The Relationship Between Chronic Kidney Disease and Weight Loss in Children

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Abstract

Background: Weight loss often occurs in children with Chronic Kidney Disease (CKD). Provision of proper nutrition is necessary for growth and development and weight gain of patients with chronic kidney disease in children.

Objectve: To aimed the relationship between chronic kidney disease and weight loss in children

Methods: An observational analytic study with a retrospective cohort design in outpatients and inpatients with chronic kidney disease aged 5 to 18 years at the H. Adam Malik Medan General Hospital and USU Hospital in December 2019 to March 2021.

Results: This study was followed by 29 CKD children. Subjects who experienced weight loss were 16 (55.2%) children and 13 (44.8%) children who did not experience weight change after 3 months follow-up. There was a significant difference between the mean weight at baseline and after the 3-month follow-up period ($p<0.001$). There was no difference in the stage of CKD between initial examination and after 3-month follow-up ($p = 0.877$). There was no significance between the stage of chronic kidney disease and weight loss ($p = 0.096$). there was no significant relationship between chronic kidney disease stage and weight loss ($p = 0.343$), with the same nutritional status after 3 months follow-up. Other results showed that there was no difference in urea and creatinine levels between the start of the study and after 3 months of follow-up ($p>0.05$). The mean delta weight loss was 0.87 kg with the largest decrease being around 3 kg and 13 subjects did not show any weight loss.

Conclusion: There was a significant association between initial weight loss and after 3 months of follow-up but not for height. There is no relationship between the initial examination stage of CKD and weight loss. There was no significant relationship between the initial examination of body weight, nutritional status, urea and creatinine levels and after 3 months of follow-up.

Keywords: Chronic Kidney Disease, CKD, Weight Loss, CKD in Children

Introduction

Weight loss often occurs in children with chronic kidney disease (CKD) (Ku E, et al., 2017). Because of the importance of nutrition in supporting children's growth, the provision of nutritional supplementation is very important for appropriate weight gain in patients with chronic kidney disease (Chazot C, et al., 2009). Surveys using nutritional status measurements show that malnutrition (wasting) is a common condition that can occur in adults with chronic kidney disease, with a prevalence of 20-75% of adults undergoing dialysis showing wasting conditions (Mak RH, et al., 2012). Currently, the prevalence of wasting in children with chronic kidney disease has limited available data (Furth SL, et al., 2006).

Several new evidences and new thinking in the field of nutrition regarding CKD children have resulted in a new definition of the term wasting (Mak RH, et al., 2012). Wasting is caused by factors other than inadequate intake and is referred to as cachexia. Cachexia has recently been defined as "a complex metabolic syndrome associated with an underlying disease and characterized by muscle loss, with or without fat loss" (Sienna JL, et al., 2010). Based on the Society for Cachexia and Wasting Disorders (SCWD) there are several diseases that cause cachexia, namely cancer, human immunodeficiency virus infection, heart failure, chronic kidney disease, and chronic obstructive pulmonary disease (Chazit C, et al., 2009).

Society for Cachexia and Wasting Disorders (SCWD) identified weight loss and growth failure as the most important clinical features in both adults and children (Ku E, et al., 2017). International Society of Renal Nutrisi and Metabolisme (ISRNM) mentions the term protein energy to describe a state of decreased protein stores and body energy fuel (body protein and fat mass) (Mak RH, et al., 2012). Several previous cross-sectional studies conducted in adults showed that body weight began to decrease around the estimated glomerular filtration rate (eGFR) of 40 mL/min/1.73 m2 (Hobbs DJ, et al., 2010). However, there are limited data for assessing the rate of weight loss that occurs in children with CKD (Wong CJ,

et al., 2012). Does body weight slowly decrease linearly as chronic kidney disease progresses or does it remain stable until the end stages of chronic kidney disease (Schwartz GJ, et al., 2009). However, the exact timing of interventions to reduce glomerular filtration rate to maintain body weight or gain appropriate weight has not been studied in children with CKD (Warady BA, et al., 2015). An observational cohort study conducted by Furth et al in 2006 on children and adolescents with CKD was followed up in a longitudinal study since 2005 with the results that the weight trajectory was not linear with the progression of chronic kidney disease but weight loss would occur after onset of advanced stage of CKD (stage 4) (Furth SL, et al., 2006). Based on these considerations, the investigators intended to determine whether there was a change in body weight when renal function decreased in children with CKD and to assess whether such weight change would be associated with an increased risk of developing end-stage chronic kidney disease as well.

Methods

This study is an analytic approach with a retrospective cohort study conducted at H. Adam Malik (HAM) Medan General Hospital dan Universitas Sumatera Utara (USU) Hospital. The time of the study was carried out from December 2020 to July 2021 involving 29 children with inclusion criteria of children aged 5-18 years, children diagnosed with chronic kidney disease based on clinical features and supporting examinations and children who had undergone hemodialysis due to chronic kidney disease.[3] The exclusion criteria were children who had chronic diseases such as tuberculosis and children who had a history of malignancies such as leukemia, immunosuppression or other serious blood diseases.

This study was approved by the Research Ethics Committee of the Faculty of Medicine, USU. All subjects were asked for approval from their parents after an explanation was made regarding the condition of the disease experienced, and the examination that had been carried out. After that, the patient was asked for information for the basic data of patient characteristics. Examination and recording of data carried out is the result of examination of kidney function and nutritional status in the form of weight, height and upper arm circumference. Measurement of the nutritional status of children using the WHO curve for children under 5 years and CDC 2000 for children over 5 years. Measurement of GFR based on the results of laboratory tests of kidney function (creatinine).

Results

This study was followed by 29 children with CKD who had met the inclusion and exclusion criteria. The characteristics of the subject can be seen in table 1.

Table 1. Characteristics of Subjects

Characteristics	**n = 29**
Sex, n (%)	
Boy	19 (65,5)
Girl	10 (34,5)
Age, n (%)	
5 – 12 years	7 (24,1)
> 12 years	22 (75,9)
Ethnics, n (%)	
Batak	14 (48,3)
Java	14 (48,3)
Karo	1 (3,4)

The results showed that there were 16 (55.2%) children who experienced weight loss and 13 (44.8%) children who did not experience a change in body weight after a 3-month follow-up. Table 2 shows the differences in body weight and height before and after a 3-month follow-up.

Table 2. Differences in Weight and Height Before and After 3-months Follow-up

	Initial Examination	**3 Months Follow Up**	**p***
Weight, kg			
Mean (SD)	36,14 (11,13)	35,28 (11,22)	<0,001
Median (Min – Max)	11,13 (15-53)	38 (14-50)	
Height, cm			
Mean(SD)	142,55 (15,81)	142,55 (15,81)	1,000
Median (Min – Max)	145 (96-168)	145 (96-168)	

*Wilcoxon

Classification of CKD at baseline and after 3-month follow-up and the relationship between CKD stage and weight loss can be seen in Tables 3 and 4.

Table 3. Classification of CKD at Baseline and After 3-months Follow-up

Stage	Initial Examination	3 Months Follow Up	p*
Stage 2	2 (6,9)	2 (6,9)	0,877
Stage 3	4 (13,8)	6 (20,7)	
Stage 4	7 (24,1)	4 (13,8)	
Stage 5	16 (55,2)	17 (58,6)	

*Wilcoxon

Table 4. Relationship between CKD Stage and Weight Loss

Stage	Weight Loss		p*
	Decreased	Unchanged	
Stage 2	1 (50)	1 (50)	0,096
Stage 3	3 (75)	1 (25)	
Stage 4	1 (14,3)	6 (85,7)	
Stage 5	11 (68,8)	5 (31,2)	

*Kruskal Wallis

The relationship between CKD stage at 3-month examination and weight loss did not show significance with p value = 0.343 (table 5). Examination of the nutritional status of the subjects can be seen in tables 6 and 7 and the delta value of changes in body weight in table 8. The results of kidney function levels are in table 9.

Table 5. Relationship between CKD Stage at 3-Month Follow-Up Examination and Weight Loss

Stage	Weight Loss		p*
	Decreased	Unchanged	
Stage 2	2 (100)	0	0,343
Stage 3	2 (33,3)	4 (66,7)	
Stage 4	3 (75)	1 (25)	
Stage 5	9 (52,9)	8 (47,1)	

*Kruskal Wallis

Table 6. Examination of Nutritional Status Before and After 3 Months Follow Up

Nutritional Status	Initial Examination	3 Months Follow Up	p*
Severe Malnutrition	10 (34,5)	10 (34,5)	1,000
Moderate Malnutrition	7 (24,1)	7 (24,1)	
Good Status	12 (41,4)	12 (41,4)	

*Wilcoxon

Table 7. Nutritional Status of CKD Patients Based on Upper Arm Circumference

Nutritional Status	Frequencies	%
Severe malnutrition	29	100
Moderate malnutrition	0	0
Good Status	0	0
Total	**29**	**100**

Table 8. Delta Value of Changes in Body Weight

Weight	n = 29
Initail weight	
Mean (SD)	36,14 (11,13)
Median (Min – Max)	11,13 (15-53)
Weight 3 Months Follow Up	
Mean (SD)	35,28 (11,22)
Median (Min – Max	38 (14-50)
Delta Values	

Mean (SD)	0,87 (0,92)
Median (Min – Max)	1 (0 – 3)

Table 9. Classification of CKD at Baseline and After 3-month Follow-up

	Initial Examination	3 Months Follow Up	p*
Ureum, mg/dL			
Mean (SD)	173,76 (174,91)	185,45 (176,15)	0,552
Median (Min – Max)	126 (36-1010)	133 (36-1010)	
Creatinine, mg/dL			
Mean (SD)	6,19 (4,01)	7,31 (4,33)	0,289
Median (Min – Mak)	7,11 (1,04-14,93)	7,41 (1,04-14,93)	

*Wilcoxon

Discussion

Children with chronic kidney disease have a high risk of malnutrition, which is characterized by loss of protein energy and micronutrient deficiencies (Lorember FM, et al., 2018). Previous studies show a high prevalence of malnutrition in children with chronic kidney disease. The study by Gupta, et al. In India, it is reported that children with chronic kidney disease stage 1-5 are around 45 children with various basic diseases, the number of boys is 40 children and the number of girls is 5 children with nutritional status problems. The age of the children studied was 1-18 years with a median age of 9 years (min-max age 13 months – 14 years). Another study by Bakr, et al. in Egypt, it was reported that 45 children with end-stage chronic kidney disease had an average age of 12 years, with 23 boys and 22 girls. The study is similar to this study where there were more men than women, about 19 children and 10 children. The total number of children with CKD in this study was around 29 children in the 5-12 year age group, 7 children and over 12 years of about 22 children.

Assessment of nutritional status is a process of examining a person's nutritional status that is measured objectively (Arisman MB, et al., 2010), one of the problems that often arises in patients with chronic kidney disease is problems with growth which can be assessed by nutritional status (Pardede SO, et al., 2009). Based on the Ministry of Health in 2016, nutritional status was assessed into three indices, namely weight for age, height for age, weight for height (Rees L, et al., 2011). The study conducted by Rees, et al. regarding the growth of children with chronic kidney disease on peritoneal dialysis reported a significant increase in body mass index in children in North America, whereas in children in Turkey there was a significant decrease in body mass index independent of enteral diet. The Rees study also reported that height does not increase during the first 6 to 12 months of life and then tends to stabilize and there is a significant association with mealtime with gastrostomy with height becoming taller over time in dialysis patients.

Another study by Conkar, et al. in Turkey reported an increase in body weight after a 3-month follow-up but there was no relationship between an increase in height after a 3-month follow-up in CKD who received continuous ambulatory peritoneal dialysis (CAPD) with nutritional support, with the result that the number of children who experienced weight gain was 9 of 10 children. The results of this study showed that there was a relationship between weight loss after 3 months of follow-up with $p < 0.001$ and no increase in height after 3 months $p = 1$, with the result that the number of children who experienced weight loss was 16 and 13 of 29 children with fixed weight. The results of the study by Conkar and the Rees study were not similar in this study. In the study, Rees received additional diet through an NGT or gastrostomy. Meanwhile, the Conkar study sample received support for a strict oral diet.

Chronic kidney disease, which is characterized by decreased kidney function, can be progressive and can eventually lead to end-stage kidney disease. Although the data in children are few, CKD is not uncommon in children with poor progression. The study by Chiou, et al. in Taiwan reported that 56 (14.7%) children experienced CKD progression due to structural abnormalities. Chiou's study was different with this study, where there was no relationship between CKD progression after 3 months with p value = 0.877. The reason for this discrepancy is that the etiology is not differentiated so that it is not possible to assess the etiology of the structural abnormalities leading to increased progression as in the Chiou's study.

Another study by Kamath, et al. in India reported that approximately 25 (38%) children had progressive CKD after 2 years of follow-up. Approximately 12 children had a >50% reduction in baseline glomerular filtration rate (GFR), 8 achieved a GFR <15 ml/min per 1.73 m2, 4 started on dialysis, and 1 child underwent kidney transplantation. The study by Kamath also showed different results in this study, where there was a longer follow-up of about 2 years while this study used a follow-up of 3 months. Chronic kidney disease has become a global public health problem due to the increasing incidence of disease, morbidity and mortality. In general, weight loss is easy in CKD children. In this study, there was no significant relationship between the stage of chronic kidney disease and weight loss in children with CKD at the beginning of the examination and follow-up for 3 months. This study is similar to the study by Ku, et al. in North America reported that there was no association between weight loss and CKD with a decrease in GFR <35/min/1.73m2 at baseline. However, the results of this study differ from other studies by Conkar, et al. in Turkey reported an increase in body weight after 3 months of follow-up in patients with CKD stage 5, this was due to the support of a strict diet that had been carried out.

This study also added an assessment of nutritional status before and after the 3-month follow-up which showed no significant difference between the nutritional status at the start of the study and the 3-month follow-up (p=1,000) with the same amount of nutritional status before and after follow-up. poor nutritional status of about 29 (100%) based on the circumference of the upper arm. The study by Silva, et al. in Brazil reported that there was no significant relationship between changes in body mass index of children with CKD stage 5, with the number of children who were malnourished as many as 15 (12.6%) children. Another study by Conkar, et al. in Turkey also reported no significant association between CKD and CAPD and body mass index after 3 months and 6 months of follow-up. Study Apostulu, et al. reported the incidence of CKD with nutritional status based on body mass index and upper arm circumference had the same number of children experiencing nutritional disorders around 6 out of 30 children with CKD.

Assessment of serum urea and creatinine is important to see the progress of CKD. This study examined urea and creatinine at baseline and after a 3-month follow-up. The results showed that there was no difference in urea and creatinine levels between the beginning of the study and after 3 months of follow-up with the Wilcoxon test (p>0.05). The study by Chiou, et al. also reported that there was no relationship between creatinine and BUN levels with the progression of CKD with the etiology of nephritis, while the etiology of structural abnormalities did not correlate with the progression of CKD. Another study by Ishikura, et al. in Japan reported a significant relationship between creatinine and BUN results and CKD stage. The difference between the results of this study and the results of the study by Chiou is that there is an assessment of the etiology of the causes of CKD making it easier to assess progression, whereas in this study the etiology was not assessed. Likewise in the study by Ishikura serum and BUN levels were assessed among staging of CKD at the same time whereas in this study no staging was performed.

This study still has limitations. This study has not been able to explain the relationship between the etiology and the progression of CKD. The etiology of CKD is important because the outcome is different.

Conclusion

There was a significant relationship between initial weight loss and after 3 months of follow-up, while for height there was no significant relationship. There was no correlation between CKD stage and baseline weight and weight loss. There was no significant relationship between the initial examination of body weight, nutritional status, urea and creatinine levels and after 3 months of follow-up.

Suggestion

It is necessary to examine the etiology of CKD in determining the progression of kidney damage and controlling nutritional support for this progression.

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References

Ku E., Kopple J., McCulloch CE., Warady BA., Furth SL., Mak RH., et al., 2017. Associations between Weight Loss, Kidney Function Decline, and Risk of ESRD in Chronic Kidney Disease in Children (CKiD) Cohort Study. American Journal Kidney Disease 71,p. 648..

Chazot C., 2009. Why are chronic kidney disease patients anorexic and what can be done about it? Seminars Nephrology 29,p.15.

Mak RH., Cheung WW., Zhan JY., Shen Q., Foster BJ., 2012. Cachexia and protein-energy wasting in children with chronic kidney disease. Pediatric Nephrology 27,p.173.

Furth SL., Cole SR., Moxey-Mims M., et al., 2006. Design and methods of the Chronic Kidney Disease in Children (CKiD) prospective cohort study. Clinical Journal of the American Society of Nephrology 1,p.1006.

Sienna JL., Saqan R., Teh JC., et al., 2010. Body size in children with chronic kidney disease after gastrostomy tube feeding. Pediatric Nephrology 25,p.2115.

Hobbs DJ., Bunchman TE., Weismantel DP., et al., 2010. Megestrol acetate improves weight gain in pediatric patients with chronic kidney disease. Journal of Renal Nutrition 20, p. 408.

Wong CJ., Moxey-Mims M., Jerry-Fluker J., Warady BA., Furth SL., 2012. CKiD (CKD in Children) prospective cohort study: a review of current findings. American Journal Kidney Disease 60,p.1002.

Schwartz GJ., Munoz A., Schneider MF., 2009. New equations to estimate GFR in children with CKD. Journal of the American Sociery of Nephrology 20,p. 629.

Warady BA., Abraham AG., Schwartz GJ., 2015. Predictors of rapid progression of glomerular and nonglomerular kidney disease in children and adolescents: the Chronic Kidney Dis- ease in Children (CKiD) Cohort. American Journal Kidney Disease 65,p. 878.

Lorember FM., 2018. Malnutrition in chronic kidney disease. Front Pediatrics 6, p.1.

Gupta A., Mantan M., Sethi M., 2016. Nutritional assessment in children with chronic kidney disease 27, p.733.

Bakr AMAE., Hasaneen BM., Bassiouni DARH., 2018. Assessment of nutritional status in children with chronic kidney disease using hand grip strength tool. Jiurnal of Renal Nutrition 28, p. 265.

Arisman MB., 2010. Buku Ajar Ilmu Gizi Dalam Daur Kehidupan. Ed 2. Jakarta: Penerbit Buku Kedokteraan EGC, p.205.

Pardede SO., Chunnaedy S., 2009. Penyakit Ginjal Kronik pada Anak. Sari Pediatri 11,p.199.

Alatas SSS., 2011. Status Gizi Anak Usia Sekolah (7-12 Tahun) DanHubungannya Dengan Tingkat Asupan Kalsium Harian Di Yayasan Kampungkids Pejaten Jakarta Selatan Tahun 2009. Jakarta, p.1.

Rees L., Azocar M., Borzych D., Watson AR., Buscher A., Edefonti A., 2011. Growth in Very Young Children Undergoing Chronic Peritoneal Dialysis. Journal of the American Society of Nephrology 22,p. 2303.

Conkar S., 2017. Effects of nutrition on residual renal functions during peritoneal dialysis. The Pan African Medical Journal 1, p.39.

Chiou YY., Lin CY., Chen MJ., Chiou YH., Wang YF., Wang HH., et al., 2016. Etiology and pediatric chronic kidney disease progression: Taiwan Pediatric Renal Collaborative Study. Journal of the Formosan Medical Association 215,p. 752.

Kamath N., Iyengar A., George N., Luyckx VA., 2019. Risk Factors and Rate of Progression of CKD in Children. Kidney Internatioanl Report 4,p. 1472.

Ku E., Kopple JD., Mc Culloch CE., Warady BA., Furth SL., Mak RH., et.al., 2018. Associations Between Weight Loss, Kidney Function Decline, and Risk of ESRD in the Chronic Kidney Disease in Children (CKiD) Cohort Study. American Journal Kidney Disease 71,p. 648.

Silva VR., Soares CB., Magalhaes JO., de Barcelos IP., Cerqueira DC., Silva ACS., 2015. Anthropometric and Biochemical Profile of Children and Adolescents with Chronic Kidney Disease in a Predialysis Pediatric Interdisciplinary Program. ScientificWorld Journal, p. 1.

Apostolou A., Printza N., Karagiozoglou-Lampoudi T., Dotis J., Papachristou F., 2014. Nutrition assessment of children with advanced stages of chronic kidney disease-A single center study. Hippokratia 18, p. 212.

Ishikura K., Uemura O., Hamasaki Y., Ito S., Wada N., Hattori M., et al., 2014. Progression to end-stage kidney disease in Japanese children with chronic kidney disease: results of a nationwide prospective cohort study. Nephrology Dialysis Transplantation 29,p. 878.