Iran J Pediatr. 2018 August; 28(4):e22029. doi: 10.5812/ijp.22029.

Published online 2018 June 29. **Research Article**

Long-Term Effect of Nephrocalcinosis on Renal Function and Body Growth Index in Children: A Retrospective Single Center Study

Zahra Pournasiri,[1,*] Abbas Madani,[1] Anahita Ghaemi,[1] Zahra Adl,[1] and Shadab Salehpour[1]

[1]Department of Pediatrics, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

[*]*Corresponding author*: Zahra Pournasiri, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran. Tel: +98-9122766955, E-mail: pournasiri.z@gmail.com

Received 2017 June 14; **Revised** 2018 January 28; **Accepted** 2018 February 21.

Abstract

Background: Nephrocalcinosis to the presence of calcium salts within renal tissue. Infants and children are more likely to have an underlying etiology for nephrocalcinosis including inherited errors of metabolism, anatomic abnormalities of the urinary tract, renal disorders, vitamin D excess, medication and prematurity. The body growth and renal function have rarely been investigated concerning children with nephrocalcinosis (NC).

Objectives: This study aimed to evaluate effect of NC on growth index and kidney function of patients according to its cause.

Methods: This study was conducted on twenty-eight now 2-27-year-old patients with NC who were admitted or referred to Loghman Hakim Hospital within 2006 and 2013. The patients' data were recorded in terms of age, gender, NC etiology, clinical presentation, GFR, standard deviation scores of height and weight, and follow-up period. Data was imported to the SPSS software version 18 and analyzed using statistical tests.

Results: Mean age of the participants was 2.5 $\pm$ 2.2, ranging from 0.1 to 9.7 years. Fourteen (47%) patients were male. Mean follow-up time period was 7.1 $\pm$ 5.2, ranging from 1.0 to 20.9 years. The most common clinical presentations leading to the NC diagnosis were urinary tract infection (25%) and growth retardation among 18% of the patients. The NC was rooted in distal renal tubular acidosis (dRTA) regarding 34.5% of the subjects, idiopathic hypercalciuria (IHC) in terms of 17.2% participants, Bartter syndrome in 10.3% and other different factors in 31.1% of the participants and cause of the NC was unknown in 6.9% of the subjects. Mean glomerular filtration rate (GFR) was 75.6 $\pm$ 29.1 in presentation and 105.7 $\pm$ 21.9 ml/min/1.73m^2 in follow-up ($P < 0.001$). There was no significant decrease in height and weight SDS from the first to last observation. Also, a significant increase of BMI was observed from first to last observation.

Conclusions: Findings revealed that nephrocalcinosis has no significant effect on growth index and glomerular filtration within a long term and its impact depends on the underlying causes.

Keywords: Nephrocalcinosis, Distal Renal Tubular Acidosis, Renal Function, Hypercalciuria

1. Background

Nephrocalcinosis (NC) represents calcification of the renal parenchyma (1). The main etiological agents of this condition are metabolic diseases such as hypoparathyroidism and hyperparathyroidism, apparent mineralocorticoid excess syndrome, idiopathic infantile hypercalcemia, glycogen storage disease type 1, glucose-galactose malabsorption, and taking certain drugs (2-8). Furthermore, renal disorders including idiopathic hypercalciuria, renal hypophosphatemia, renal tubular acidosis, Dent disease, familial hypomagnesemia with hypercalciuri, and nephrocalcinosis, hypocitraturia, cystinuria, primary hyperoxaluria and renal hypouricemia (9), vitamin D excess medication and prematurity; sometimes it is incidentally and radiographically found in individuals with normal kidney function (10-12). Appreciation of the processes involved in calculus formation aids in the understanding the diagnosis and management of the disease, the most important of which are intratubular factors explaining crystal retention and adhesion to the tubular epithelium such as decreased urine volume, urinary supersaturation, the presence of insufficient concentrations of crystal inhibitors including citrate, magnesium and various proteins (such as uromodelin, osteopontin, bikunin, and urinary prothrombin fragment) (1). Decreased urinary excretion of a potent inhibitor, known as uromodelin, in patients with nephrolithiasis was demonstrated by Jaggi M et al. (13). On the other hand, some experimental and clinical studies strongly suggest that crystals only adhere to injured and regenerated epithelial cells expressing a

variety of crystal-binding molecules such as annexin II, osteopontin, hyaluronan, sialic acid-containing proteins and/or phospholipids, phosphatidyl serine and nucleolin-related protein on the luminal surface of the tubular epithelium (14-16). In addition to these studies, the NC etiology, pathogenesis and clinical course remain unclear concerning some diseases and its prognosis is not well-defined (17).

Additionally, few studies have been conducted on the identification and underlying causes of NC and on whether it has any impact on body growth and renal function in children (10, 18). Al-Riyami MS et al. found severe renal failure as initial presentation among 39% of children with primary hyperoxaluria type 1 with nephrocalcinosis in comparison with 22% among those without it (19). Hence, the present retrospective study was carried out to examine the causes of NC and its effect on renal function and body growth as well as its follow-up findings in children.

2. Methods

This is a retrospective longitudinal study of all children with bilateral nephrocalcinosis attending our center for 7 years (2006 - 2013).

The study consists of 30 children. Children with unilateral nephrocalcinosis, focal nephrocalcinosis and history of urinary tract obstruction, and urinary system anomaly were excluded. Furthermore, children with a follow-up time less than 2 years were also excluded. The diagnosis of NC in all children were extracted from ultrasonography reports. The medical records of patients were evaluated for gender, age, birth weight, history of prematurity, laboratory findings, family history of nephrocalcinosis, clinical presentation, etiology of NC and follow-up period. Weight and height standard deviation scores (wSDS, hSDS), body mass index (BMI) and glomerular filtration rate (GFR) were calculated in the first and last examination. GFR was estimated using the Schwartz formula (20) and the normal level was considered as > 90 ml/min/1.73 m^2. Height and weight SDS were calculated based on the published national standards and heights and weights below -2 SD was taken as lower than the normal limit (21). The most frequently underlying causes of NC were distal renal tubular acidosis (dRTA) in patients by hyperchloremic metabolic acidosis, hypokalemia, hypercalciuria, high urine pH (> 5.5) and positive urinary anion; idiopathic hypercalciuria in those with elevated urinary calcium in relation to age (defined as Ca/creatinine ratio $\geq$ 0.8, $\geq$ 0.6, $\geq$ 0.4 and $\geq$ 0.2mg/mg in children < 6 months, 6 - 12 months, 1 - 2 years and > 2 years of age, respectively, in random urine samples (10)), absence of other tubular defects and normal levels of calcium (9 - 12 mg/dl); Bartter syndrome in patients with metabolic alkalosis, hypokalemia and elevated urinary potassium and chloride excretion; Hypercalcemia in patients with serum calcium more than 12 mg/dl, Dent's disease in male patients with hypercalciuria, low molecular weight proteinuria and bilateral medullary NC in addition to proximal tubule dysfunction findings; proximal renal tubular acidosis (pRTA) in patients with normal anion gap metabolic acidosis and negative urine anion gap and urine pH less than 5.5; methylmalonic acidemia (MMA) in those with high anion gap metabolic acidosis and high urine methylmalonic aciduria, primary hyperoxaluia with urine oxalate more than 90 mg/1.73m^2/day; and x-linked hypophosphatemia rickets in males with hypophosphatemia rickets and high urine phosphate.

2.1. Statistical Analysis

Data were presented as mean±standard deviation and range values. Comparison of hSDS, wSDS, BMI and GFR at presentation and last visits was made by using t-test. Statistical analyses between the groups were carried out using chi-square test, Fisher exact test and Pearson correlation. Analyses were done with the Statistical Package for Social Sciences (SPSS version 18.0, Chicago, USA) software and $P < 0.05$ was considered statistically significant.

3. Results

Among the 30 patients with NC, 14 (46.7%) subjects were male and 16 (53.3) female. No data was available regarding the two patients; therefore, 28 patients with NC were included in the final analysis. The mean follow-up period was 7.1 ± 5.2 (1.0-20.9) years. The detailed description of the spectrum is summarized in Table 1.

Table 1. Growth Features and Renal Function at Presentation and Last Follow-Up

Parameter	At Presentation	At Last Presentation	P Value
Mean age, y	2.5 ± 2.2 (0.1-9.7)	9.2 ± 5.7 (2.1-27.6)	< 0.001
wSDS	-0.74 ± 2.4 (-4.5-8.5)	0.87 ± 3.2 (-2.6-10.3)	0.001
hSDS	0.73 ± 1.6 (-4.1-2.8)	-0.44 ± 1.4 (-4.2-1.8)	0.259
BMI	16.2 ± 4.5 (8.5-33.1)	19.3 ± 5.2 (12.8-30.3)	0.001
GFR	75.6 ± 29.1 (29.8-132)	105.7 ± 21.9 (43.2-143.9)	< 0.001

Abbreviations: BMI, body mass index; GFR, glomerular filtration rate; hSDS, height standard deviation scores; wSDS, weight standard deviation scores.

A wide range of renal tubular disorders were seen. Distal renal tubular acidosis (34.5%), idiopathic hypercalciuria (17.2%) and Bartter syndrome (10.3%) were common causes encountered.

Other observed causes were hypercalcemia, Dent disease, proximal renal tubular acidosis, methymalonic

acidemia, glycogen storage disease, x-linked hypophosphatemic rickets, nephritic syndrome and primary hyperoxaluria type I. The causes of NC were unknown in two patients.

3.1. Clinical and Laboratory Findings

Most frequently encountered initial symptoms were urinary tract infection (25%), followed by growth retardation (17.8%), enuresis (7.1%) and abdominal pain (3.6%). The NC was incidentally detected in one case during the diagnostic procedures adopted for abdominal pain.

Three patients (10%) had a history of prematurity. family history of NC was seen in 4 children. Family history of microlithiasis was also noted in 13.8% of patients. Ninety-seven percent of urinalysis in the last observation was abnormal and consisted of pyuria in 51.7%, hematuria in 34.5% and proteinuria in 6.9%. Also, abnormal urine solute such as hypercalciuria (65.9%), hyperoxaluria (51.7%), hyperuricosuria (48.3%), and hypocitraturia (34.5%) was also frequently observed.

3.2. Growth

Fourteen point three percent of NC patients had heights below the normal limit (-2 SDS) at presentation and had no change at last observation (P = 0.481). Thirty-nine point seven percent and 35.7% of these children had weights below the normal limit (-2 SDS) at first and the last investigation with significant improvement in mean SD from -0.7 $\pm$ 2.4 to 0.87 $\pm$ 3.2 (P-value 0.001). Mean score of height and weight SDS in NC patients are summarized in Table 2 according to the most frequent underlying disease at first and last observations. The most severe initial growth retardation was observed in patient with dRTA and Bartter's syndrome. Although some improvement in height SDS was generally recorded, a decrease was reported in distal RTA patients.

Mean body mass index in NC patients is also presented in Table 3 with regard to the most common underlying disease at first and last observation. There was a significant increase in BMI in patients with dRTA from first to last observations.

3.3. Renal Function

A statistically significant increase ranging from 75.6 to 105.7 ml/in/1.73m^2 (P < 0.001) was found in mean GFR score of the patients.

At the first presentation, 19 (65.5%) patients had GFR less than 90 ml/in/1.73 m^2; however, 7 (24.1%) patients had GFR less than 90 ml/in/1.73 m^2 in the last investigation and GFR < 60 ml/min/1.73 m^2 was not observed in these patients. Table 4 shows the mean GFR in NC patients according to the most common underlying causes of disease in the first and last observations. As it is presented, the GFR increased in all of patients and it was more significant in patients with dRTA.

4. Discussion

This is a single-center survey on the etiology of NC and its impact on renal function and body growth of NC in Iranian children. In our study, most of the NC children were girls and this is inconsistent with some other studies [18]. In this regard, 13.7% of patients had at least one family member with nephrocalcinosis, which is lower than in the Germany series (17).

Although growth retardation was the most common clinical presentation in patients with nephrocalcinosis in a majority of studies (10, 17, 18, 22), urinary tract infection was the major reason for referral (25%) followed by growth retardation as the second cause (17.8%) in this study. In Ronnefarth et al.'s study, more than one-third of the patients suffered from UTI (17).

In contrast to the adults, for whom environmental factors are the major cause of NC, the genetic and/or metabolic disorders are the main cause of childhood nephrocalcinosis and microlithiasis.

The most frequent underlying conditions associated with NC in this study were dRTA and idiopathic hypercalciuria (IHC) with an incidence frequency of 34% and 17%, respectively. In studies conducted in India, Turkey and Italy (10, 18, 22), dRTA was the most often mentioned cause of NC. High incidence of dRTA in these countries may be due to high prevalence of consanguineous marriages. Ronnefarth et al. found that 34% of 152 patients with NC had IHC (17). Further, the IHC was the most common cause of NC in Habbig's et al.'s study (12). The mean age for the dTRA diagnosis was 3 years (2 months- 9.5 year) and these findings are in line with those obtained by Ronnefarth et al. (17). Underlying cause of the NC was unknown in 7% of the participants and this is consistent with those found in Germany (17) and much lower than the values reported by Ammenti et al. (24.4%) and Mantan et al. (12.5%) (18, 22). The difference may be due to the extent of the investigation and existing laboratory facilities.

The role of abnormal urine solutes including hypercalciuria, hyperuricosuria, hyperoxaluria and hypocitraturia alone or associated with other known genetic diseases are demonstrated as a predisposing and accelerant factor to establish NC (11, 23-26). Dogan's et al. reported hypercalciuria in 25 (92.6%) patients in the first observation (10). In the current presentation, the hypercalciuria and hypercalcemia in the first observation were seen in 65.5% and 20.7% of the participants, respectively. Hypercalcuria was found

Table 2. Comparison of Mean Height and Weight SDS in Children with NC According to the Most Significant Underlying Disorders at First and Last Observations[a]

Underlying Disease	Height SDS			Weight SDS		
	Observation		P Value	Observation		P Value
	First	Last		First	Last	
Distal renal tubular acidosis (dRTA)	-0.5 ± 1.5	-0.62 ± 1. 6	0.772	-0.3 ± 1.8	0. 9 ± 2.2	0.070
Idiopathic Hypercalciuria (IHC)	-0.2 ± 1.1	0.42 ± 0.8	0.173	-0.4 ± 1.1	0.8 ± 2.3	0.237
Bartter syndrome	-3.5 ± 0.7	-0.95 ± 1.2	0.087	-4.0 ± 0.7	-0.9 ± 1.6	0.122
Total	-0.73 ± 1.6	-0.44 ± 1.4	0.259	-0.74 ± 2.4	0.87 ± 3.2	0.001

[a]Values are expressed as mean ± SD.

Table 3. Comparison of Mean BMI in Children with NC According to the Most Underlying Disorders at First and Last Observations[a]

Underlying Disease	BMI		P Value
	First observation	Last observation	
Distal renal tubular acidosis (dRTA)	16.43 ± 3.12	20.27 ± 5.47	0.026
Idiopathic Hypercalciuria (IHC)	16.16 ± 1.65	16.63 ± 3.17	0.670
Bartter syndrome	10.85 ± 2.04	15.88 ± 1.84	0.092
Unknown	19.87 ± 7.06	27.25 ± 3.50	0.742

[a]Values are expressed as mean ± SD.

Table 4. Comparison of Mean GFR in Children with NC According to the Most Common Underlying Causes of Disorders in the First and Last Observations[a]

Diagnosis	First Observation	Last Observation	P Value
Distal renal Tubular acidosis	82.2 ± 31.1	119.8 ± 17.5	0.001
Idiopathic Hypercalciuria	82.4 ± 25.59	113.2 ± 13.49	0.105
Bartter syndrome	37.71 ± 6.9	91.07 ± 41.89	0.123
Total (28 patient)	75.6 ± 29.1	105.7 ± 21.9	< 0.001

[a]Values are expressed as mean ± SD.

in a majority of the current NC patients, indicating its importance as a predisposing factor of NC (17, 18). The frequency of hyperoxaluria in NC patients was reported 7.3 - 7.7% in various studies (17, 18) and this is greater than the present study's (3.4%).

In this study, the mean GFR of the patients in the first and last observation was 75.6 and 105 ml/min/1.73 m^2, respectively (P < 0.001; however, Dogan et al. reported mean GFR of 114.9 and 115.1ml/min/1.73 m^2 for their patients in the first and last investigation, respectively (10). In Mantan et al.'s study, GFR value decreased from 82 to 70.8 ml/min/1.73 m^2 in a mean follow-up period of 35 months (18). Nearly two-thirds of the patients had GFR values less than 90 ml/min/1.73 m^2 in the first presentation and an improvement less than one-fourth in the last observation after correct diagnosis and treatment of NC cases (27-29). Dogan et al. found that GFR was < 90 ml/min/1.73 m^2 in 18.5% of the cases at the end of the study (10). In Italy, 41% of the patients in the first and 29% in the last investigation had a GFR less than 80 ml/min/1.73 m^2 (22). In India, 83% of the subjects had a normal GFR (> 80 ml/min/1.73 m^2) (18).

The mean weight SD S scores and BMI improved during the follow-up period and the differences were statistically significant with a mean value of 7 years. The mean Z-score height for the patients in the current study was -0.73 in the first and 0.44 in the last investigation (P > 0.05). These values for the study carried out in Italy were -2.2 and -1.0, respectively (22). In Ronnefarth et al.'s study, 41% of the patients during the diagnosis and 32% of patients during the last observation had a 2 height SD less than the normal height (17). Also, 54% of 28 NC patients in Ammenti et al. series had hSDS < -2 in the first and 22% in the last observation (22). In Turkey, about half of the patients had hSDS < -2 at presentation, which decreased about one-fourth in the last investigation (10).

Although growth retardation has been a recognized

problem in tubular disorders at initial presentation, however, with adequate treatment, good catch-up growth has been demonstrated. In our series, there was a trend toward improvement in growth standard deviation. The present study showed that height and weight Z-scores show no decrease in long term because of nephrocalcinosis and their dependence on underlying causes.

4.1. Limitations

The limitations of this study include lack of access to a sufficient amount of patients' information, not referring of the patients to continue treatment, ultrasonography by different radiologists and ultrasound equipment, and non-reported nephrocalcinosis procedures adopted by them.

4.2. Conclusion

According to the findings, it can be concluded that the dRTA and IHC are the most frequent

causes underlying the NC in these children. Findings show that nephrocalcinosis has no significant effect on growth index and glomerular filtration in long term and its impact is dependent upon underlying causes.

Due to the limitation of this study including small sample size and ultrasonography performed by different radiologists, conducting a multi-center prospective study with a larger sample size is recommended.

Acknowledgments

We would like to acknowledge the contributions of the Clinical Research Development Center of Loghman-Hakim Hospital, Shahid Beheshti University of Medical Sciences,Tehran, Iran.

References

1. Wrong O. *Nephrocalcinosis. In: Oxford Textbook of Clinical Nephrology, Davison AM, Cameron JS, Grunfeld J, et al (Eds)*. Oxford: Oxford University Press; 2005. 1375 p.
2. Lopes MP, Kliemann BS, Bini IB, Kulchetscki R, Borsani V, Savi L, et al. Hypoparathyroidism and pseudohypoparathyroidism: etiology, laboratory features and complications. *Arch Endocrinol Metab*. 2016;**60**(6):532–6. doi: 10.1590/2359-3997000000221. [PubMed: 27901178].
3. Nair CG, Babu M, Jacob P. Renal dysfunction in primary hyperparathyroidism; effect of parathyroidectomy: A retrospective cohort study. *Int J Surg*. 2016;**36**(Pt A):383–7.
4. Moudgil A, Rodich G, Jordan SC, Kamil ES. Nephrocalcinosis and renal cysts associated with apparent mineralocorticoid excess syndrome. *Pediatr Nephrol*. 2000;**15**(1-2):60–2. [PubMed: 11095013].
5. Smit GPA, Rake JP, Akman HO, Mauro S. *The glycogen storage diseases and related disorders. In: Fernandes J, Saudubray JM, Berghe G, Walter JH, editors. Inborn Metabolic Diseases: Diagnosis and Treatmen*. Heidelberg: Springer; 2006.
6. Pahari A, Milla PJ, van't Hoff WG. Neonatal nephrocalcinosis in association with glucose-galactose malabsorption. *Pediatr Nephrol*. 2003;**18**(8):700–2. [PubMed: =].
7. Saadah OI, Alghamdi SA, Sindi HH, Alhunaitti H, Bin-Taleb YY, Alhussaini BH. Congenital glucose-galactose malabsorption: a descriptive study of clinical characteristics and outcome from Western Saudi Arabia. *Arab J Gastroenterol*. 2014;**15**(1):21–3. doi: 10.1016/j.ajg.2014.01.004. [PubMed: 24630509].
8. Pronicka E, Ciara E, Halat P, Janiec A, Wojcik M, Rowinska E, et al. Biallelic mutations in CYP24A1 or SLC34A1 as a cause of infantile idiopathic hypercalcemia (IIH) with vitamin D hypersensitivity: molecular study of 11 historical IIH cases. *J Appl Genet*. 2017;**58**(3):349–53. doi: 10.1007/s13353-017-0397-2. [PubMed: 28470390]. [PubMed Central: PMC5509812].
9. Shavit L, Jaeger P, Unwin RJ. What is nephrocalcinosis? *Kidney Int*. 2015;**88**(1):35–43. doi: 10.1038/ki.2015.76. [PubMed: 25807034].
10. Dogan CS, Uslu-Gokceoglu A, Comak E, Alimoglu E, Koyun M, Akman S. Renal function and linear growth of children with nephrocalcinosis: a retrospective single-center study. *Turk J Pediatr*. 2013;**55**(1):58–62. [PubMed: 23692833].
11. Hoppe B, Kemper MJ. Diagnostic examination of the child with urolithiasis or nephrocalcinosis. *Pediatr Nephrol*. 2010;**25**(3):403–13. doi: 10.1007/s00467-008-1073-x. [PubMed: 19104842]. [PubMed Central: PMC2810372].
12. Habbig S, Beck BB, Hoppe B. Nephrocalcinosis and urolithiasis in children. *Kidney Int*. 2011;**80**(12):1278–91. doi: 10.1038/ki.2011.336. [PubMed: 21956187].
13. Jaggi M, Nakagawa Y, Zipperle L, Hess B. Tamm-Horsfall protein in recurrent calcium kidney stone formers with positive family history: abnormalities in urinary excretion, molecular structure and function. *Urol Res*. 2007;**35**(2):55–62. doi: 10.1007/s00240-007-0083-7. [PubMed: 17345077].
14. Asselman M, Verhulst A, Van Ballegooijen ES, Bangma CH, Verkoelen CF, De Broe ME. Hyaluronan is apically secreted and expressed by proliferating or regenerating renal tubular cells. *Kidney Int*. 2005;**68**(1):71–83. doi: 10.1111/j.1523-1755.2005.00382.x. [PubMed: 15954897].
15. De Yoreo JJ, Qiu SR, Hoyer JR. Molecular modulation of calcium oxalate crystallization. *Am J Physiol Renal Physiol*. 2006;**291**(6):F1123–31. doi: 10.1152/ajprenal.00136.2006. [PubMed: 17082348].
16. Verhulst A, Asselman M, De Naeyer S, Vervaet BA, Mengel M, Gwinner W, et al. Preconditioning of the distal tubular epithelium of the human kidney precedes nephrocalcinosis. *Kidney Int*. 2005;**68**(4):1643–7. doi: 10.1111/j.1523-1755.2005.00584.x. [PubMed: 16164641].
17. Ronnefarth G, Misselwitz J. Nephrocalcinosis in children: a retrospective survey. Members of the Arbeitsgemeinschaft fur padiatrische Nephrologie. *Pediatr Nephrol*. 2000;**14**(10-11):1016–21. [PubMed: 10975319].
18. Mantan M, Bagga A, Virdi VS, Menon S, Hari P. Etiology of nephrocalcinosis in northern Indian children. *Pediatr Nephrol*. 2007;**22**(6):829–33. doi: 10.1007/s00467-006-0425-7. [PubMed: 17285294].
19. Al Riyami MS, Al Ghaithi B, Al Hashmi N, Al Kalbani N. Primary hyperoxaluria type 1 in 18 children: genotyping and outcome. *Int J Nephrol*. 2015;**2015**:634175. doi: 10.1155/2015/634175. [PubMed: 25918646]. [PubMed Central: PMC4396551].
20. Schwartz GJ, Munoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, et al. New equations to estimate GFR in children with CKD. *J Am Soc Nephrol*. 2009;**20**(3):629–37. doi: 10.1681/ASN.2008030287. [PubMed: 19158356]. [PubMed Central: PMC2653687].
21. Abtahi M, Doustmohammadian A, Abbdollahi M. Construction of national standards of weight and height and growth charts of Iranian children: a review article. *Int J Prev Med*. 2011;**2**(3):122–6. [PubMed: 21811652]. [PubMed Central: PMC3143523].
22. Ammenti A, Pelizzoni A, Cecconi M, Molinari PP, Montini G. Nephrocalcinosis in children: a retrospective multi-centre study. *Acta Paediatr*. 2009;**98**(10):1628–31. doi: 10.1111/j.1651-2227.2009.01401.x. [PubMed: 19572991].

23. Tang X, Bergstralh EJ, Mehta RA, Vrtiska TJ, Milliner DS, Lieske JC. Nephrocalcinosis is a risk factor for kidney failure in primary hyperoxaluria. *Kidney Int*. 2015;**87**(3):623–31. doi: 10.1038/ki.2014.298. [PubMed: 25229337]. [PubMed Central: PMC4344931].
24. Karaolanis G, Lionaki S, Moris D, Palla VV, Vernadakis S. Secondary hyperoxaluria: a risk factor for kidney stone formation and renal failure in native kidneys and renal grafts. *Transplant Rev (Orlando)*. 2014;**28**(4):182–7. doi: 10.1016/j.trre.2014.05.004. [PubMed: 24999029].
25. Hoppe B, von Unruh GE, Blank G, Rietschel E, Sidhu H, Laube N, et al. Absorptive hyperoxaluria leads to an increased risk for urolithiasis or nephrocalcinosis in cystic fibrosis. *Am J Kidney Dis*. 2005;**46**(3):440–5. doi: 10.1053/j.ajkd.2005.06.003. [PubMed: 16129205].
26. Tasic V, Gucev Z. Nephrolithiasis and Nephrocalcinosis in Children - Metabolic and Genetic Factors. *Pediatr Endocrinol Rev*. 2015;**13**(1):468–76. [PubMed: 26540764].
27. Kurt-Sukur ED, Ozcakar ZB, Fitoz S, Yilmaz S, Hoppe B, Yalcinkaya F. Primary Hyperoxaluria Type 1: A Cause for Infantile Renal Failure and Massive Nephrocalcinosis. *Klin Padiatr*. 2015;**227**(5):293–5. doi: 10.1055/s-0035-1554638. [PubMed: 26090995].
28. Deeb A, Abood SA, Simon J, Dastoor H, Pearce SH, Sayer JA. A novel CLDN16 mutation in a large family with familial hypomagnesaemia with hypercalciuria and nephrocalcinosis. *BMC Res Notes*. 2013;**6**:527. doi: 10.1186/1756-0500-6-527. [PubMed: 24321194]. [PubMed Central: PMC3867415].
29. Kanabus M, Shahni R, Saldanha JW, Murphy E, Plagnol V, Hoff WV, et al. Bi-allelic CLPB mutations cause cataract, renal cysts, nephrocalcinosis and 3-methylglutaconic aciduria, a novel disorder of mitochondrial protein disaggregation. *J Inherit Metab Dis*. 2015;**38**(2):211–9. doi: 10.1007/s10545-015-9813-0. [PubMed: 25595726].