

## THE ASSOCIATION BETWEEN STUNTING AND CALCIUM INTAKE IN CHILDREN WITH NEPHROTIC SYNDROME

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### ABSTRACT

**Aims:** To determine the association between stunting and calcium intake in children with nephrotic syndrome.

**Methods:** A cross-sectional study was conducted on 53 pediatric patients diagnosed with nephrotic syndrome at the Department of Nephrology - Endocrinology, Children Hospital No.2, from April 25 to June 26, 2022. Stunting and height faltering were classified according to the height-for-age and sex standards of World Health Organization. Calcium intake from the diet and medications was collected through dietary logs, prescription reviews, and calculated using the Eiyokun software, based on the Vietnamese food composition table and the recommended calcium intake by the Vietnamese National Institute of Nutrition. Other data such as blood albumin levels, disease duration, and corticosteroid resistance status were collected from inpatient and outpatient treatment records.

**Results:** The prevalences of moderate stunting and severe stunting were 20.8% and 13.2%, respectively. The rate of height faltering was 30.2%. Fulfillment of the recommended daily calcium intake was 50.1% from diet alone and 75.5% after supplementation with medications. There was a significant association between stunting and calcium intake from diet at level >50% of the requirement (OR=0.28,  $p=0.001$ ).

**Conclusion:** Stunting and height faltering were commonly observed in children with nephrotic syndrome at Children Hospital No.2. Those with calcium intake exceeding 50% of the daily requirement had a lower prevalence of stunting. It is essential to educate and counsel both the family and the children on appropriate nutrition, emphasizing the importance of adequate calcium intake from daily dietary sources.

**Keywords:** *nephrotic syndrome, stunting, height faltering, calcium intake*

### I. INTRODUCTION

Children with nephrotic syndrome (NS) undergoing long-term treatment with medication and dietary disturbance are at risk of impaired height growth, and stunting; and malnutrition adversely affect the treatment prognosis of NS in children. Long-term use of corticosteroids can lead to numerous side effects, such as bone decalcification due to urinary calcium and phosphorus

leakage; statural growth retardation due to growth factor inhibition; osteonecrosis due to demineralisation; hypothyroidism due to decreased thyroid secretion and muscle atrophy. Children with NS are prone to both macro and micronutrient deficiency and are at risk of poor growth, muscle mass depletion and cognitive impairment.

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There are few works on assessing the nutritional status of children with nephrotic syndrome, especially stunting in the world [1–4]. But, there has been limited research relating stunting in pediatric NS patients in Vietnam. Children Hospital No.2 (CH2), is one of tertiary pediatric hospital in the South of Vietnam, which provides hemo-dialysis and kidney transplantation, manages many pediatric patients with severe nephrotic syndrome. It is essential to have strategies to ensure the most effective treatment, including the prevention and treatment of malnutrition,

especially in preventing stunting and height faltering. Therefore, we conducted this study to determine the prevalence of stunting, height faltering and calcium intake level from diet and medication, and the relationship between stunting and calcium intake in pediatric NS patients under treatment at the Nephrology-Endocrinology Department of CH2. This study aims to serve as a foundation for developing more appropriate nutritional guidelines to improve the stunted status in children with NS.

## II. METHODS

### 2.1. Study design and subjects

The cross-sectional study was conducted from April 25 to June 26, 2022. The study subjects were children with NS treated at the Nephrology - Endocrinology Department of Children Hospital Number No.2.

**Inclusion criteria:** All children with NS treated at the Nephrology-Endocrinology Department of CH2

whose families agreed to participate in the study and signed the informed consent form.

**Exclusion criteria:** Children with spinal deformities, bone deformities, or those whose height cannot be measured or being in severe underlying conditions (heart disease, liver diseases, or hematologic malignancies...)

### 2.2. Sample size and sampling method

\* Sample size was calculated using the formula for estimating a single proportion.

$$n = \frac{Z_{1-\alpha/2}^2 p(1-p)}{d^2}$$

$\alpha=0.05$ : type I error;  $Z_{(1-\alpha/2)}=1.96$ ,  $p=0.1475$ : the stunting prevalence in children with NS according to the study by Solari et al.) [5];  $d=0,10$ : margin of error. The sample size was calculated,  $n=49$ . The total of 53 patients of NS were recruited for the study.

### 2.3. Data collection and processing

The child's guardian was directly interviewed using a research questionnaire. To measure the length of children less than 2 years, a measuring board with a headboard and sliding foot

piece was used and for children 2 years and above, height was measured using an stadiometer, with an accuracy of 0.1 cm. Stunting and height faltering were compared to the WHO growth reference

among children aged under 5 years [6] and children aged 5-19 years [7]. Calcium intake from the diet by 24h recall method and medications was collected through dietary logs, prescription reviews, and calculated using the Eiyokun software, based on the Vietnamese food composition table and

## 2.4. Variables and indicators

Categorical data were shown as frequency (%). Continuous data were reported as mean and standard deviation with a normal distribution or median and interquartile range with a non-normal distribution.

The height-for-age Z-score (HAZ) was calculated. The child was classified as moderate stunting and severe stunting, respectively, when HAZ below 2 SD and

## 2.5. Data analysis

Data were entered using EpiDATA 3.1 and Eiyokun software. Statistical analysis was performed using Stata 16.0 software.

Chi-square test or Fisher's exact test was used to examine the relationship

## 2.6. Ethical Considerations

The study protocol was approved by the Ethics Committee in Biomedical Research of Children's Hospital No. 2, approval number 409/GCN-BVND 2, dated May 31, 2022.

The research did not interfere with the treatment process of the patients. The child's guardians were informed about

the recommended calcium intake by the Vietnamese National Institute of Nutrition. Other data such as blood albumin levels, disease duration, and corticosteroid resistance status... were collected from inpatient and outpatient treatment records.

3 SD from the WHO Child Growth Standards median. The height faltering was identified when  $-2SD \leq HAZ < -1SD$  and not stunted when  $HAZ \geq -1SD$  [6, 7].

Independent variables included calcium intake from diet (mg), calcium intake from diet and medication (mg), percentage of calcium requirement intaken(%).

between the level of calcium intake and stunting ratio. The relationship was estimated and presented as prevalence ratio (PR) with 95% confidence interval (95%CI). A *p*-value under 0.05 was considered significant.

the purpose and procedures of the study and were notified about the benefits, risks, and disadvantages of participating in the research. Patient identifying information was coded and kept completely confidential. The data was used solely for research purposes.

## III. RESULTS

Of the total 53 children recruited in the study, 37 boys accounted for 69.8%. The rates of children in age group < 1, 1-5 ,

6-10 , and > 10 years, respectively were 1.9, 20.8, 35.8, and 41.5 %.

**Table 1.** Characteristics of diseases in the study population (n=53)

Characteristics	Frequency	Percentage
Edema (current)	41	77.4
Hypertension	8	15.1
Corticosteroid-resistant diagnosis	21	39.6
Renal failure	2	3.8
Serum albumin		
Normal	17	32.1
Hypoalbuminemia	36	67.9
Number of hospital admissions since diagnosis of nephrotic syndrome (times)	3 (2 – 6)*	
=< 2 times	24	45.3
>2 times	29	54.7
Duration of illness (months)	33 (13 – 63)*	
=< 2 years	22	41.5
>2 years	31	58.5

\* Median (interquartile range)

Table 1 shows that the proportion of children currently with edema was 77.4%. Most children did not have hypertension. The proportion of children diagnosed with corticosteroid resistance was 39.6%, accounting for one-third of the total patients. Most children did not have renal failure. A total of 67.9% of children had serum albumin levels below normal. The median number of hospital admissions since being diagnosed with

NS was 3 times, with an interquartile range of 2 – 6 times. The proportion of children with 0-2 hospital admissions since being diagnosed with NS was 45.3%, and over 2 times was 54.7%. The median duration of illness was 33 months, with an interquartile range of 13 – 63 months. The proportion of children with a disease duration of up to 2 years was 41.5%, and over 2 years was 58.5%.

**Table 2.** Stunting prevalence in children with nephrotic syndrome (n=53)

Characteristics	Frequency	Rate (%)
No stunting (HAZ> -1SD)	19	35.8
Height faltering (-2SD ≤ HAZ< -1SD)	16	30.2
Moderate stunting (-3SD ≤ HAZ< -2SD)	11	20.8
Severe stunting (HAZ< -3SD)	7	13.2

Table 2 shows that 64.2% of children had height problems, with height faltering accounting for 30.2%, moderate stunting for 20.8%, and severe stunting for 13.2%. The elemental calcium

amount was calculated from dietary intake surveys and recorded calcium supplements used at the time of the study (Table 3).

**Table 3.** Daily calcium intake in children with nephrotic syndrome (n=53)

Characteristics	Value	Min	Max
Average daily calcium intake from diet (mg)	828 (639 – 970)*	127	2286
Calcium from supplements (mg)	300 (150 – 500)*	0	1800
No supplementation	4 (7.6 %)		
With supplementation	49 (92.5%)		
Total calcium from diet and supplements (mg)	1128 (885 – 1394)*	277	2757

Data are in n (%), except for \* Median (interquantil range)

**Table 4.** Relationship between stunting and calcium intake in children with nephrotic syndrome (n=53)

Characteristics	Stunting n = 18	No stunting n = 35	p-value	Prevalence ratio (95%CI)
Enough calcium intake from diet, n (%)				
Yes	6 (23.1)	20 (76.9)	0.101	0.52 (0.24 – 1.14)
No	12 (44.4)	15 (55.6)		1.0
Enough calcium intake from diet and supplements, n (%)				
Yes	11 (27.5)	29 (72.5)	0.081*	0.51 (0.24 – 1.10)
No	7 (53.8)	6 (46.2)		1.0
Intake >50% of calcium daily requirement from diet, n (%)				
Yes	11 (24.4)	34 (75.6)	0.001	0.28 (0.14 – 0.58)
No	7 (87.5)	1 (12.5)		1.0
Intake >50% of calcium daily requirement from diet and supplements, n (%)				
Yes	16 (32.0)	34 (68.0)	0.263*	0.48 (0.15 – 1.56)
No	2 (66.7)	1 (33.3)		1.0

p-value by Chisquare test, except for \*p-value by Fisher's exact test

The provision of calcium from diet and supplements was associated to the rate of stunting in children with NS. Notably, meeting more than 50% of calcium daily requirement from the diet showed a strong association with stunting in children with NS. Total patient with inadequate calcium intake from diet was 27 (50.1%) and adequate calcium intake was 26 (49.1%). Total patient with inadequate calcium intake

from diet and supplements was 13 (24.5%) and adequate calcium intake was 40 (75.5%).

From the 24-hour dietary survey of the pediatric patients, we observed that the meal composition and the balance of food groups were of lower quality in stunted children compared to non-stunted children. Children who did not receive enough calcium from their diet had a higher rate of stunting (44.4%)

compared to children who receive adequate calcium (23.1%).

The frequency of consumption of calcium-rich food groups, including milk, dairy products, calcium-rich seafood, and the variety and quality of meals, differed between the two groups. Stunted children consumed milk less frequently, only about 1 to 2 small cartons (110ml) per day or none at all, compared to non-

stunted children who typically consumed 3-4 larger cartons (180 ml) per day. For stunted children, the calcium-rich seafood/animal choice was often shrimp, but the frequency per week was low, and the amount consumed was small (only about 1-2 pieces per meal). In contrast, non-stunted children had a more diverse diet that included various fish types.

## IV. DISCUSSION

### 4.1. Characteristics of the study population

The average age of children in the study was  $8.89 \pm 3.85$  years, similar to the study by Vu Thi Chi et al. [1], conducted on 52 children treated at Bac Ninh Maternity and Children's Hospital with an average age of 6.75 years, and in the study of Ndongo et al. [2] with an average age of 8 years and the results of Solarin et al. [5] conducted on 61 pediatric patients at the nephrology clinic of Lagos State University Hospital, Ikeja, showed an average age of  $6.73 \pm 3.52$  years.

The rate of NS was higher in boys than in girls. In this study, boys accounted for 69.81% (male/female ratio was 2.31/1). In the study by Vu Thi Chi et al., the male/female ratio was 2.05/1 (with 17 females and 35 males), Ndongo with ratio 1.6 and the study by Solarin (2018) reported a ratio of 2.05/1 (with 41 boys and 20 girls) [1, 2, 5]. The high rates of edema, hypoalbuminemia, recurrent NS, and corticosteroid resistance were due to our hospital being a tertiary pediatric hospital, thus receiving more severe cases.

### 4.2. Stunting rate in children with nephrotic syndrome hospitalized at CH2

Children with NS were prone to deficiencies in both micronutrients and macronutrients, leading to poor growth, muscle mass loss, and stunting. Short stature occurred due to the disease process, poor diet, steroid therapy, which contribute to increased morbidity and mortality in children with NS. In our study, the stunting prevalence was 34%, and height faltering accounted for 30.2%. That means 66% of children with NS having height problems. That the stunting rate was 14.75% in the study of Solarin et al. [5], was lower than that in our study as our subjects were mainly

hospitalized patients, with many cases of relapse or complications, making them more severe than outpatient children. This could be explained by racial characteristics of Asians compared to Europeans, Africans, and Americans, along with dietary differences. Asians typically did not consume calcium-rich products like milk and dairy products as part of their diet, leading to calcium deficiency from food, while children with NS were already prone to hypocalcemia due to poor absorption and increased loss [3, 4, 5, 8].

The rate of height faltering ( $-2SD \leq HAZ < -1SD$ ) in our study was 30.2%, which was quite high among children with NS. It should be noted and appropriately prevented. These children

were at risk of becoming stunting if not promptly identified and intervened with counseling to help them return to normal height.

### 4.3. Calcium intake in children with NS and its relation to stunting prevalence

Most children in the study were supplemented with calcium through oral medications (92.5%), similar to the study by of Ndongo et al. [2] with 97.8% having calcium supplementation, indicating that the physicians were concerned about the height and calcium metabolism of children with NS and had preventive measures in place for calcium deficiency. However, the fulfillment of the recommended daily calcium intake from diet alone for all children was 49.1%, indicating that the diet of these children was inadequate. After supplementation with medications, the rate of meeting the adequate calcium intake increased to 75.5%. Calcium-rich foods are often high in protein and minerals, which help maintain strong bones and promote healthy growth. Increasing calcium intake from food provides the body with more essential nutrients for overall health than simply supplementing with calcium pills. Pediatric NS patients and their caregivers should receive additional nutritional counseling to improve calcium intake from food. The diversity and quality of meals were also contributing factors.

The prevalence of stunting among children consuming less than 50% of their daily calcium requirement from dietary sources was very high (87.5%) compared to that in the others (24.4%), with PR (95%CI) = 0.28 (0.14–0.58) and  $p$ -value = 0.001. This indicates that ensuring at least 50% of the daily calcium requirement from dietary

sources may be a crucial factor in reducing the risk of stunting malnutrition in children. This demonstrates the crucial role of dietary calcium in bone development in children, especially in pediatric patients with nephrotic syndrome (NS). These children were affected by impaired ossification and bone loss due to medications and were often coupled with nutritional deficiencies and metabolic disorders [2, 3, 4, 9, 10]. Based on these findings, the role of nutritional therapy is essential and should be implemented regularly from the beginning of treatment to ensure optimal development for pediatric patients with NS. When considering consumption of  $>50\%$  of the daily calcium requirement from both dietary sources and supplements, the prevalence of stunting in the insufficient calcium group (66.7%) remained higher than in the sufficient calcium group (32.0%), with PR (95%CI) = 0.48 (0.15–1.56) and  $p$ -value = 0.263. Although this difference is not statistically significant due to small sample size of the study, the results continue to support the hypothesis that sufficient calcium intake from both dietary sources and supplements may help reduce the risk of stunting. The study by Nguyen Thi Le Thuy reported that 74.5% of children with NS had hypocalcemia, due to protein loss in urine as well as reduced calcium absorption in the intestines, along with deficiency from inadequate intake. Therefore, to minimize calcium deficiency, which in the long term

affects nerve, muscle function, and bone development, it is crucial not only to control the disease but also to provide adequate calcium from the diet as well as vitamin D [3, 4, 9, 10].

The study had the limitation of a small sample size and short duration, which may not fully represent children with nephrotic syndrome. Larger studies are needed to determine the relationship between calcium intake and stunting in children with nephrotic syndrome.

## V. CONCLUSION

Stunting and height faltering are commonly observed in children with nephrotic syndrome in Childre Hospital No.2. Those with calcium intake exceeding 50% of the daily requirement had a lower prevalence of stunting. It is

essential to educate and counsel both the family and the children on appropriate nutrition, emphasizing the importance of adequate calcium intake from daily dietary sources.

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