Research Article

J Ped. Nephrology 2017;5(3)
http://journals.sbmu.ac.ir/jpn

Etiology of Renal Tubulopathy in Iranian Children-A Nationwide Survey

How to Cite This Article: Hooman N, Derakhshan A, Javadilarijani F, et al. Etiology of Renal Tubulopathy in Iranian Children-A Nationwide Survey. J Ped. Nephrology 2017;5(3)

Hooman N,[1*] Derakhshan A,[2] JavadiLarijani F,[3] Mortazavi F,[4] Falakaflaki B,[5] Sadeghi-Bojd S,[6] Nikibakhsh AA,[7] Esteghamati M,[8] Ghassemi K,[8] Mohkam M,[9] Ghane-Sharbaf F,[10] Ghazanfari F,[11] Sorkhi H,[12] Safaeian B,[13] Yousefichaijan P,[14] Kajbafzadeh AM,[15] Safaei-Asl A,[16] Shakiba M,[17] Shajari A,[17] Valavi E,[18] Sharif MR,[19] Akhavan-Sepahi M,[20] Momtaz HE,[21] Eskandarifar AR,[22] GhasemiKh,[23] Otukesh H,[1] Hosseini Shamsabadi R,[1] Nickavar A,[1] Basiratnia M,[2] Fallahzadeh MH,[2] Madani A,[3] Esfahani ST,[3] Ataei N,[3] Razavi MR,[20] Naghshizadian R.[22]

[1]Ali-Asghar Clinical Research Development Center, Iran University of Medical Sciences, Tehran, Iran, [2]Shiraz nephro-urology research center, Shiraz University of Medical Sciences, Shiraz, Iran, [3]Pediatric Chronic Kidney Disease Research Center, Children's Hospital Medical Center, Tehran University of Medical Sciences, Tehran, Iran, [4]Tabriz University of Medical Sciences, Tabriz, Iran, [5]Zanjan University of Medical Sciences, Zanjan, Iran, [6]Children and Adolescent Health Research Center, Zahedan University of Medical Sciences, Zahedan, Iran, [7]Urumieh University of Medical Sciences, Urumieh, Iran, [8]Hormozgan University of Medical Sciences , Bandarabas, Iran, [9] Shahid Beheshti University of Medical Sciences, Tehran, Iran, [10] Mashad University of Medical Sciences, Mashah, Iran, [11]Kerman University of Medical Sciences, Kerman, Iran, [12]Non-Communicable Pediatric Disease Research Center, Health Research Institute, Babol University of Medical Science, Babol, Iran, [13]Neonatal & Children's Health Research Center, Golestan University Medical Sciences, Gorgan, Iran, [14] Arak University of Medical Sciences, Arak, Iran,[15]Pediatric Urology and Regenerative Medicine Research Center, Section of Tissue Engineering and Stem Cells Therapy, Children's Medical Center, Pediatric Center of Excellence, Tehran University of Medical Sciences, Tehran, Iran, [16] Guilan University of Medical Sciences, Rasht, Iran, [17] Shahid Sadoughi University of Medical Sciences, Yazd, Iran, [18] Chronic Renal Failure Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran, [19] Kashan University of Medical Sciences, Kashan, Iran, [20] Qom University of Medical Sciences, Qom, Iran, [21]Hamadan University of Medical Sciences, Hamadan, Iran, [22]Kurdistan University of Medical Sciences, Sanandaj, Iran, [23] Bushehr University of Medical Sciences, Bushehr, Iran.

*** Corresponding Author**
Nakysa Hooman, Consultant Pediatric Nephrology, Ali-Asghar Children Hospital, Vahid-Dasgerdi st. Tehran, Iran.
Email: hooman.n@iums.ac.ir Tel:+98(21)23046210)

Received: June-2017
Revised: Aug-2017
Accepted: Aug-2017

Introduction: Inherited and acquired renal tubular disorders including cystic Kidney disease, cystinosis, Bartter's syndrome, Liddle syndrome, Gordon syndrome, nephrogenic diabetes insipidus, and drug-induced tubular injury are the frequent causes of end stage renal disease (ESRD) in children manifesting with chronic kidney disease (CKD). This is a report of the etiology and incidence of tubulopathies in a cohort of Iranian children across the country.

Materials and Methods: This descriptive observational study was conducted from March 2013 to October 2013. A list of tubulopathy disorders was emailed to 70 members of the Iranian Society of Pediatric Nephrology in different provinces of Iran practicing in both university affiliated and non-affiliated hospitals. They were requested to report the number of patients with specific International Classification of Disease (ICD-10) codes admitted to their hospitals between 2006 and 2013. Data are presented as numbers and percentages.

Results: Of 31 participating centers, 23 completed and returned the spreadsheets. Of the 2940 reported cases, the three most frequent tubulopathies were renal tubular acidosis (RTA) (33%), calcium disorders (27%), and cystic diseases (17%). Considering Tehran and Shiraz as referral centers, RTA and cystinosis were mostly reported from Kerman and Urmia, respectively. Furthermore, idiopathic hypercalciuria, cystinuria, and hyperoxaluria were the most common causes of hereditary kidney stone in 281 children reported from Bandarabas, Tabriz, and Shiraz, respectively

Conclusions: Our findings regarding the high incidence and different etiologies of inherited tubulopathies may provide a basis for designing targeted therapeutic interventions in the future and strategies for gene therapy of these complex disorders.

Keywords: Kidney Tubules; Disease; Acidosis; Renal Tubule; Kidney disease; Cyst; Diabetes Insipidus; Urolithiasis; Bartter syndrome.

Running Title: Renal Tubulopathy in Iranian Children

Introduction

The Renal Tube Network, which collects the clinical and genetic data of more than 200 patients mainly from Latin America and Spain, has reported that the most common tubulopathies in a descending order are distal renal tubular acidosis, classic barter syndrome, familial hypomagnesemia with hypercalciuria and nephrocalcinosis, and Gitelman syndrome [1]. Many of these inherited diseases are lifelong disorders accompanied by some co-morbidities and complications in adulthood [2]. There are a few case reports of specific tubular disorders in Iran. About 18-22% of ESRDs in young Iranian children are due to tubular disorders including cystic disease, cystinosis, hyperoxaluria, and tubulointerstitial nephritis [3,4]. The aim of this survey was to evaluate the frequency of various renal tubular disorders in different provinces of Iran.

Materials and Methods

This descriptive study was conducted from March 2013 to October 2013. A list of 34 renal tubulopathies (TP) was emailed to 70 members of the Iranian Society of Pediatric Nephrology (IranSPN) in 31 centers of Iran and the recipients were requested to report the number of patients with specific International Classification of Disease (ICD-10) codes admitted between 2006 and 2013 to their hospitals. Three reminders were emailed within eight weeks. The following ICD codes were used: Q61(1,3, 5,8) E72 (0,4,5,6,8), E26.8, E83 (4,5), E27.8, W25.8, E23.2, E10.8, E74.8, I15.2, N10, N4.9, W20 (0,9), N13.7, Q61.3, E83 (0,5). Data were presented as numbers and percentages. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of IranSPN. A review of the literature in the Pubmed and Google Scholar databases was done to collect information about known genes in each tubular disease in Iranian subjects [5-27].

Results

Of 31 centers, 23 completed and returned the list of diseases, comprising a total of 2940 patients. According to www.amar.org.ir, the number of children aged below 15 years old was 17.5 million in 2013. The incidence of tubulopathy (TP) was 168 per million population (PMP) of children. Figure 1 shows the contributing provinces. Table 1 shows the number of patients with each renal tubular disorder in different parts of Iran.

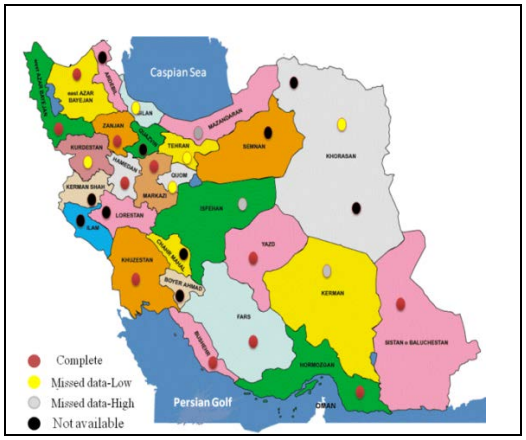

Figure 1. Collaborated Centers (n-23) in different provinces of Iran

Renal tubular disorders comprised one third of nephropathic disorders. Interestingly, the incidence of renal tubular acidosis was approximately 55.9 PMP of children aged below 15 years of age. Figure 2 shows the distribution of each class of tubular disorder reported from different centers of Iran.

Discussion

This survey showed the most frequent tubulopathies were renal tubular acidosis, calcium disorders, and cystic diseases of kidney. The estimated incidence of renal tubular acidosis and Bartter like group, cystic kidney diseases including medullary sponge kidney disease, and hereditary urolithiasis (cystinuria, primary hyperoxaluria, and hypercalciuria) was 66.3, 34.6, and 16 PMP of children below 15 years of age, respectively.

Distal renal tubular acidosis (dRTA) is the most common tupulopathy according to the Renal Tube Network [1]. Renal tubular acidosis is a rare disease defined by a normal anion gap and metabolic acidosis and is classified as distal, proximal, and type IV. Its clinical presentation is failure to thrive, rickets, renal stone, and deafness. A recent cohort of 89 patients with dRTA revealed genetic mutations in 72% of them. ATP6V1B1 and ATP6V0A4 mutations had an equal frequency [28]. Observational studies have shown dRTA in one third to half of the children with RTA [20,29-30]. Consanguineous marriage is one the most common reasons of the high rate of inherited diseases in some provinces. The genes already

detected in Iranian children with dRTA are ATP6V1B1 and KEA1 [19-21].

Cystinosis comprised 13% of the causes of RTA and had an estimated incidence of 7.42 PMP of children below 15 years in the present study. The quality of life and the knowledge of physicians and patients have been improving about cystinosis by annually holding cystinosis patient days in Iran [31]. So far, the diagnosis of cystinosis had been based on clinical findings, crystal detection in bone marrow aspiration, or corneal cystine crystal accumulation detected on ophthalmologic exam. Recently, the measurement of cystine in leukocyte and genetic study has been available in some laboratories of Iran. [24, 25, 32]. Shiraz and Tehran are the major tertiary centers for monitoring these patients. Cystinosis is a rare metabolic disorder with renal and extra-renal involvement. A worldwide survey on 213 cystinosis patients from 30 nations by Bertholet-Thomas A *et al*. showed discrepancies in the management of developing and developed countries [33].

Pafery et al. conducted an epidemiological study for genetic and clinical presentations of autosomal dominant, autosomal recessive and complex forms of inherited kidney disease in Newfoundland [34]. About 17% of patients in the present study group had **cystic kidney disease**; among them the incidence of **PKD** was 13 PMP of children.

ADPKD comprises 4.4% of the causes of CKD in Iran [35]. Gene studies have been already done for ADPKD in Iranian affected families [8-13]. There is few study about ARPKD in Iran [36].

Cystinuria includes 3% (Gilan, Mazandaran, Khuzestan) to 6% (Qom, Mashahd, Yazd, Tehran) of the causes urolithiasis in Iranian children [37-41]. Its estimated incidence was 5.8 PMP in children less than 15 years old in present survey. Gene studies in Iranian children have shown some new mutations in SLCA31 and SLC7A9 [15-18,42].

Previous studies in Iran showed the majority of tubulointerstitial nephritis was secondary to inherited tubular disorders or glomerulonephritis. Although drug induced TIN (DITIN) is a major concern and comprises 6% of acute kidney injuries in Iranian children [43], there is scare report on it [44]. As in the present survey, TIN including DITIN comprised only 0.6% of total cases. There are some studies in Iranian literatures about tubular dysfunction due to chemotherapy and beta thalassemia but TIN induced by over the counter medications and antibiotics are less considered for study [45-47].

Major concerns for rare inherited diseases are the unknown genetic cause, heterogeneity in presentation, lack of biomarkers, insufficient ontogeny, carrier state, etc [48].This was a first nationwide survey on tubular disorders in Iran. This information might help to prioritize the local investigation, promote collaboration to unveil the unknown points, to guide to draw schema of knowledge transfer to public, to policy making in health, etc.

This study had some limitations like duplicate hospital admissions and lack of information on age category and gender of the reported cases. We added the genetic studies already done in Iranian families with hereditary tubulopathies as an appendix to Table 1. There is still no published information about genetic analysis of nephrogenic DI, Bartter syndrome, Gitelman syndrome, hyperoxaluria, and calcium and magnesium disorders.

Conclusions

This survey showed renal tubular acidosis, calcium disorders, and renal cystic disease were the most frequently diagnosed tubulopathies in different centers of Iran

Our findings regarding the high incidence and different etiologies of inherited tubulopathies may provide a basis for designing targeted therapeutic interventions in the future and strategies for gene therapy of these complex disorders.

Acknowledgement

The abstract of this study was presented orally in the 3rd International Congress of Iranian Society of Pediatric Nephrology held on 29-31 October 2013 in Tehran, Iran [49]. We would like to thank Professor Farahnak Assadi for critical review of the draft of the manuscript and his precise comments.

Conflict of Interest

None declared.

Financial Support

None declared.

Table 1. Summaries of the Tubular Disorders in Iran

	Geographical division						Incidence PMP age < 15 yrs old	Gene Study [5-27]
	North	South	West	East	Center	Total		
Cystic Disease, n(%)	**85 (16)**	**107 (21)**	**73 (14)**	**31 (6)**	**208 (41)**	**504 (17)**	**28.8**	
Nephronophtisis	6	48	21	12	43	130		(**NPHP1**) [5-6]
								NPHP5 / (c.1504C > T, p. R502) [7] (**NPHP5/IQCB1**)
Polycystic Kidney Disease	23	34	38	16	118	229		**PKD1** (c.3057 GTG>ATG) [8-11] (c.2241ACA > GCA) / (c.3710 CAC > AAC) KG8, 16AC2.5 D6S1344, D16S283, KG8 /D4S423 D16S521,SM7,Kh8
								PKD2 (c.1094+1G>A) [8-13] c.1142delG AFM224x6 D4S395, D4S1534, D4S423,D4S414
Other cystic disease	56	25	14	3	47	145		**BBS3** (3p13p12) [14]
Amminoaciduria & Glycosuria, n(%)	**18 (12)**	**35 (22)**	**41 (26)**	**20 (13)**	**41 (26)**	**155 (5)**	**8.85**	
Aminoaciduria	3			12	1	16		
Glycosuria	9	8	11	5	4	37		
Cystinuria	6	27	30	3	36	102		**SLC3A1 /rBAT** (c.-29A>G) [15-17] (G105R) M467K /G38G, c. 610 + 169C>T c. 610 + 147C>G
								SLC7A9 (c.272-273 insA) [16,18] c.1136+2/3delT
Renal Tubular Disorder of Electrolyte regulation, n(%)	**9 (0.03)**	**54 (20)**	**24 (0.08)**	**33 (12)**	**152 (55.8)**	**272 (9)**	**15.5**	
Bartter syndrome	7	34	19	27	44	131		
Gitelman syndrome	2	7	3	1	59	72		
Liddle syndrome		6	1	1	1	9		
GRA				3		3		
Pseudohypoaldosteronism I		4	1		34	39		
Gordon II		3		1	14	18		
Calcium Disorders, n(%)	**54**	**271**	**62**	**37**	**366**	**790 (27)**	**45**	
Hypocalcemic Hypercalciura Familial			20	7	121	148		
Hypocalcemia -AR				3	123	126		
Hypercalciuria- Idiopathic	54	271	42	27	122	516		
Magnesium Disorders, n(%)	**0**	**11**	**2**	**1**	**7**	**21(0.7)**	**1.2**	
Hypomagnesemia					7	7		
Hypomagnesemic Hypercalciuria			1	1		2		
Hypomagnesemic-Hypocalcemia		10	1			11		
Hypomagensemia mitochondrial		1				1		

Renal Tubular Acidosis (RTA),n(%)	**43**	**140**	**130**	**225**	**447**	**979 (33)**	**55.9**	
RTA	19	80	52	106	177	434		ATP6V1B1 /[19,20] (P385fsX441) (P346R) (KAE1) [21]
Lowe Syndrome	1	2		1		4		
Idiopathic Fanconi Syndrome	1	6	3	69		79		
Secondary Fanconi Syndrome	9	28	11	20	177	245		
Fanconi bickel			3		32	35		**GLUT2** [22-23] (c.1061_1066del6, p.V355_S356del2) (P.A229QFsX19)
Von Gierke		1	6		1	8		
Cystinosis	2	21	35	12	60	130		**CTNS** [24-25] (c.153-155insCT), (c.923G>A c.18–21delGACT, c.1017G>A, c.681G>A) (c.969C>A; p. N323K) (c.257-258delCT; p.S86FfsX37 (c.661insT; p.V221CfsX6 , c.92insG; p.V31GfsX28 c.120delC; p.T40TfsX10
Medullary Sponge Kidney	11	2	10	17		40		
Diabetes Insipidus, n(%)	16	11	12	13	27	**79(3)**	**4.5**	
Nephrogenic DI	15	8	9	6	20	58		
Wolfram	1	3	3	7	7	21		(**WFS1**) [26=27] Exon8 “c.2173_2177dupTCTTC” d c.1185 C>T, c.2433 G>A, c.2565 A>G (neutral), c.997 A>G (I332V), c.1762 T>G (W588G), c.1832 G>A (H611R), c.1963 G>A (E655K)
Hyperoxaluria, n(%)	**6**	**12**	**10**	**3**		**31(1)**	**1.7**	
Tubulointerstitial Nephritis (TIN), n(%)	**17**	**29**	**39**	**19**	**9**	**113(4)**	**6.4**	
Acute TIN	7	17	7	5	8	44		
Chronic TIN	3	6	2	8	1	20		
Drug induced Tubulopathy	7	6	30	6		49		

PMP: Per million populations, GRA: glucocorticoid remediable aldosteronism, DI: Diabetes Insipidus

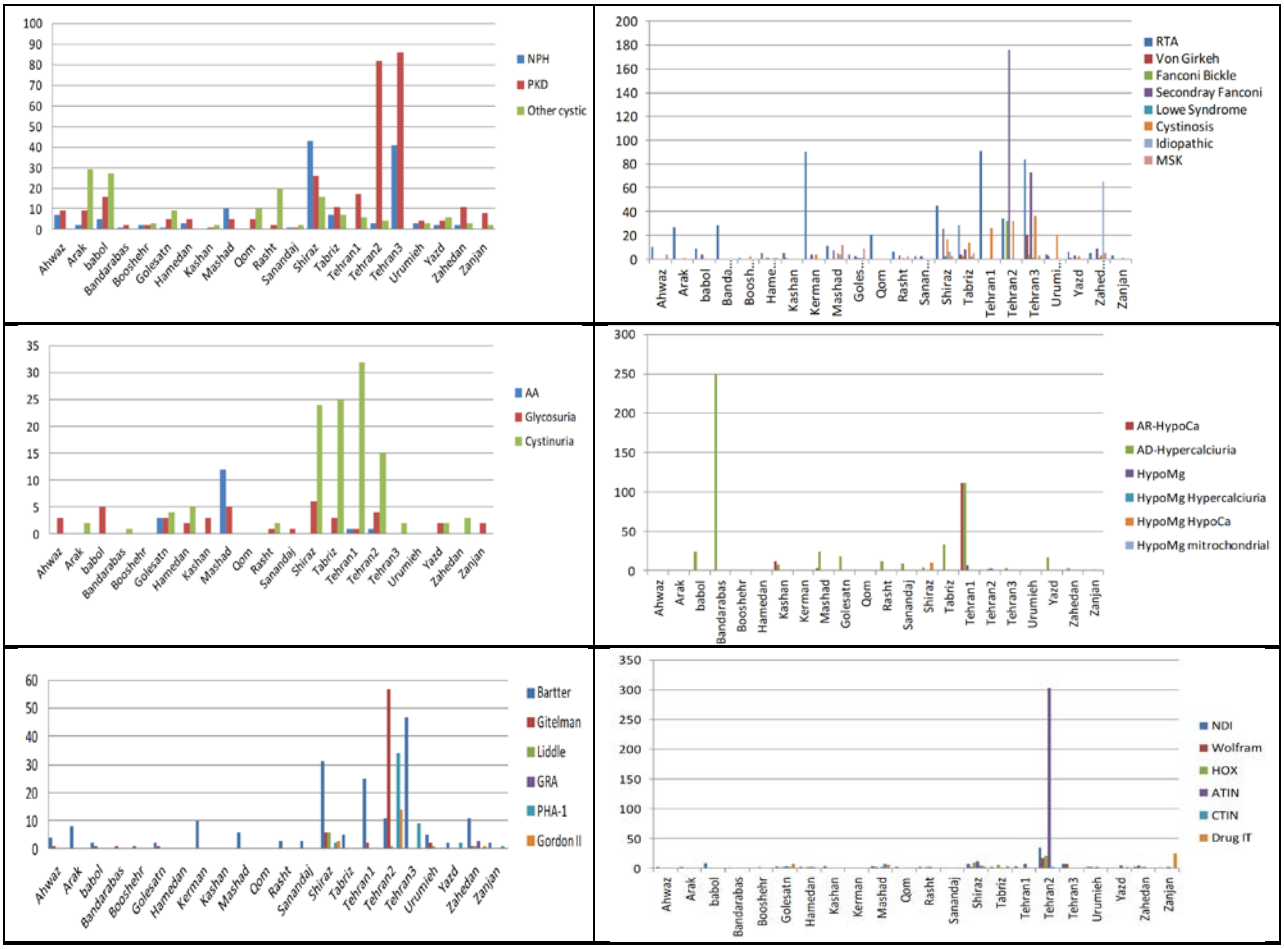

Figure 2. The distribution of each class of tubular disorder reported from different centers of Iran

References

1. Mejía N, Santos F, Claverie-Martín F, García-Nieto V, Ariceta G, CastañoL. RenalTube group. Renal Tube: a network tool for clinical and genetic diagnosis of primary tubulopathies. Eur J Pediatr. 2013 Jun;172(6):775-80. doi:10.1007/s00431-013-1934-6. Epub 2013 Feb 7. PubMed PMID:23389821.
2. Khosravi M, Walsh SB. The long-term complications of the inherited tubulopathies: an adult perspective. Pediatr Nephrol. 2015;30(3):385-95. doi: 10.1007/s00467-014-2779-6. Epub 2014 Feb 25. Review. PubMed PMID: 24566812.
3. Hooman N, Esfahani ST, Mohkam M, Derakhshan A, Gheissari A, VazirianS, Mortazavi F, Ghane-Sherbaff F, Falak-Aflaki B, Otoukesh H, Madani A, Sharifian-Dorcheh M, Mahdavi A, Esmaeile M, Naseri M, Azhir A, Merikhi A, Mohseni P, Ataei N, Fallahzadeh MH, Basiratnia M, Hosseini-Al-Hashemi G. The outcome of Iranian children on continuous ambulatory peritoneal dialysis: the first report of Iranian National Registry. Arch Iran Med. 2009 Jan;12(1):24-8. PubMed PMID: 19111025.
4. Mortazavi F, Rafiee A, 2010. Etiology of Pediatric Chronic Kidney Diseases in North-West of Iran. Pakistan Journal of Biological Sciences, 13: 456-459. **DOI:**10.3923/pjbs.2010.456.459.
5. Gheissari A, Harandavar M, Hildebrandt F, Braun DA, Sedghi M, Parsi N, Merrikhi A, Madihi Y, Aghamohammadi F. Gene mutation analysis in Iranian children with nephronophthisis: a two-center study. Iran J Kidney Dis. 2015 Mar;9(2):119-25. PubMed PMID: 25851290.
6. Haghighi A, Savaj S, Haghighi-Kakhki H, Benoit V, Grisart B, Dahan K. Identification of an NPHP1 deletion causing adult form nephronophthisis. Ir J Med Sci. 2016;185(3):589-95. doi: 10.1007/s11845-015-1312-7. Epub 2015 Jun 4. PubMed PMID: 26037636.
7. Haghighi A, Al-Hamed M, Al-Hissi S, Hynes AM, Sharifian M, Roozbeh J, Saleh-Gohari N, Sayer JA. Senior-Loken syndrome secondary to NPHP5/IQCB1 mutation in an Iranian family. NDT Plus. 2011 Dec;4(6):421-3. doi: 10.1093/ndtplus/sfr096. Epub 2011 Aug 18. PubMed PMID: 25984213; PubMed Central PMCID: PMC4421651.

8. Hafizi A, Khatami SR, Galehdari H, Shariati G, Saberi AH, Hamid M. Exon sequencing of PKD1 gene in an Iranian patient with autosomal-dominant polycystic kidney disease. Iran Biomed J. 2014 Jul;18(3):143-50. PubMed PMID: 24842140;PubMed Central PMCID: PMC4048478.
9. Radpour R, Haghighi MM, Ohadi M, Broumand B, Najmabadi H, Asghar Hagibeigi A. Molecular Study of Pkd1 & Pkd2 Genes by Linkage Analysis And Determining The Genotype iphenotype Correlations In Several Iranian Families With Autosomal Dominant Polycystic Kidney Disease. Medical Journal of the Islamic Republic of Iran. MIIRI, 2005;19(1):65-75.
10. Akhavan-Sepahi M, Saghafi H, Mousavi Movahed SM, Haeri MR, Shokrollahi SMR, Hakimelahi J, Movahedi Z, Houshmand M, Gharehbeglou M. An Investigation on Linkage Analysis in Autosomal Dominant Polycystic Kidney Patients in Qom Province in 2014. Bimonthly Journal of Sabzevar University of Medical Sciences 2015;22(5):740-747.
11. Jabbarpour Bonyadi M; Emamalizadeh A; Argani H; Omrani O; Association analysis of autosomal dominant polycystic kidney disease in familial type in East-Azerbaijan. Medical Journal of Tabriz University of Medical Sciences and Health Services. 2007; 29(2);31-37.
12. Entezam M, Khatami MR, Saddadi F, Ayati M, Roozbeh J, Keramatipour M. PKD2 mutation in an Iranian autosomal dominant polycystic kidney disease family with misleading linkage analysis data. Kidney Res Clin Pract. 2016 Jun;35(2):96-101.doi: 10.1016/j.krcp.2016.02.003. Epub 2016 Feb 27. PubMed PMID: 27366664; PubMed Central PMCID: PMC4919558.
13. Vazifehmand R, Rossetti S, Saber S, Khorshid HR, Harris PC. Molecular analysis of a consanguineous Iranian polycystic kidney disease family identifies a PKD2 mutation that aids diagnostics. BMC Nephrol. 2013 Sep 8;14:190. doi:10.1186/1471-2369-14-190. PubMed PMID: 24011172; PubMed Central PMCID:PMC3846117.
14. Ghadami M, Tomita HA, Najafi MT, Damavandi E, Farahvash MS, Yamada K, Majidzadeh-A K, Niikawa N. Bardet-Biedl syndrome type 3 in an Iranian family: clinical study and confirmation of disease localization. Am J Med Genet. 2000 Oct 23;94(5):433-7. PubMed PMID: 11050632.
15. Markazi S, Kheirollahi M, Doosti A, Mohammadi M, Koulivand L. A Novel Mutation in SLC3A1 Gene in Patients With Cystinuria. Iran J Kidney Dis. 2016 Jan;10(1):44-7. PubMed PMID: 26837681.
16. Koulivand L, Mohammadi M, Ezatpour B, Salehi R, Markazi S, DashtiS, Kheirollahi M. Mutation analysis of SLC3A1 and SLC7A9 genes in patients with cystinuria. Urolithiasis. 2015 Oct;43(5):447-53. doi: 10.1007/s00240-015-0794-0.Epub 2015 Jun 30. PubMed PMID: 26123750.
17. Markazi S, Kheirollahi M, Doosti A, Mohammadi M. Report of *SLC3A1*/rBAT gene mutations in Iranian cystinuria patients: A direct sequencing study. J Res Med Sci2017;22:33.
18. Fazaeli S, Ashouri S, Kheirollahi M, Mohammadi M, Fazilati M. A Novel Mutation in SLC7A9 Gene in Cystinuria. Iran J Kidney Dis. 2017 Mar;11(2):138-141. PubMed PMID: 28270646.
19. Zeinali F, Mohseni M, Fadaee M, Fattahi Z, Najmabadi H, Otukesh H, KahriziK. Investigation of ATP6V1B1 and ATP6V0A4 genes causing hereditary hearing loss associated with distal renal tubular acidosis in Iranian families. J Laryngol Otol. 2014 128(12):1056-9 doi: 101017/S0022215114002540. PubMed PMID:25498251.
20. Sharifian M, Esfandiar N, Mazaheri S, Kariminejad A, Mohkam M, Dalirani R, Esmaili R, Ahmadi M, Hassas-Yeganeh M. Distal renal tubular acidosis and its relationship with hearing loss in children: preliminary report. Iran J Kidney Dis. 2010 Jul;4(3):202-6. PubMed PMID: 20622307.
21. Hooman N, Otukesh H, Fazilaty H, Torktaz I, Hosseini R, Behnam B. A novel mutation pattern of kidney anion exchanger 1 gene in patients with distal renal tubular acidosis in Iran. Iran J Kidney Dis. 2015 May;9(3):230-8. PubMed PMID:25957428.
22. Abbasi F, Azizi F, Javaheri M, Mosallanejad A, Ebrahim-Habibi A, Ghafouri-Fard S. Segregation of a novel homozygous 6 nucleotide deletion in GLUT2 gene in a Fanconi-Bickel syndrome family. Gene. 2015 Feb 15;557(1):103-5. doi:10.1016/j.gene. 2014.12.024. Epub 2014 Dec 15. PubMed PMID: 25523092.
23. Hadipour F, Sarkheil P, Noruzinia M, Hadipour Z, Baghdadi T, Shafeghati Y. Fanconi Bickel syndrome versus osteogenesis imperfeeta: An Iranian case with a novel mutation in glucose transporter 2 gene, and review of literature. Indian J Hum Genet. 2013;19(1):84–86. doi: 10.4103/09716866.112906.
24. Shahkarami S, Galehdari H, Ahmadzadeh A, Babaahmadi M, Pedram M. The first molecular genetics analysis of individuals suffering from nephropatic cystinosis in the Southwestern Iran. Nefrologia.2013;33(3):308-15. doi: 10.3265/Nefrologia.pre2012.11558. Epub 2013 Feb 15. PubMed PMID:23640116.
25. Ghazi F, Hosseini R, Akouchekian M, Teimourian S, Ataei Kachoei Z, Otukesh H, Gahl WA, Behnam B. CTNS molecular genetics profile in a Persian nephropathic cystinosis population. Nefrologia. 2017 Feb 23. pii: S0211-6995(17)30006-1. doi: 10.1016/j.nefro.2016.11.024. [Epub ahead of print] English, Spanish. PubMed PMID:28238446.
26. Sobhani M, Tabatabaiefar MA, Rajab A, Kajbafzadeh AM, Noori-Daloii MR. Molecular characterization of WFS1 in an Iranian family with Wolfram syndrome reveals a novel frameshift mutation associated with early symptoms. Gene. 2013 Oct 10;528(2):309-13. doi: 10.1016/j.gene.2013.06.040. Epub 2013 Jul 8. PubMed PMID: 23845777.
27. Alimadadi A, Ebrahim-Habibi A, Abbasi F, Amoli M, Sayahpour FA, Larijani B. Novel mutations of wolframin: a report with a look at the protein structure. Clin Genet. 2011 Jan;79(1):96-9. doi: 10.1111/j.1399-0004.2010.01511.x. PubMed PMID:21143470.
28. Palazzo V, Provenzano A, Becherucci F, Sansavini G, Mazzinghi B, Orlandini V, Giunti L, Roperto RM, Pantaleo M, Artuso R, Andreucci E, Bargiacchi S, Traficante G, Stagi S, Murer L, Benetti E, Emma F, Giordano M, Rivieri F, Colussi G, Penco S, Manfredini E, Caruso MR, Garavelli L, Andrulli S, Vergine G, Miglietti N, Mancini E, Malaventura C, Percesepe A, Grosso E, Materassi M, Romagnani P, Giglio S. The genetic and clinical spectrum of a large cohort of patients with distal renal tubular acidosis. Kidney Int.2017;91(5):1243-1255.doi: 10.1016/j.kint.2016.12.017.

29. Ahmad-Zadeh A. Renal tubular acidosis in children: Report of 25 cases from Ahwaz Scientific Medical Journal of Ahwaz University of Medical Sciences 1378;(26):66-76.
30. Mortazavi F, Ghergherehchi R. Causes of Nephrocalcinosis in Children Referring to Children's Hospital of Tabriz. Urmia Medical Journal 1391; 23(2): 172-177.
31. Basiratnia M. Cystinosis Patient Day in Iran. J Ped. Nephrology 2014;2(3):104-106.
32. Hosseini S, Kalantar E. Measurement of Cystine in PMN Cells by Liquid Chromatography –Tandem Mass Spectrometry. J Ped. Nephrology, Suppl1: 2013;10.
33. Bertholet-Thomas A, Berthiller J, Tasic V, Kassai B, Otukesh H, Greco M, Ehrich J, de Paula Bernardes R, Deschênes G, Hulton SA, Fischbach M, SoulamiK, Saeed B, Valavi E, Cobenas CJ, Hacihamdioglu B, Weiler G, Cochat P, Bacchetta J. Worldwide view of nephropathic cystinosis: results from a survey from 30 countries. BMC Nephrol. 2017 Jul 3;18(1):210. doi: 10.1186/s12882-017-0633-3. PubMed PMID: 28673276; PubMed Central PMCID: PMC5496396.
34. Parfrey PS, Davidson WS, Green JS. Clinical and genetic epidemiology of inherited renal disease in Newfoundland. Kidney Int. 2002 Jun;61(6):1925-34. Review. PubMed PMID: 12028433.
35. Ebner K, Schaefer F, Liebau MC; ARegPKD Consortium. Recent Progress of the ARegPKD Registry Study on Autosomal Recessive Polycystic Kidney Disease. Front Pediatr. 2017;16(5):18. doi: 10.3389/fped.2017.00018. eCollection 2017. PubMed PMID: 28296980; PubMed Central PMCID: PMC5327862.
36. Nafar M, Mousavi SM, Mahdavi-Mazdeh M, Pour-Reza-Gholi F, Firoozan A, Einollahi B, Lessan-Pezeshki ML, Asbaghi-Namini S, Farrokhi F. Burden of chronic kidney disease in Iran: a screening program is of essential need. Iran J Kidney Dis. 2008 Oct;2(4):183-92. PubMed PMID: 19377235.
37. Kheradpir MH, Bodaghi E. Childhood urolithiasis in Iran with special reference to staghorn calculi. Urol Int. 1990;45(2):99-103. PubMed PMID: 2330666.
38. Sepahi MA, Heidari A, Shajari A. Clinical manifestations and etiology of renal stones in children less than 14 years age. Saudi J Kidney Dis Transpl2010;21:181-4.
39. Naseri M, Varasteh AR, Alamdaran SA. Metabolic factors associated with urinary calculi in children. Iran J Kidney Dis. 2010 Jan;4(1):32-8. PubMed PMID:20081302.
40. SafaeiAsl A, Maleknejad S. Pediatric urolithiasis: an experience of a single center. Iran J Kidney Dis. 2011 Sep;5(5):309-13. PubMed PMID: 21876306.
41. Mohammadjafari H, Barzin M, Salehifar E, KhademiKord M, Aalaee A, Mohammadjafari R. Etiologic and epidemiologic pattern of urolithiasis in north iran;review of 10-year findings. Iran J Pediatr. 2014 Feb;24(1):69-74. Epub 2014 Jan 1. PubMed PMID: 25793048; PubMed Central PMCID: PMC4359607.
42. Koulivand L, Mohammadi M, Ezatpour B, Kheirollahi M. Cystinuria in a patient with a novel mutation in SLC7A9 gene. Iran J Kidney Dis. 2015 Jan;9(1):63-6. PubMed PMID: 25599739.
43. Hooman N. Acute Kidney Injury in Iranian Children - What Do We Know About It? - Part 2. J Ped. Nephrology 2014;2(3):98-103.
44. Koochak A, Babaheidarian P, Hooman N, Mehrazma M. Clinicopathological Findings in Pediatric Tubulointerstitial Nephritis: Iranian Experience. J Ped. Nephrology 2015;3(4):139-142.
45. Arjmandi Kh, Hooman N. , Vossough P. Evaluation Of Renal Proximal Tubular Function In Children Undergoing Chemotherapy In Ali Asghar Children's Hospital. The Razi Journal of Medical Sciences 1386;14(55): 197-205.
46. Zareifar S, Jafari H, Geramizadeh B, Basiratnia M, Golafshan H, Cohan N, Mehravar Z, Hamidi R. The evaluation of cisplatin effect on tubular function in children on chemotherapy. Pediatr Hematol Oncol. 2013;30(1):18-24. doi: 10.3109/08880018.2012.737093. Epub 2012 Nov 19. PubMed PMID: 23163346.
47. Naderi M, Sadeghi-Bojd S, Valeshabad AK, Jahantigh A, Alizadeh S, Dorgalaleh A, Tabibian S, Bamedi T. A prospective study of tubular dysfunction in pediatric patients with Beta thalassemia major receiving deferasirox. Pediatr Hematol Oncol. 2013;30(8):748-54. doi: 10.3109/08880018.2013.823470. PubMed PMID: 24134694.
48. Devuyst O, Knoers NV, Remuzzi G, Schaefer F; Board of the Working Group for Inherited Kidney Diseases of the European Renal Association and European Dialysis and Transplant Association. Rare inherited kidney diseases: challenges, opportunities, and perspectives. Lancet. 2014 May 24;383(9931):1844-59. doi:10.1016/S0140-6736(14)60659-0. Review. PubMed PMID: 24856029; PubMed Central PMCID: PMC4135047.
49. Hooman N, Derakhshan A, Javadilarijani F, Mortazavi F, Falakaflaki B, Sadeghi-Bojd S, Nikibakhsh AA, Esteghamati M, Ghassemi K, Mohkam M, Ghaneh- Sherbaf F,Ghazanfari F, Sorkhi H,Safaiyan B, Yousefichaijan P, Kajbafzadeh A, Safaei-Asl A, Shakiba M, Shajari A, Valavi E, Sharif MR, Akhavan-Sepahi M, Momtaz HE, Eskandarifar AR, Ghasemi Kh, Iranian Society of Pediatric Nephrology. The Etiology of Tubulopathy in Iranian Children- Iranian Society of Pediatric Nephrology Collaboration. J Ped. Nephrology 2013; Sup1(1):2.