Original Research

ASSOCIATION BETWEEN STUNTING AND CALCIUM INTAKE IN CHILDREN WITH NEPHROTIC SYNDROME

Nguyen Thi Thu Hau[1,✉], Nguyen Thi Yen Vy[2], Vo Van Tam[2] Huynh Thi Vu Quynh[2]

[1] *Department of Nutrition, Children's Hospital No. 2*
[2] *University of Medicine and Pharmacy at Ho Chi Minh City*

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 medical treatment records.

Results: The prevalence of moderate stunting and severe stunting was 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 at risk of poor growth, muscle mass depletion and cognitive impairment.

✉ Corresponding author: Nguyen Thi Thu Hau
Email: thuhaunt@gmail.com
Doi: 10.56283/1859-0381/709
Received: May 20, 2024 Revised: June 1, 2024
Accepted: September 6, 2024
Published online: September 15 , 2024

Research investigating the nutritional status of children with NS, especially stunting has been conducted in some nations [1–4]. The data relating stunting in pediatric NS patients in Vietnam, however, has been limited. Children Hospital No.2 (CH2), is one of the tertiary pediatric hospitals in the South of Vietnam, which provides hemo-dialysis and kidney transplantation, manages pediatric patients with severe NS. 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, and the relationship between stunting and calcium intake in pediatric NS patients under treatments at the Nephrology-Endocrinology Department of CH2. Findings will serve as a foundation for developing nutritional guidelines to improve the stunting status in children with NS.

II. METHODS

2.1. Study design and subjects

A cross-sectional study was conducted from April 25th to June 26th, 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 and their 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.

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

$\alpha = 0.05$: 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. Apply all the values above to the equation, the desired sample size was 49. At the end of the sampling stage, we recruited 53 patients with NS.

2.3. Data collection and processing

The child's guardian was directly interviewed using a constructed research questionnaire. Children's height was measured by a stadiometer, with an accuracy of 0.1 cm, according to the standard procedure. Length of children under 24 months and height of children greater than 24 months were measured by separate stadiometer. Daily calcium intake was collected by 24h food recall method and dietary logs, from medications was collected through prescription reviews. The total daily calcium intake was 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 medical records.

2.4. Variables and indicators

Categorial data were shown as frequency (%). Continuous data were reported as mean and standard deviation with a normal distribution or median and interquartile range (IQR) with a abnormal distribution.

The height-for-age Z-score (HAZ) was calculated by WHO Anthro and WHO Anthro Plus software. The child was classified as moderate stunting and severe stunting, respectively, if HAZ below -2 and -3 from the WHO Child Growth Standards median. The height faltering was indentified if $-2 \leq HAZ < -1$ and not stunted if $HAZ \geq -1$ [6, 7].

Dependent variables included calcium intake from diet alone, diet and supplements, and intakes exceeding 50% of the daily requirement from diet alone, and diet and supplements.

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

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

III. RESULTS

Of the 53 children in the study, 37 (69.8%) were boys. Age distribution was as follows: <1 year, 1.9%; 1-5 years, 20.8%; 6-10 years, 35.8%; and >10 years, 41.5%.

As shown in Table 1, 77.4% of children presented with edema. The majority did not have hypertension or renal failure. Corticosteroid resistance was diagnosed in 39.6% of the children, and 67.9% exhibited serum albumin levels below the normal concentration (<35-55 g/L). The median number of hospital admissions since NS diagnosis was 3 (IQR: 2-6), with 45.3% of children admitted 0-2 times and 54.7% admitted more than twice. The median duration of illness was 33 months (IQR: 13-63), with 41.5% of children having a disease duration of up to 2 years and 58.5% exceeding 2 years.

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	3 (2 – 6)*	
≤ 2 times	24	45.3
>2 times	29	54.7
Duration of illness	33 (13 – 63)*	
=< 2 years	22	41.5
>2 years	31	58.5

** Median (interquartile range)*

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

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

Table 2 shows that 34 (64.2%) children had height problems: height faltering, 30.2%; moderate stunting, 20.8%; and severe stunting, 13.2%. The elemental calcium amount from dietary intake surveys was 828 mg/day, and recorded calcium supplements used at the time of the study was 300 mg/day (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. *Association 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 Chi square test, except for *p-value by Fisher's exact test*

In children with NS, calcium intake from diet and supplements was related to stunting rate. Notably, meeting over 50% of calcium daily requirement through diet is strongly associated with stunting. Dietary calcium intake was inadequate in 50.1% of patients and adequate in 49.1%. When considering both diet and supplements, inadequate calcium intake was observed in 24.5% of patients, while adequate intake was present in 75.5%.

From the 24-hour dietary survey, 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 (110 ml) 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 ± 3.85 years, similar to the study conducted by Vu Thi Chi et al. [1] on 52 children treated in 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, with average age of 6.73 ± 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 from this research might be a result from the selection bias, because the 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 of both micronutrients and macronutrients, leading to poor growth, muscle mass loss, and stunting. Short stature occurred due to the disease process, poor diet, and 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 had height problems. The stunting rate was 14.75% in the study of Solarin et al. [5], which 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. Vietnamese Asians typically did not consume as much calcium-rich products such as milk and dairy products as part of the diet of Europeans [8]. This may contribute to low dietary calcium intake and calcium deficiency, while children with NS were already prone to hypocalcemia due to poor absorption and increased loss [3, 4, 5, 9].

The rate of height faltering in our study was 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 catchup to normal height.

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

Most children in the study were supplemented with calcium, through oral medications (92.5%), similar to the findings from Ndongo et al. [2] with 97.8% having calcium supplementation. These high percentage of calcium supplement indicate that the physicians were concerned about calcium metabolism among children with NS and had preventive solutions in place for controlling of 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.

Children consuming less than 50% of their daily calcium requirement from dietary sources had a significantly higher prevalence of stunting (87.5%) compared to those consuming at least 50% (24.4%) (PR=0.28, 95%CI=0.14-0.58, p=0.001). This indicates that ensuring at least 50% of the daily calcium requirement through dietmay be a crucial for reducing stunting risk, emphasizing the importance of dietary calcium for bone development, particularly in pediatric NS patients. 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, 10, 11]. 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. However, the trend supports the hypothesis that adequate calcium intake, including supplements, may reduce stunting risk. Given the prevalence of hypocalcemia in children with NS, stemming from protein loss in urine and reduced calcium absorption in intestines (Nguyen Thi Le Thuy), adequate calcium and vitamin D intake, alongside disease management, are crucial for nerve, muscle function, and bone development [3, 4, 10, 11].

The study's limitations, including small sample size and short duration, necessitate larger studies to further investigate the relationship between calcium intake and stunting in children with nephrotic syndrome.

V. CONCLUSION

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

References

1. Vu Thi Chi, Ta Thi Thanh Phuong, Pham Trung Kien. Results of treatment of children with idiopathic nephrotic syndrome at Bac Ninh Obstetric and Children's Hospital. *Journal of Community Medicine*. 2021;62(5):23-31.
2. Ndongo AA, Boiro D, Basse I, et al. Factors Affecting the Statural Growth Retardation in Children using Steroids in Idiopathic Nephrotic Syndrome. *Asian Journal of Pediatric Research*. 2021;7(4):70-76. Doi: 10.9734/ajpr/2021/v7i430225.
3. Nguyen Thi Le Thuy, Le Thy Phuong Anh, Hoang Thi Thuy Yen, Nguyen Thi Hong Duc. Electrolyte disorders in nephrotic syndrome in children. *Ho Chi Minh City Journal of Medicine*. 2018;22(4):50-55.
4. Soliman AT, Hamed N, De Sanctis V, et al. The Long-term (five years) Effects of Prednisone Therapy in Children with Frequently Relapsing Nephrotic Syndrome: A Controlled Study of Anthropometric Parameters and Metabolic Abnormalities. *Acta Biomed*. 2022; 93(5):e 2022303. Doi: 10.23750/abm.v93i5.13459.
5. Solari AUS, Motunrayo OA, et al. Nutritional assessment of children with nephrotic syndrome in a tertiary institution: A case controlled study. *Trop J Nephrol*. 2018;13(2):97-103.
6. WHO child growth standards: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development. Geneva: World Health Organization; 2006. Retrieved from http://www.who.int/childgrowth/standards/technical_report/en/.
7. de Onis M, Onyango W A, Borghi E et al. Development of a WHO growth reference for school-aged children and adolescents. Bulletin of the World Health Organization. 2007;85:660-667. Laillou A, Wieringa F, Tran TN, et al. Hypovitaminosis D and mild hypocalcaemia are highly prevalent among young Vietnamese children and women and related to low dietary intake. *PLoS One*. 2013;8(5):e63979.doi: 10.1371/journal.pone.0063979.
8. Tran Thi Hong Minh, Nguyen Van Son. Evaluation of treatment outcomes for primary nephrotic syndrome in children in Thai Nguyen. *Vietnam Journal of Medicine*. 2023;16(5):23-31.
9. Hossain A, Mostafa G, Mannan KA, Deb KP, Hossain MM, Alam S. Correlation between serum albumin level and ionized calcium in idiopathic nephrotic syndrome in children. *Urol Nephrol Open Access J*. 2016; 3(2):111-115. Doi: 10.15406/unoaj.2016.03.00070.
10. Hussain N, Zello JA, Vasilevska-Ristovska J, et al. The rationale and design of Isight into Nephrotic Syndrome: Investigating Genes, Health and Therapeutics (INSIGHT): a prospective cohort study of childhood nephrotic syndrome. *BMC nephrology*. 2013:1-11. Doi: 10.1186/1471-2369-14-25.