with level lowest found in the phase relapse and increase back to phase remission until approach normal values , which means zinc has the potential made into as a biomarker of travel disease . Apart from that , there are connection positive between zinc and albumin levels , which indicate that low albumin levels in syndrome nephrotic No only affect the status of plasma proteins , but also reduce capacity zinc transport in circulation so that make things worse condition deficiency . On the other hand , it was found correlation negative between zinc levels and proteinuria , where the more the severity of proteinuria , the more low measured serum zinc levels , a phenomenon that can explained through mechanism zinc loss due to excretion urine in amount increase and decrease zinc binding to albumin under conditions hypoalbuminemia . Findings This confirm that syndrome nephrotic is condition systemic that is not only related with disturbance filtration kidneys , but also has implications for the

balance nutrition micronutrients , especially zinc , which plays a very important role in guard Power stand body children . Zinc deficiency in patients syndrome nephrotic proven influential to increasing vulnerability to infection and high number relapse , so that make things worse quality life patient as well as add burden care . With Thus , monitoring zinc levels should be entered in evaluation routine patient clinical child with syndrome nephrotic , especially in the phase active disease , while zinc supplementation can considered as an additional strategy in governance comprehensive For repair function immune , lowering frequency relapse , and improve prognosis . Although study This give description important about there is a relationship between zinc , albumin and proteinuria limitations in the form of design cut latitude that is not allows withdrawal causality in a way direct , amount relative sample limited , and Not yet analyzed other possible micronutrients play a role . Therefore that , research advanced with longitudinal design , number more samples big , and approach more nutrition comprehensive is very much needed For strengthen proof scientifically . overall , research This confirm that zinc levels , albumin , and proteinuria are interrelated related close in journey clinical syndrome nephrotic in children , with zinc deficiency is dominant in the phase relapse , so that integration zinc monitoring and intervention nutrition can become part important from effort management disease this is in the future .

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