Original Article

Bone Mineral Disorders in Children with Predialysis Chronic Kidney Disease Correlates with Short Stature

Ghina Rania[1], Henny Adriani Puspitasari,[2] Eka Laksmi Hidayati,[2] Cut Nurul Hafifah[3]

[1]Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

[2]Nephrology Division, Department of Child Health, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia

[3]Nutrition and Metabolic Diseases Division, Department of Child Health, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia

e-ISSN: 2830-5442

Corresponding author:
Cut Nurul Hafifah
cutnurulhafifah@gmail.com

Published:
29th February 2024

DOI:
https://doi.org/10.58427/apghn.3.1.2024.12-23

Citation:
Rania G, Puspitasari HA, Hidayati EL, Hafifah CN. Nutritional Status of Children with Chronic Kidney Disease in Stage 3-5 Predialysis: Identifying Influential Factors. *Arch Pediatr Gastr Hepatol Nutr.* 2024;3(1).12-23

Abstract:

Background: The increasing prevalence of malnutrition and growth impairment among children with CKD could impact the prognosis and the preferred intervention. Therefore, this study aimed to identify the nutritional status of children with CKD and its relating factors.

Method**:** A cross-sectional study was conducted in a tertiary, national-referral teaching hospital in Jakarta. Sociodemographic and laboratory data were obtained from medical records. Body weight and height of participants were measured using digital scale and stadiometer, respectively. Growth and nutritional status indicators such as BMI-for-age, weight-for-height, height for age, and weight for age were quantified and plotted using WHO Anthro and Anthroplus application.

Result: A total of 18 participants aged 3-17 years old with CKD stage 3 – 5 were included in this study. BMI measurements showed a z-score average of -1.02, while the mean z-score for height-for-age was of -2.71. Our study demonstrated a significant association between the height-for-age and mineral bone in children with CKD ($p = 0.005$). However, we found no association between mineral bone disorder with other indicators of nutritional status. Furthermore, our study also found no significant relation between nutritional status and other influencing factors including the stage of CKD, duration of CKD, age, gender, primary etiological factor, hypertension, anemia, age, familial economic status, disease duration, and parental education level demonstrates no significant correlation ($p > 0.05$).

Conclusion**:** Children with stage 3 – 5 CKD in the pre-dialysis phase are shown to be underweight and short statured but with normal nutritional status. Mineral bone disorder was revealed to be significantly associated with height-for-age in children with CKD.

Keywords: children, chronic kidney disease, nutritional status, pre-dialysis, influential factors

Introduction

Chronic kidney disease (CKD) poses a major health concern, affecting an estimated 13.4% of the global population and influencing 18.5-58.3 per 1 million children worldwide.[1] Data upon the prevalence of pediatric CKD in Indonesia were still limited; however, an increased trend of the disease incidence was identified from several referral centers across the country.[2] The escalating number of CKD cases had raised concerns, as children with CKD face a higher risk of malnutrition, potentially leading to growth failure. The prevalence of malnutrition in children with CKD is approximately 20-45%. Furthermore, malnutrition not only impacts growth but also elevates the risk of morbidity and mortality in CKD patients.[3]

Nutrition plays a crucial role in preventing infections, hospitalizations, depression, weakness, and cardiovascular diseases in children with CKD.[4] However, the nutritional challenges in pediatric CKD cases extend beyond reduced intake and involve other factors such as decreased appetite, increased catabolism, hormonal imbalances, inflammation, and nutrient loss in dialysate fluid.[3] The accumulation of metabolic by-products due to the kidney's inability to clear it also plays a role in metabolic dysfunction among CKD patients.[3] In addition, the progression of the disease further determines the risk of malnutrition. Study in India had illustrated an increase in the incidence of malnutrition corresponding to the progression of CKD stages.[5] This concludes that nutritional imbalances and metabolic disturbance had happened among CKD patients, even from the pre-dialysis stage.

Management and renal replacement therapy also contribute to growth disturbances in CKD patients. Research in Nigeria indicated a 46.7% prevalence of malnutrition in pre-dialysis CKD patients, higher than those without kidney dysfunction (25.7%).[6] In Iran, a study reported malnutrition in 19 out of 42 pediatric CKD patients, with 4 cases occurred in the pre-dialysis phase, 5 cases were reported in dialysis phase (peritoneal and hemodialysis).[7] Studies have found that one of CKD therapies, hemodialysis, could induce increased CRP, protein muscle breakdown, and oxidative stress that could further affect growth and nutritional status.[3] However, studies have also linked chronic inflammation, characterized by increased TNF-alpha cytokines in CKD patients since the pre-dialysis phase, to bone mineral disorders affecting patients' stature.[8] Therefore, further study must be conducted to find the most ideal intervention to prevent worsening nutritional status.

Given the high prevalence of malnutrition in children with CKD, identifying factors influencing the nutritional status is crucial to prevent malnutrition and growth disturbances. Therefore, this study aims to investigate the nutritional status of pre-dialysis pediatric CKD patients and its relation to multiple factors. In the long run, the result of this study could be used to identify whether early diagnosis and intervention from pre-dialysis stage can improve the nutritional outcomes among children with CKD.

Methods

Data collection This is a cross-sectional study conducted in October 2022 at a tertiary, national-referral, teaching hospital in Jakarta, Indonesia. The study was approved by the local ethics committee with approval number of KET-915/UN2.F1/ETIK/PPM.00.02/2022. We included all pediatric patients aged 0-18 years in pre-dialysis phase of CKD (stage 3-5) for a minimum of three months prior the study. CKD patients who underwent kidney transplant and whose parents did not provide consent were excluded from the study. This study is a part of a larger study focusing on nutritional status of children with CKD, with the main difference of the participants which are divided into three according to the characteristics; patients who undergo predialysis, hemodialysis (Metasyah, et al)[9], or continuous ambulatory peritoneal dialysis (Amirah, et al).[10]

Calculation of growth and nutritional status indicators. Anthropometric measurements were performed using a combined digital weight scale and stadiometer (SECA 730). Indicators of nutritional status, including weight for height, weight for age, height for age, and body mass index (BMI) for age were calculated in form of z-score using WHO Anthro for participants below 5 years of age and WHO Anthroplus for participants aged 5-18 years old. The result of z-scores were then categorized based on the classification determined based on the Indonesian Minister of Health Regulation No. 2 of 2020. Secondary data comprises of disease stage, duration of disease, primary etiological factors, as well as past medical history of anemia, hypertension, and bone mineral disorder were recorded from medical records. Sociodemographic data, such as parental education levels, family economic status, age, and gender, were obtained through parent/guardian interviews and the completion of the Case Report Form (CRF).

Statistics. Data were analyzed using SPSS Statistic ver. 25. Normality test was performed using Saphiro-Wilk test. All numeric data with normal distribution were presented with mean and standard deviation, while data with abnormal distribution were presented in median and interquartile range. Correlation between the indicators of nutritional status with associated factors such as age and duration of disease were quantified using Pearson test for the normally distributed data and Spearman test for data with abnormal distribution. ANOVA test and Kruskal-Wallis test were used to analyze the relationship between the indicators of nutritional status with other factors such as stages of CKD, primary etiological factors, and comorbidities. Meanwhile, independent t-test and Mann-Whitney were used to analyze the indicators of nutritional status with gender of participants.

Results

A total of 18 patients were enrolled in this study. Majority of the participants were male (61.1%) with the median age of 13.5 years. The educational level of both parents was mainly high school or equal (38.9%) and most participants came from family with income below the minimum wage (55.6%). Patients were predominantly diagnosed with stage 5 CKD (38.9%) with median duration of disease of 8.5 months. Other baseline characteristics of participants were illustrated in Table 1.

Table 1. Characteristics of Participants

Variables	Frequency (n (%))
Age (years)*	13.5 (3.0-17.0)
Gender	
Male	11 (61.1)
Female	7 (38.9)
Mother's educational level	
Primary school or equivalent	2 (11.1)
Middle high school or equivalent	5 (27.8)
Senior high school or equivalent	7 (38.9)
University	4 (22.2)
Father's Level of Education	
Primary school or equivalent	2 (11.1)
Middle high school or equivalent	5 (27.8)
High school or equivalent	7 (38.9)
University	4 (22.2)
Family Economic Status	
Below the minimum wage	10 (55.6)
Above the minimum wage	8 (44.4)
Duration of Disease*	8.5 (3.0-26.0)
Stage of CKD	
G3a	5 (27.8)
G3b	3 (16.7)
G4	3 (16.7)
G5	7 (38.9)
Primary Etiological Factors	
CAKUT	5 (27.8)
SRNS	6 (33.3)
Chronic glomerulonephritis	2 (11.1)
Renal ciliopathies	1 (5.6)
Thrombotic microangiopathies	1 (5.6)
Others	3 (16.7)
Systolic Blood Pressure (mmHg)**	108.44 ± 20.11
Diastolic Blood Pressure (mmHg)**	65.44 ± 16.30

Variables	Frequency (n (%))
Hemoglobin (g/dL)**	10.48 ± 2.57
Mineral Bone Disorder	
Yes	2 (11.1)
No	16 (88.9)

Saphiro-Wilk test was used to analyze the normality of data distribution. *Data presented in median (minimum-maximum). **Data presented in mean ± standard deviation. CKD: chronic kidney disease, CAKUT: congenital anomalies of the kidney and urinary tract, SRNS: Steroid-Resistant Nephrotic Syndrome

The relation between the nutritional status indicator with the influencing factors were illustrated in **Table 2, 3 and 4**. Our study evaluated the relation between the indicators of pediatric nutritional status with CKD and various influencing factors. These factors include age, gender, parents' level of education, family economic status, stage of CKD, duration of disease, primary etiological factors, and comorbidities such as hypertension indicated by systolic and diastolic blood pressure, anemia represented by hemoglobin level, as well as bone mineral disorder. The findings indicated no significant correlation between nutritional status and the influencing factors, except for height for age, which demonstrated a significant correlation with bone mineral disorders (p = 0.005).

Table 2. Correlation between nutritional status indicators with age, duration of CKD, systolic blood pressure (SBP), diastolic blood pressure (DBP), and hemoglobin

	Weight-for-Height (n: 3)[a]	**Weight-for-Age** (n: 8)[b]	**Height-for-Age** (n: 18)[a]	**BMI-for-Age** (n: 18)[a]
Age	r: 0.866 p: 0.333	r: -0.217 p: 0.606	r: -0.900 p: 0.722	r: -0.126 p: 0.618
Duration of CKD	r: 0.500 p: 0.667	r: 0.292 p: 0.483	r: -0.196 p: 0.437	r: -0.044 p: 0.863
Systolic Blood Pressure	r: -0.130 p: 0.917	r: -0.335 p: 0.417	r: -0.275 p: 0.270	r: 0.035 p: 0.892
Diastolic Blood Pressure	r: -0.541 p: 0.636	r: -0.395 p: 0.333	r: -0.369 p: 0.132	r: -0.241 p: 0.334
Hemoglobin	r: 0.581 p: 0.605	r: 0.168 p: 0.691	r: -0.155 p: 0.538	r: -0.035 p: 0.890

[a] analyzed using Pearson correlation test. [b] analyzed using Spearman correlation test. CKD: chronic kidney disease, BMI: body mass index.

Table 3. Relation between nutritional status indicators with stage of CKD, primary etiological factors, and parents' educational level.

	Weight-for-Age[a]		Height-for-Age[b]		BMI-for-Age[b]	
	Mean rank	p	Mean square	p	Mean square	p
Stage of CKD		0.362	1.516	0.646	0.538	0.789
G3a	6.00					
G3b	3.00					
G4	8.00					
G5	3.80					
Primary Etiological Factors		0.297	1.386	0.789	2.704	0.249
SRNS	3.67					
CAKUT	5.75					
Others	2.00					
Mother's Level of Education		0.570	0.399	0.937	3.152	0.201
Primary school or equivalent	-					
Middle high school or equivalent	4.50					
High school or equivalent	3.75					
University	6.00					
Father's Level of Education		0.240	0.735	0.854	3.254	0.186
Primary school or equivalent	8.00					
Middle high school or equivalent	1.00					
High school or equivalent	4.75					
University	4.00					

[a] analyzed using ANOVA. [b] analyzed using Kruskal Wallis. CKD: chronic kidney disease, BMI: body mass index, SRNS: Steroid-Resistant Nephrotic Syndrome, CAKUT: congenital anomalies of the kidney and urinary tract

Table 4. Relation between nutritional status indicators with gender, bone mineral disorder, and family economic status

	Weight-for-Age[a]		Height-for-Age[b]			BMI-for-Age[b]		
	Mean Rank	p	Mean	Levene's Test	p	Mean	Levene's Test	p
Gender		0.127		0.568	0.420		0.444	0.568
Male	4.00		-2.96			-1.17		
Female	8.00		-2.32			-0.78		
Bone Mineral Disorder		0.827		0.738	0.005		0.957	0.767
Yes	5.00		-5.43			-0.62		
No	4.43		-2.37			-1.07		
Family Economic Status		0.386		0.729	0.657		0.158	0.935
Above the minimum wage	5.25		-2.52			-0.99		
Below the minimum wage	3.75		-2.86			-1.04		

[a] analyzed using Mann-Whitney test. [b] analyzed using independent t-test. BMI: body mass index

Discussion

Based on the BMI-for-age indicator, the average of nutritional status between participants in this study was -1.02, indicating a good nutritional status. This finding is aligned with a study in Brazil which reported that 79.8% of pediatric patient in the pre-dialysis phase of CKD had good nutritional status. Furthermore, the study also indicated that the nutritional status during the initial diagnosis and during follow-up did not exhibit significant changes, with majority maintaining good nutritional status.[11] Another study in Canada also documented a good nutritional status between children in the pre-dialysis phase of CKD, irrespective of gender, with the average z-score between male and female were 0.34±1.20 and 0.40±1.06, respectively.[12] Meanwhile, the nutritional status results among participants, based on height-for-age indicator, indicate short stature, with an average z-score of -2.71. The outcome is also consistent with a study in Brazil, which stated that 54% of children in pre-dialysis phase of CKD were classified as having very short stature.[11]

This study found no direct correlation between CKD stages and body weight, stature, and overall nutritional status. This contrasts with prior studies in the United States and Canada, which demonstrates that a decrease in GFR of 10 ml/min per 1.73m2 was associated with a reduction in height and weight in children, regardless of gender.[12] A study in Brazil also reported a decline in overall nutritional status along with the progression of CKD stages.[11] This was hypothesized to be caused by anorexia resulting from reduced food intake among advanced CKD patients and exacerbated by insulin resistance, leading to protein catabolism and muscle wasting.[3] This discrepancy could be caused by the small number of samples and the concentration of sample in certain CKD stages. Nutritional status was also not correlated with duration of CKD, which is inconsistent with previous study by Sozeri et al. However, the previous study also included patients undergoing dialysis as their participants, which differentiates their population from our study.[7] Another study by Greenbaum et al. reported similar results to our findings.[14] The nutritional status of children with CKD is primarily affected by the hormonal imbalance caused by the decrease of GFR due to kidney dysfunction. However, it is also influenced by the type of therapy received and patients' current condition. Hence, assessing the relation between nutritional status and the duration of disease is better to be conducted on patients with the same stages of diseases.[3]

Our study also found no correlation between nutritional status and several indicators, including age, genders, primary etiological factors, and family economic status, which is consistent with previous studies.[6, 7, 15, 16] The absence of correlation between nutritional status and age could be attributed to other factors influencing the disease. Hogan et al. revealed that nutritional status is not related to the age of patient if the patient has already developed CKD before others, supporting the finding.[17] Additionally, there is no specific phase of growth that could lead to a different nutritional status between male and female children, confirming our result. The difference in growth between boys and girls is relatively minor during the critical growth phase in the first 1000 days of life.[18] Furthermore, there is no significant difference in the nutritional needs of both genders during the prepubertal phase. Despite experiencing growth spurt at different times and having different nutritional needs, both genders eventually undergo growth spurts and changes in body composition, leading to similar nutritional status.[19] Nutritional status is also not associated with the primary etiological factors of CKD. This could be due to the mechanism of malnutrition in CKD being directly related to the consequence of kidney dysfunction, regardless of its primary etiology.[3, 15] The lack of correlation between nutritional status and family economic status is expected, as economic status should not be a barrier for families to seek appropriate healthcare for patients with CKD, with the existence of national health insurance in Indonesia.[20] However, there is currently no government funding that covers the expenses of daily food for children, which is essential for their growth. Particularly for children with CKD, supplementary food is often needed despite its high cost, which is also not covered by the government.[21] Thus, we do acknowledge that family economic status may indirectly affect the conditions of patients with CKD if the expenses are not prioritized wisely.

This study also reported that parents' level of education is not associated with the nutritional status of children with CKD in the pre-dialysis stage. This is because parents' level of education only partially influences parental upbringing. Parenting styles could be affected by several factors, such as the number of children, antenatal and postnatal care, as well as the family's economic status. Additionally, the quality of education should also be considered. Alderman et al. suggest that parents with a history of education in areas with better educational quality had children with better nutritional status.[22] This concludes that parental education is only one of the various factors influencing the decision-making in child-rearing and is not directly related to nutritional status.

There is no association between nutritional status with anemia and hypertension in this study. This funding is aligned with study by Rodig et al. and Flyyn et al. which demonstrated that there is no significant correlation between nutritional status with anemia and hypertension.[13, 23] Both anemia and hypertension in CKD occurs as a result of a multifactorial process which does not directly cause the chronic malnutrition in children necessary to impair their growth and overall nutritional status.[23, 24]

Conversely, this study revealed a significant correlation between bone mineral disorders and the average of height-for-age during the pre-dialysis phase of children with CKD ($p = 0.005$). Bone mineral disorders is often found in pediatric patient with CKD as CKD induces growth hormone abnormality which may impact the height of children through the increase of TNF alpha cytokine levels induced by chronic inflammation in patients. This elevation is known to inhibit RUNX2, a transcription factor associated with osteoblast differentiation, and stimulate osteoclastogenesis, ultimately leading to disturbances in bone mineralization.[8] Changes in bone mineralization are monitored through numerous laboratory testing, such as serum calcium levels, PTH, phosphate, and alkaline phosphatase activities, since the stage G2 of CKD. This is also done along with routine anthropometric measurement at least every 1 to 3 months. Additionally, certain organizations such as the European ad hoc Committee on Assessment of Growth and Nutritional Status in Peritoneal Dialysis recommending a more intense anthropological monitoring of once monthly measurement for children under the age of 5 and every two months for older children and every 6 – 12 months for bone mineralization marker examinations.[25] The target therapy for bone mineral disorder is a normal level of phosphate and calcium according to age. For patient experiencing growth disturbance, recombinant human growth hormone is recommended as treatment.[26]

As this study is a pilot study in Indonesia, this study possesses several advantages and drawbacks. This study aimed to determine the correlation between CKD stages and malnutrition in children which could provide novel information about the impact of CKD progression in a child's overall nutrition and growth status especially among children with pre-dialysis and dialysis stages of CKD. Despite these advantages, this study also possesses several limitations such as small sample size and small sample variability as the majority of the samples are male children with stage 5 CKD. Lack of samples variability also made it impossible to identify whether certain groups of CKD stages and certain genders possess better nutritional status than others. Therefore, further study with more variations in CKD stages and nutritional status is still needed in the future to help validate the findings of this study.

Conclusion

In conclusion, children with CKD stage 3 – 5 pre-dialysis have normal nutritional status according to BMI for age and weight for height. However, according to weight for age and height for age, these children are underweight with short stature. Therefore, BMI alone should not be used to evaluate nutritional status. Bone mineral disorders is also found to be correlated with short stature. For this reason, early detection and intervention in addressing growth faltering among children with CKD is paramount to improve their quality of life.

Conflict of Interest

None declared

Funding Statement

The authors received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

References

1. Lv JC, Zhang LX. Prevalence and Disease Burden of Chronic Kidney Disease. Adv Exp Med Biol. 2019;1165:3-15.https://doi.org/10.1007/978-981-13-8871-2_1.
2. Direktorat Jenderal Pencegahan dan Pengendalian Penyakit Kementerian Kesehatan RI. Peran pemerintah dalam pencegahan dan pengendalian gangguan ginjal anak. Jakarta: Kementerian Kesehatan Republik Indonesia 2018.
3. Iorember FM. Malnutrition in Chronic Kidney Disease. Front Pediatr. 2018;6:161.https://doi.org/10.3389/fped.2018.00161.
4. Panggabean MS. Nutrisi Pasien Anak dengan Chronic Kidney Disease (CKD). Cermin Dunia Kedokteran. 2022;49(6):320-6.https://doi.org/10.55175/cdk.v49i6.240.
5. Anupama SH, Abraham G, Alex M, Vijayan M, Subramanian KK, Fernando E, et al. A multicenter study of malnutrition status in chronic kidney disease stages I-V-D from different socioeconomic groups. Saudi J Kidney Dis Transpl. 2020;31(3):614-23.https://doi.org/10.4103/1319-2442.289448.

6. Oluseyi A, Enajite O. Malnutrition in pre-dialysis chronic kidney disease patients in a teaching hospital in Southern Nigeria. Afr Health Sci. 2016;16(1):234-41.https://doi.org/10.4314/ahs.v16i1.31.
7. Sozeri B, Mir S, Kara O, Dincel N. Growth impairment and nutritional status in children with chronic kidney disease. Iran J Pediatr. 2011;21:271-7.
8. Meza K, Biswas S, Zhu YS, Gajjar A, Perelstein E, Kumar J, et al. Tumor necrosis factor-alpha is associated with mineral bone disorder and growth impairment in children with chronic kidney disease. Pediatr Nephrol. 2021;36(6):1579-87.https://doi.org/10.1007/s00467-020-04846-3.
9. Metasyah N, Hidayati EL. Nutritional Status in Children with End-Stage Kidney Disease Undergoing Hemodialysis and Other Related Factors. Arch Pediatr Gastr Hepatol Nutr. 2023;2(3):13-24.https://doi.org/10.58427/apghn.2.3.2023.13-24
10. Amirah P, Puspitasari HA, Hafifah CN.Analysis of the Impact of Continuous Ambulatory Peritoneal Dialysis on Nutritional Status in Pediatric Chronic Kidney Disease. Arch Pediatr Gastr Hepatol Nutr. 2023;2(4).1-10.https://doi.org/10.58427/apghn.2.4.2023.1-10
11. Kementerian Kesehatan Republik Indonesia. Peraturan Menteri Kesehatan Republik Indonesia No. 2 Tahun 2020. Jakarta: Kementerian Kesehatan Republik Indonesia; 2020.
12. Silva VR, Soares CB, Magalhaes JO, de Barcelos IP, Cerqueira DC, Simoes e Silva AC, et al. Anthropometric and biochemical profile of children and adolescents with chronic kidney disease in a predialysis pediatric interdisciplinary program. ScientificWorldJournal. 2015;2015:810758.https://doi.org/10.1155/2015/810758.
13. Gao T, Leonard MB, Zemel B, Kalkwarf HJ, Foster BJ. Interpretation of body mass index in children with CKD. Clin J Am Soc Nephrol. 2012;7(4):558-64.https://doi.org/10.2215/CJN.09710911.
14. Rodig NM, McDermott KC, Schneider MF, Hotchkiss HM, Yadin O, Seikaly MG, et al. Growth in children with chronic kidney disease: a report from the Chronic Kidney Disease in Children Study. Pediatr Nephrol. 2014;29(10):1987-95.https://doi.org/10.1007/s00467-014-2812-9.
15. Greenbaum LA, Munoz A, Schneider MF, Kaskel FJ, Askenazi DJ, Jenkins R, et al. The association between abnormal birth history and growth in children with CKD. Clin J Am Soc Nephrol. 2011;6(1):14-21.https://doi.org/10.2215/CJN.08481109.
16. Hamasaki Y, Ishikura K, Uemura O, Ito S, Wada N, Hattori M, et al. Growth impairment in children with pre-dialysis chronic kidney disease in Japan. Clin Exp Nephrol. 2015;19(6):1142-8.https://doi.org/10.1007/s10157-015-1098-y.
17. Yaya S, Uthman OA, Kunnuji M, Navaneetham K, Akinyemi JO, Kananura RM, et al. Does economic growth reduce childhood stunting? A multicountry analysis of 89 Demographic and Health Surveys in sub-Saharan Africa. BMJ Glob Health. 2020;5(1):e002042.https://doi.org/10.1136/bmjgh-2019-002042.
18. Hogan J, Schneider MF, Pai R, Denburg MR, Kogon A, Brooks ER, et al. Grip strength in children with chronic kidney disease. Pediatr Nephrol. 2020;35(5):891-9.https://doi.org/10.1007/s00467-019-04461-x.
19. Pietrobelli A, Agosti M, MeNu G. Nutrition in the First 1000 Days: Ten Practices to Minimize Obesity Emerging from Published Science. Int J Environ Res Public Health. 2017;14(12).https://doi.org/10.3390/ijerph14121491.
20. World Health Organization. Adolescent nutrition: a review of the situation in selected south-east asian countries. New Delhi: WHO; 2006.
21. Badan Penyelenggara Jaminan Sosial Kesehatan. Panduan Layanan Bagi Peserta Jaminan Kesehatan Nasional Kartu Indonesia Sehat (JKN-KIS). Jakarta: BPJS Kesehatan; 2022.
22. Badan Pengawas Obat dan Makanan Republik Indonesia. Peraturan Badan Pengawas Obat dan Makanan Nomor 1 Tahun 2018 Tentang Pengawasan Pangan Olahan Untuk Keperluan Gizi Khusus. Jakarta: BPOM; 2018.
23. Alderman H, Headey DD. How Important is Parental Education for Child Nutrition? World Dev. 2017;94:448-64.https://doi.org/10.1016/j.worlddev.2017.02.007.
24. Flynn JT, Mitsnefes M, Pierce C, Cole SR, Parekh RS, Furth SL, et al. Blood pressure in children with

chronic kidney disease: a report from the Chronic Kidney Disease in Children study. Hypertension. 2008;52(4):631-7.https://doi.org/10.1161/HYPERTENSIONAHA.108.110635.

25. Erlianda D, Rizal MF. Pertumbuhan Dan Perkembangan Anak Penderita Penyakit Ginjal Kronik. Dentika: Dental Journal. 2016;19(1):78-82.https://doi.org/10.32734/dentika.v19i1.157.
26. National Kidney Foundation. KDOQI Clinical Practice guideline for nutrition in children with CKD: 2008 update. American Journal of Kidney Diseases. 2009;53(3).https://doi.org/10.1053/j.ajkd.2008.11.017.
27. Kidney Disease Improving Global Outcomes (KDIGO). Summary of recommendation statements. Kidney Int Suppl. 2013;3(1):5-14.https://doi.org/10.1038/kisup.2012.77.