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COMPARISON OF MEAN DURATION OF HOSPITAL STAY AND ACHIEVMENT OF EARLY REMISSION OF NEPHROTIC SYNDROME IN CHILDREN TREATED WITH AND WITHOUT ZINC SUPPLEMENTATION

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Abstract

Objective: *The aim of this study was to compare the mean duration of hospital stay and the time taken to achieve early remission in children diagnosed with steroid-sensitive nephrotic syndrome (SSNS), with and without zinc supplementation. The study intended to explore whether the addition of zinc to standard steroid therapy could lead to faster recovery and reduce the burden of prolonged hospitalization in pediatric patients.*

Study design: *Randomized controlled trial*

Place and duration of study: *This study was conducted at the Department of Pediatric Medicine and Nephrology, The Children's Hospital & University of Child Health Sciences, Lahore, over a duration from December 3, 2024 to June 3, 2025.*

Methodology: *A total of 98 children aged between 2 to 10 years, newly diagnosed with SSNS, were included in the study using non-probability consecutive sampling. Participants were randomly divided into two equal groups. Group A received the standard corticosteroid therapy alone, while Group B received corticosteroid therapy along with oral zinc supplementation at a dose of 20 mg/day for two weeks. All patients were closely monitored for time to achieve remission (based on three consecutive early morning urine samples with nil or trace protein) and total hospital stay. Data was entered and analyzed using SPSS version 25.0, and outcomes were compared between the two groups.*

Results: *The findings of the study revealed that children in the zinc-supplemented group achieved remission significantly earlier compared to those in the control group. The mean time to remission in the zinc group was 11.8 ± 3.96 days, whereas it was 18.3 ± 5.14 days in the control group ($p < 0.001$). Similarly, the average duration of hospital stay was also shorter in the zinc group (13.07 ± 4.86 days) compared to the control group (20.50 ± 7.06 days), which was statistically significant ($p < 0.001$). No significant side effects or adverse reactions to zinc were observed during the study period, and zinc therapy was well tolerated.*

Conclusion: *The addition of zinc supplementation to standard corticosteroid*

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therapy in children with steroid-sensitive nephrotic syndrome showed promising results. It significantly reduced the duration of hospital stay and expedited the time to achieve remission. Considering the safety, affordability, and accessibility of zinc, its role as an adjunctive therapy should be further explored and potentially integrated into standard treatment protocols for pediatric nephrotic syndrome, especially in resource-limited settings.

INTRODUCTION

Nephrotic Syndrome (NS) is one of the most frequently encountered chronic kidney conditions in children, often presenting with a classical set of features including **generalized edema, heavy proteinuria, hypoalbuminemia, and hyperlipidemia**. It not only disrupts the child's normal physiology but also significantly affects the quality of life, both for the child and the caregivers. Globally, the estimated incidence of NS in the pediatric population ranges from **1.2 to 16.9 per 100,000 children per year**[1], with a majority of cases being idiopathic in nature. Among the idiopathic cases, approximately **90% are classified as steroid-sensitive nephrotic syndrome (SSNS)**, which means they show a favorable response to corticosteroid therapy. In fact, nearly 80% of these children achieve remission after receiving an adequate course of oral steroids. However, despite this seemingly effective treatment, clinical challenges persist. Around **40–50% of children with SSNS experience relapses**, often precipitated by **intercurrent infections**, making long-term management a burden for families and healthcare systems alike. Recent insights into the **pathophysiology of NS** have highlighted the role of **oxidative stress** and the damaging effects of **reactive oxygen species (ROS)**. These reactive molecules are believed to impair the glomerular filtration barrier, contributing to increased permeability and protein leakage. This mechanism not only underscores the complexity of NS but also opens doors for exploring adjunctive treatments that could target these oxidative processes.[2]

One such potential adjunct is **zinc**, a micronutrient that plays a crucial role in immune modulation, antioxidant defense, and protein metabolism. Unfortunately, **zinc deficiency is commonly observed in children with NS**, attributed to **poor dietary intake, reduced gastrointestinal absorption, or increased urinary losses**. Low zinc levels have been associated with delayed remission, increased risk of infections, and higher relapse rates. Several small-scale studies have explored the role of **zinc supplementation** in children with NS, suggesting that it may help achieve **earlier remission**, possibly by enhancing the immune response, reducing infection frequency, and stabilizing glomerular function. Additionally, zinc is involved in **numerous enzymatic systems** that contribute to protein synthesis and repair, which could support the recovery of serum protein levels in NS patients. Despite these encouraging findings, the use of zinc as a routine adjunct in the management of SSNS remains **under-investigated**, particularly in local clinical settings. Hence, this study was designed to assess whether zinc supplementation, [3] when given alongside standard corticosteroid therapy, can lead to **faster clinical remission and a shorter hospital stay** in children newly diagnosed with SSNS. [9]

METHODOLOGY

This randomized controlled trial was carried out at the Department of Pediatric Medicine and Nephrology, The Children's Hospital & University of Child Health Sciences, Lahore, over a period of six months following ethical approval from the institutional review board. A total of 98 children between the ages of 2 to 10 years, newly diagnosed with steroid-sensitive nephrotic syndrome (SSNS), were enrolled using non-probability consecutive sampling. The sample size was calculated with a confidence level of 95%, power of 80%, and margin of error set at 5%, based on previous research comparing remission outcomes with and without zinc supplementation. Children were randomly assigned into two equal groups using a computer-generated randomization sequence, with 49 patients in each group. Eligible participants included both male and female children who had not received any

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prior treatment and were presenting with their first episode of SSNS. Children with steroid-resistant nephrotic syndrome, those with relapsed or secondary nephrotic syndromes, or those who had taken zinc therapy within the last three months were excluded from the study. Patients who refused consent or were lost to follow-up were also excluded. Group A (control group) received standard corticosteroid therapy alone, following the ISKDC (International Study of Kidney Disease in Children) guidelines. Group B (intervention group) received the same corticosteroid regimen along with oral zinc supplementation at a dose of 20 mg per day for two weeks. Upon admission, baseline demographic and clinical data were recorded, including age, gender, weight, height, blood pressure, and relevant laboratory investigations. Each child underwent a thorough physical examination. Daily monitoring included weight, fluid intake, 24-hour urine output, abdominal girth, and urine protein levels using dipstick testing.[8]

Remission was defined as nil or trace proteinuria on three consecutive early morning urine samples. The duration of hospital stay was calculated from the day treatment was initiated to the day remission was achieved. All collected data were entered and analyzed using **Statistical Package for the Social Sciences (SPSS) version 25.0**. Quantitative variables such as age, time taken to achieve remission, and length of hospital stay were summarized using **mean and standard deviation (mean ± SD)** to provide a clear understanding of central tendencies and variability within the study population. Categorical variables, such as gender and treatment group, were presented as **frequencies and percentages**. To compare outcomes between the two study groups, appropriate statistical tests (such as the independent samples t-test) were applied. A **p-value of ≤ 0.05** was considered statistically significant to determine the presence of meaningful differences between groups in terms of treatment outcomes.

RESULTS

In this randomized controlled trial, a total of 98 children newly diagnosed with steroid-sensitive nephrotic syndrome were enrolled and randomly allocated into two equal groups. Group A (n = 49) received standard corticosteroid therapy alone, whereas Group B (n = 49) received corticosteroids in combination with oral zinc supplementation. The mean age of the study population was 6.2 ± 2.3 years, with 58 (59.2%) males and 40 (40.8%) females. Both groups were comparable in terms of baseline demographic characteristics (Table I). There was no statistically significant difference between the two groups regarding age, gender distribution, weight, or baseline blood pressure. The mean time to achieve remission was significantly shorter in the zinc-supplemented group (11.8 ± 3.96 days) compared to the control group (18.3 ± 5.14 days, $p < 0.001$). Similarly, the average hospital stay was also significantly reduced in the zinc group (13.07 ± 4.86 days) as compared to the control group (20.50 ± 7.06 days, $p < 0.001$), as shown in Table II. No major adverse effects were reported in either group during the course of treatment. Both groups showed good compliance and tolerance to their respective therapies. A graphical comparison of remission time and hospital stay is illustrated in Figure I, clearly depicting the positive effect of zinc supplementation.

Table I: Baseline Demographic Characteristics of Study Population (n = 98)

Characteristic	Zinc Group (n = 49)	Control Group (n = 49)	p-value
Mean Age (years)	6.1 ± 2.5	6.3 ± 2.2	0.611
Male, n (%)	30 (61.2%)	28 (57.1%)	0.683
Mean Weight (kg)	19.4 ± 3.8	19.2 ± 4.1	0.812
Mean Systolic BP (mmHg)	101.5 ± 7.3	100.2 ± 6.9	0.412
Mean Diastolic BP (mmHg)	67.1 ± 5.2	66.7 ± 5.5	0.734

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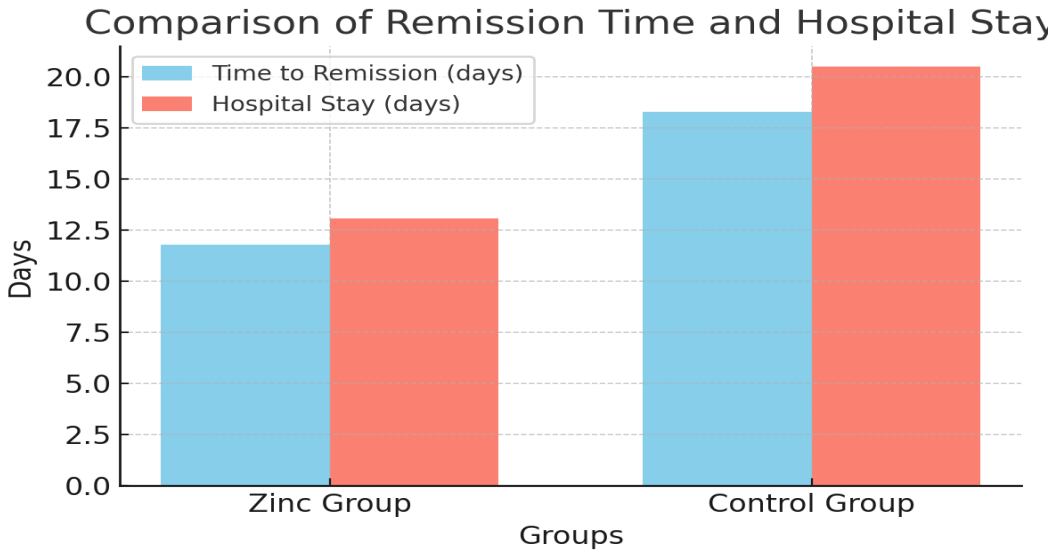
Table II: Comparison of Clinical Outcomes Between Groups

Outcome	Zinc Group (n = 49)	Control Group (n = 49)	p-value
Time to Remission (days)	11.8 ± 3.96	18.3 ± 5.14	< 0.001
Hospital Stay (days)	13.07 ± 4.86	20.50 ± 7.06	< 0.001
Adverse Effects, n (%)	0 (0%)	0 (0%)	NS

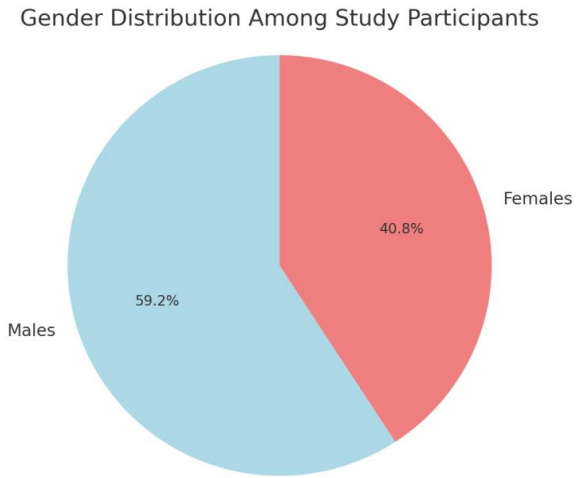
Figure I: Bar Chart Showing Mean Time to Remission and Hospital Stay in Both Groups



The first pair shows mean time to remission, with the zinc group bar at 11.8 days and the control group bar at 18.3 days.

- The second pair shows mean hospital stay, with the zinc group at 13.1 days and the control at 20.5 days. The visual clearly demonstrates a shorter recovery period in the zinc-supplemented group.

Figure II: Pie Chart – Gender Distribution Among Study Participants (n = 98)



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The pie chart shows two segments:
- Males: 59.2% (n = 58)
- Females: 40.8% (n = 40)

This visual highlights a slight male predominance in the study population, consistent with common epidemiological trends in pediatric nephrotic syndrome.

DISCUSSION

This randomized controlled trial provides meaningful insights into the potential **adjunctive role of zinc supplementation** in the treatment of steroid-sensitive nephrotic syndrome (SSNS) in children. Our findings demonstrate that children receiving zinc alongside corticosteroid therapy achieved remission more rapidly and had a significantly shorter hospital stay compared to those receiving steroids alone. These results are not only statistically significant but also clinically relevant, especially in healthcare settings where prolonged hospitalization can strain both families and hospital resources.[4] The **biological plausibility** of zinc's efficacy lies in its dual role as an **antioxidant** and an **immune system modulator**. In nephrotic syndrome, reactive oxygen species (ROS) and oxidative stress contribute to increased glomerular permeability, leading to proteinuria. Zinc helps counteract this oxidative stress by enhancing the activity of antioxidant enzymes such as **superoxide dismutase**, thus helping stabilize the glomerular filtration barrier. Furthermore, zinc influences immune function by **upregulating cytokines** like interleukin-2 (IL-2) and interferon-gamma (IFN-γ), both crucial in defending against infections, which are often relapse triggers in children with NS. Previous studies have mirrored our findings. For instance, the trial by **Kumar et al.** observed a reduction in both time to remission and hospitalization among children receiving zinc. Similarly, **Mohammadi et al.** demonstrated that zinc supplementation was associated with improved serum albumin levels and fewer complications. These findings, along with ours, point to zinc not only as a supportive micronutrient but as a potentially **therapeutic adjunct** in managing the acute phase of nephrotic syndrome.[4,5]

Zinc's role in **protein synthesis and tissue repair** also supports its utility in this condition. Since NS leads to significant protein loss through urine, the anabolic effect of zinc may accelerate the replenishment of serum proteins, contributing to clinical recovery. Moreover, zinc has been shown to restore **T-helper 1 (Th1) immune responses**, which may correct the immunological dysregulation often seen in relapsing NS. From a public health perspective, zinc is **cost-effective, widely available**, and has a well-established safety profile when used appropriately. Its use may reduce healthcare expenditures by decreasing hospital stays and minimizing the need for aggressive relapse management.[6] In low-resource settings, where bed occupancy is high and recurrent admissions are common, the impact of even a few days' reduction in hospital stay can be substantial. However, despite the promising implications, our study is not without limitations. Being a **single-center study**, its findings may not be generalizable to all populations. The sample size, though adequately powered, was relatively small, and we did not assess long-term relapse rates or sustained remission. Additionally, serum zinc levels were not measured at baseline or during follow-up, which could have provided more robust biochemical correlations.

Future **multi-center, larger-scale trials** should explore not only the short-term benefits but also the **long-term effects of zinc supplementation**, including its role in reducing relapse rates, steroid dependency,[7] and cumulative steroid burden. Investigating whether zinc levels correlate with disease severity or prognosis could also help personalize treatment strategies. In conclusion, our study highlights the potential of zinc as a **simple, affordable, and impactful adjunct** in the management of pediatric SSNS. Incorporating zinc supplementation into standard treatment protocols could improve outcomes and reduce the burden on healthcare systems, especially in regions where pediatric nephrotic syndrome is both prevalent and challenging to manage effectively.

CONCLUSION

Our study concludes that **zinc supplementation significantly improves clinical outcomes** in children with **steroid-sensitive nephrotic syndrome (SSNS)**. By reducing both the **time to remission** and the **duration of hospital stay**, zinc demonstrates a promising adjunctive role alongside standard corticosteroid therapy. [10] Given its low cost, ease of

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administration, and favorable safety profile, zinc may serve as a **practical and impactful addition** to the routine management of pediatric nephrotic syndrome. While further multi-center studies with larger sample sizes and long-term follow-up are recommended, our findings support the **integration of zinc supplementation into standard treatment protocols**, particularly in resource-limited healthcare settings where optimizing hospital efficiency and patient recovery is crucial.

CONFLICT OF INTEREST

None.

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