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Original Article

Analyses of ultrasound-guided percutaneous pediatric kidney biopsy results: A single center experience

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Abstract

Aim: Percutaneous pediatric kidney biopsies (KB) performed in our center for the past 5 years were evaluated retrospectively. The relationship was examined between histopathological results and variables such as age, gender and ethnicity (Turkish and Syrian children).

Material and Methods: A total 330 ultrasound-guided percutaneous pediatric KBs were performed in our center between January 2015 and September 2019. The study included 318 pediatric patients comprising 152 females and 178 males with a mean age of 9.50 ± 4.89 years (range, 2 months- 18 years). Indications, results and complications of the KBs were retrospectively evaluated. Histopathological results were statistically compared between genders and three age groups (0-2, 2-12 and 12-18 years of age). Comparisons were made between the ethnicities and histopathological results.

Results: The most common indication for KB was nephrotic syndrome (n: 220, 66.7%). In the biopsy results, the most common primary (n: 230, 69.7%) and secondary (n: 74, 22.4%) glomerular diseases were focal segmental glomerulosclerosis (n: 101, 30.6%) and Henoch-Schönlein purpura nephritis (n: 41, 12.4%), respectively. A statistically significant relationship was determined between the biopsy results and age and gender. No statistically significant relationship was observed between the biopsy results and ethnicity.

Conclusion: KB is an important intervention for the identification of glomerular diseases, requiring appropriate treatment in children. The ethnic origin of the patients had no effect on the frequency of the type of the diseases.

Keywords: Childhood; glomerulonephritis; nephrotic syndrome; renal biopsy

INTRODUCTION

After congenital obstructive urinary system anomalies, glomerulonephritis (GN) is the second leading reason for chronic kidney disease (CKD) in childhood. Reported etiological differences related to parenchymal diseases of the kidney depend on geographic, environmental, cultural, genetic and ethnic variables. Epidemiological information, and the clinical and histopathological features of the glomerular diseases provide accurate diagnosis and determine the appropriate therapy options (1,2).

Kidney biopsy (KB) is an invasive method for diagnostic and prognostic assessment of pediatric parenchymal kidney diseases. It provides essential information to the clinicians for diagnosis, evaluation and monitoring of the disease, and planning the treatment options (3). However, the procedure carries a risk of some complications, including perirenal hematoma, arteriovenous fistula, infection, or loss of the kidney (4).

The aim of this study was to retrospectively evaluate the indications, results and complications of KBs in a pediatric population in a single center of a south-eastern Anatolian city in the past 5 years. The possible relationships were investigated of the histopathological results of KBs with gender, biopsy age and different ethnicities.

MATERIAL and METHODS

This study was carried out after the approval of the Local Ethics Committee (Gaziantep University, 2019/307).

A retrospective analysis was made of 330 KBs, performed in 318 pediatric patients, between January 2015 and September 2019, in a single center in Southeastern Anatolia. Patients were excluded from the study if they were aged>18 years, or if there was missing demographic or laboratory information or data about previous clinical history.

As soon as clinical diagnoses and indications were determined by the pediatric nephrologist, biopsy procedures were planned. First, analysis was performed of essential serum parameters, such as platelet count, prothrombin time, partial thromboplastin time and INR

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(international normalized ratio) values. Eligible patients were instructed to fast for 6-8 hours. After informing the parents of the patients (Syrian refugees were informed in Arabic by a translator), a signed consent form was obtained before the procedures.

All biopsies were performed percutaneously with local anesthesia after monitoring vital signs. A Toshiba Famio (SSA-530A) system (2005, Japan) with a 3.75 Mhz convex probe was used for ultrasound guidance. For children aged ≤14 years, the procedure was initiated after obtaining intravenous (IV) sedation with IV slow infusion of 1mg/kg ketamine hydrochloride with cardiopulmonary monitoring. The procedure was explained to children aged 14-18 years and sedation was not given if the child accepted it. Each child was preferably laid in the left decubitus position, with sterile draping followed by local site cleaning with povidone iodine. The right kidney was evaluated completely with ultrasound guidance and the safest biopsy route was selected for the lower pole of the kidney in the right flank region.

After local anesthesia, 2 biopsy materials (rolls) were obtained with 2 percutaneous punctures using an 18-gauge Tru-Cut needle inserted in a fully automatic spring-loaded biopsy gun. The rolls were protected between saline-impregnated surgical sponges and taken immediately to the pathology unit. The specimen evaluated by the pathologist was considered sufficient if it contained 10 or more glomeruli. All biopsy materials were examined under a light and immunofluorescence microscope, as electron microscopy is not available at our center.

The main clinical indications of KB were nephrotic syndrome (NS), acute nephritic syndrome (ANS), hematuria and/or proteinuria of unknown cause, acute kidney failure, CKD, rapidly progressive glomerulonephritis (RPGN), systemic lupus erythematosus (SLE) classification and evaluation of cyclosporine toxicity.

After the biopsy procedure, monitoring of the patients continued and after at least 24 hours they were discharged if no complications had occurred.

The data were collected related to indications, histopathological diagnosis, hospitalization time, date of biopsy and procedure complications for KB. Kidney ultrasounds performed before and after the procedure were analyzed.

Statistical analyses

The data obtained in the study were evaluated with SPSS Version 22.0 software. Numerical values were expressed as mean ± standard deviation (SD) values or number of cases (n) and percentage (%). Relationships between categorical variables were tested with the Chi-square test. A value of $p<0.05$ was considered statistically significant.

RESULTS

A total of 330 KBs were performed in 318 pediatric patients between January 2015 and September 2019. The 318 patients who underwent biopsy had a mean age of 9.50 ± 4.89 years (range, 2 months-18 years). The whole patient population consisted of 152 females with a mean age of 9.13 ± 4.87 years (range, 4 months-18 years) and 178 males with a mean age of 9.81 ± 4.89 years (range, 2 months-17.75 years). The data of the 330 KBs were analyzed retrospectively from clinical records.

Biopsies were most commonly performed in the 2-12 years age group (n: 198, 60%), the second most frequently in patients >12 years of age (n: 112, 33.9%), and at the lowest rate in the 0-2 years age group (n: 20, 6.1%).

The clinical follow-up periods of the patients were variable according to the underlying diseases.

Of the total KB cases, 50 patients (15.2%) were refugee children from Syria, and 278 (84.2%) were citizens of the Republic of Turkey (predominantly from Gaziantep and less commonly from other neighboring cities of southeastern Anatolia). The demographic characteristics of the patients are shown in Table 1.

Table 1. Demographic characteristics of the patients undergoing biopsy

Number of patients (n)	318
Number of biopsies (n)	330
Gender	
Female n (%)	152 (46.1%)
Male n (/%)	178 (53.9%)
Age (mean±SD) (min-max)	9.50±4.89 (2 months-18 years)
0-2 years n (%)	20 (6.1%)
2-12 years n (%)	198 (60%)
> 12 year n (%)	112 (33.9%)
Nationality	
Turkish	278 (84.2%)
Syrian	50 (15.2%)
Other*	2 (0.6%)

* 1 Iraqi, 1 from Turkish Republic of Northern Cyprus

The most common indication for KB was NS in 220 (66.7%) patients, followed by RPGN in 45 (13.6%) patients, ANS in 28 (8.5%) patients, hematuria and/or proteinuria in 11 (3.3%) patients, acute kidney failure in 5 (1.5%) patients, CKD in 9 (2.7%) patients, SLE classification in 3 (0.9%) patients and evaluation of cyclosporine toxicity in 9 (2.7%) patients (Table 2).

The number of the biopsies performed between January 2015 and December 2019 by years were; 55 patients (16.7%) in 2015, 73 patients (22.1%) in 2016, 71 patients (21.5) in 2017, 81 patients (24.5%) in 2018, and 50 patients (15.2%) in 2019.

Table 2. Renal biopsy indications

Renal biopsy indications	n (%)
Nephrotic syndrome	220 (66.7%)
RPGN	45 (13.6%)
Acute nephritic syndrome	28 (8.5%)
Hematuria/ proteinuria	11 (3.3%)
Acute renal injury	5 (1.5%)
Chronic renal disease	9 (2.7%)
SLE classification	3 (0.9%)
Evaluation cyclosporine toxicity	9 (2.7%)

RPGN: Rapidly Progressive Glomerulonephritis, SLE: Systemic Lupus Erythematosus

No complications developed in 298 patients (90%) after biopsy. Self-limited macroscopic hematuria developed in 32 patients (9.7%). Perirenal hematoma was observed in 3 patients and intravesical clot retention in 1 patient. In the follow-up of patients who developed hematoma, an improvement was observed within 3 months. No patient required transfusion (Table 3). No significant relationship was found between age at biopsy and biopsy complications (p= 0.66).

Table 3. Complications rate and treatment outcome in renal biopsy

Complications	n (%)	Outcome
Major complications	-	
Minor complications	32 (9.7%)	
Perirenal hematoma, self-limited	3 (0.9%)	Recovery
Isolated macroscopic hematuria, self-limited	28 (8.4%)	Recovery
Macroscopic hematuria with intravesical clot retention, self-limited	1 (0.3%)	Recovery

The histopathological diagnoses of the KBs were as follows; primary glomerular diseases were detected in 230 (69.7%) patients and glomerular diseases secondary to systemic diseases in 74 (22.4%) patients. The most common primary glomerular disease detected in the KB was focal segmental glomerulosclerosis (FSGS) in 101 (30.6%) patients. This was followed by minimal change disease (MCD) in 36 (10.9%) patients, IgA nephritis (IgAN) in 23 (7%), acute poststreptococcal glomerulonephritis (APSGN) in 21 (6.4%) and membranoproliferative glomerulonephritis (MPGN) in 20 (6.1%). The most common secondary glomerular disease was Henoch-Schönlein purpura nephritis (HSPN) detected in 41 (12.4%) patients followed by systemic lupus erythematosus nephritis (SLEN) in 30 (9.4%) patients. The distribution of histopathological diagnoses detected in KBs is shown in Table 4.

Table 4. Determination of histopathological findings

Histopathological findings	Female n=152	Male n=178	Total n (%) n=330
Primary glomerular diseases	105	125	230 (69.7%)
FSGS	55	46	101 (30.6%)
MCD	12	24	36 (10.9%)
IGAN	8	15	23 (7%)
APSGN	6	15	21(6.4%)
MPGN	13	7	20 (6.1%)
IGMN	2	12	14 (4.2%)
MesPGN	5	2	7 (2.1%)
MGN	4	1	5 (1.5%)
C1QN	0	2	2 (0.6%)
Congenital NS	0	1	1 (0.3%)
Secondary glomerular diseases			
HSP	16	25	41 (12.4%)
SLE	18	12	30 (9.4%)
Amyloidosis	2	1	3 (0.9%)
Chronic Glomerulonephritis	4	3	7 (2.1%)
Tubulointerstitial nephritis	3	4	7 (2.1%)
Undefined*	0	6	6 (1.8%)
Other**	2	1	3 (0.9%)
Normal***	1	0	1 (0.3%)
Insufficient	1	1	2 (0.6%)

FSGS: Focal Segmental Glomerulosclerosis, MCD: MCD: Minimal Change Disease, IGAN: IGAN: IgA Nephritis, APSGN: Acute Post Streptococcal Glomerulonephritis, MPGN: Membranoproliferative Glomerulonephritis, IGMN: IgM Nephropathy, MesPGN: Mesengioproliferative Glomerulonephritis, MGN: Membranous Glomerulonephritis, C1QN: C1Q Nephropathy, NS: Nephrotic Syndrome, HSP: Henoch–Schonlein Purpura, SLE: Systemic Lupus Erythematosus. * Pathological diagnosis could not be determined clearly but later genetically determined (4 Alport Syndrome, 2 Nephronophytosis), **1 hyperoxaluria and 2 acute cellular rejection, *** The pathological result of the biopsy was completely normal and this patient was later diagnosed with Nutcracker syndrome.

Statistical analysis was made of the relationship of gender, age groups and ethnic variables with the 3 most common biopsy indications (NS, RPGN, ANS) and the 7 most frequently detected histopathological results (FSGS, MCD and HSPN, SLEN, IgAN, APSGN, MPGN).

No statistically significant relationship was found between gender, age groups and ethnic variables and the 3 most common biopsy indications (p>0.05).

A statistically significant relationship was found between gender and the 7 most frequently detected histopathological results (p= 0.03). MCD, APSGN, IgAN and HSPN were detected at a higher rate in males, and FSGS, MPGN, and SLEN rates were higher in females (Table 5).

Table 5. Evaluation of the relationship between histopathological diagnosis and gender

			Histopathological Results									p
			FSGS	MCD	HSPN	SLEN	IGAN	APSGN	MPGN	Others	Total	
Gender	Female	n	55	12	16	18	8	6	13	24	152	0.030
		(%)	54.5%	33.3%	39%	60%	34.8%	28.6%	65%	41.4%	46.1%	
	Male	n	46	24	25	12	15	15	7	34	178	
		(%)	45.5%	66.7%	61%	40%	65.2%	71.4%	35%	58.6%	53.9%	
Total		n	101	36	41	30	23	21	20	58	330	
		(%)	100%	100%	100%	100%	100%	100%	100%	100%	100%	

FSGS: Focal Segmental Glomerulosclerosis, MCD: Minimal Change Disease, IGAN: IgA Nephritis, APSGN: Acute Post Streptococcal Glomerulonephritis, MPGN: Membranoproliferative Glomerulonephritis, HSPN: Henoch–Schonlein Purpura Nephritis, SLEN: Systemic Lupus Erythematosus Nephritis

Table 6. Evaluation of the relationship between histopathological diagnosis and age

			Histopathological Results									p
			FSGS	MCD	HSPN	SLEN	IGAN	APSGN	MPGN	Others	Total	
Age	0-2	n	15	0	0	1	0	0	1	3	20	0.001
		(%)	14.9%	0%	0%	3.3%	0%	0%	5%	5.2%	6.1%	
	2-12	n	66	26	27	11	15	14	12	27	198	
		(%)	65.3%	72.2%	65.9%	36.7%	65.2%	66.7%	60%	46.6%	60%	
	> 12	n	20	10	14	18	8	7	7	28	112	
		(%)	19.8%	27.8%	34.1%	60%	34.8%	33.3%	35%	48.3%	33.9%	
Total		n	101	36	41	30	23	21	20	58	330	
		(%)	100%	100%	100%	100%	100%	100%	100%	100%	100%	

FSGS: Focal Segmental Glomerulosclerosis, MCD: Minimal Change Disease, IGAN: IgA Nephritis, APSGN: Acute Post Streptococcal Glomerulonephritis, MPGN: Membranoproliferative Glomerulonephritis, HSPN: Henoch–Schonlein Purpura Nephritis, SLEN: Systemic Lupus Erythematosus Nephritis

A statistically significant relationship was determined between age groups and histopathological results (p=0.001). FSGS, MCD, MPGN, IgAN, APSGN, and HSPN were seen most commonly between the ages of 2-12 years and SLEN was most commonly seen in patients aged > 12 years (Table 6).

DISCUSSION

This study presents the statistical information about childhood renal diseases proven with percutaneous biopsy in a tertiary university hospital in the region of southeastern Anatolia, Turkey.

As in previously reported series, idiopathic NS was the most common indication for KB in the current study (2, 5, 6). In order of frequency, other indications were as follows; RPGN, ANS, hematuria and/or proteinuria, acute kidney failure, CKD, SLE classification and evaluation of cyclosporine toxicity.

There was a male predominance in the overall population of this paediatric study. With the exception of FSGS, MPGN and SLEN, other primary or secondary glomerular diseases were detected more often in males. Cakici et al. reported that the most common histopathological diagnosis in children aged >13 was IgAN (2). In this current study, the most common diagnosis was FSGS in all age groups. The frequency of SLEN was seen to be relatively higher in children aged >12 years, while the other 6 most frequent GNs were seen in younger patients. This finding was consistent with the study of Imtiaz et al (7).

Possible complications of KB include gross hematuria, peri-pararenal hematoma, infection, arterio-venous fistulas, injury of the major vascular structures of the renal hilum, and adjacent organ (liver, spleen, colon etc.) injuries (2,8). Reported overall complication rates range from 2.6% to 43% in different series. These rates may change due to different imaging guidance, different caliber needles and postprocedural follow-up and control imaging (2,3,9-14).

Macroscopic hematuria requiring blood transfusion or visceral injuries requiring endovascular intervention or nephrectomy surgery are major complications which may be encountered following KB (15). In the current study, no major complication developed in any patient. Minor complications were seen as self-limited macroscopic hematuria with or without perirenal hematoma in 32 cases, all of which spontaneously healed. No complication such as hypoxia due to iv sedation developed in any patient. The success and complication rates were determined to be 99% and 9.7%, respectively. Insufficient sampling which required repeated biopsies was determined in 2 cases (0.6%).

While MCD is the leading reason for steroid sensitive NS, FSGS is the common cause of steroid resistant NS (16,17). Demircin et al reported from Ankara (central Anatolian city) that MPGN was the most common primary GN, and HSPN was the most common secondary GN (18). In the current study, the most frequent primary GN was FSGS and the leading secondary GN was HSPN, as in a recently published study from Ankara (from the same clinic as Demircin et al, but in a different date range). They associated the time-varying prevalence in the histological types of GN, with differences in the biopsy approach due to increasing response to the steroid and new treatment options (2). In a study by Yavaşcan et al. from Izmir (western Anatolian city) and in another study by Cakmakci et al. from Istanbul (the largest city, located in north-western Turkey) FSGS was reported to be the most common result, followed by the MCD (19,20). There seems to be an increasing rate of steroid-resistant NS in Turkey. The histopathological results of paediatric KBs may differ in other countries (21). In studies from both China and the UK, MCD was the most common primary GN and HSPN was the most common secondary GN (6, 8). The article previously mentioned from Pakistan, reported that MCD was the most common primary GN and SLEN was the most common secondary GN in their samples (7). In a study from Italy it was reported that IgAN was the most common primary GN followed by MCD (22).

Studies have revealed that complex interactions of genetic and environmental influences affect the incidence of childhood NS in different races and ethnicities. A study from Canada reported that the incidence of childhood NS was significantly higher among South Asian children (from India, Bangladesh, and Pakistan) compared with European and East/Southeast Asian children (23,24). More than 50 genes have been determined in relation to NS in different populations (16,25). There is an increased risk of recessive inherited diseases emerging due to consanguineous marriages (26). A recent genetic-based study proved the relationship between childhood-onset FSGS and mutation of an autosomal recessive gene (CD2AP) in siblings born to consanguineous parents, both in human and in a created mice model (27). Parental consanguinity is a common status in southeastern Turkey and in Arabic countries (28,29), although there have been no studies on NS and associated genes in these regions as yet. As a limitation of the current study, there were no data available about the parental consanguinity of the patients. Thus, its relevance to the results could not be investigated. Genetic examinations were performed in only a few children whose histopathological results were insufficient to determine underlying disease. Although there were relatively few Syrian refugee children, there was no statistically significant difference in respect of the frequency of the histopathological results compared to the ethnic Turkish children.

There were some limitations of this study, primarily that it was retrospective in design. Second, some patients were lost to follow-up so detailed information about the course of the disease, therapy results and prognosis was not available. Third, since electron microscopy was not available in our center, the diagnosis in some cases could not be made from KB. Fourth, the lack of knowledge about parental consanguinity prevented more detailed investigation. Finally, the sample size of the refugee children was relatively small.

Nevertheless, this study provides useful epidemiological information. It was aimed to present the indications, histopathological results and complications of paediatric KBs performed in the past 5 years, in a single center. The results were examined in respect of the gender, age and ethnicity variables of the children.

CONCLUSION

KB is an important intervention for identification of glomerular diseases requiring urgent and appropriate treatment, determination of renal involvement of some systemic diseases, and the diagnosis of rare familial nephropathies. Some GNs are observed more frequently in females or males and some are more common in different age ranges. Similar rates of various GNs can be seen in children living in neighboring countries.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: This study was carried out after the approval of the Local Ethics Committee (Gaziantep University, 2019/307).

REFERENCES

1. Warady BA, Chadha V. Chronic kidney disease in children: the global perspective. Pediatr Nephrol 2007;22:1999-2009.
2. Cakici EK, Yazilitas F, Uner C, et al. Indications and Outcomes of Renal Biopsies in Children: A Single-Center 12-Year Experience. Turk J Nephrol 2019;28:250-6.
3. Feneberg R, Schaefer F, Zieger B, et al. Percutaneous renal biopsy in children: a 27-year experience. Nephron 1998;79:438-46.

4. Tondel C, Vikse BE, Bostad L, et al. Safety and complications of percutaneous kidney biopsies in 715 children and 8573 adults in Norway 1988-2010. Clin J Am Soc Nephrol 2012;7:1591-7.
5. Hod Feins R, Tobar A, Davidovits M. Yield and complications of kidney biopsy over two decades in a tertiary pediatric center. Pediatr Int 2017;59:452-7.
6. Yin XL, Zou MS, Zhang Y, et al. Twenty-three-year review of disease patterns from renal biopsies: an experience from a pediatric renal center. J Nephrol 2013;26:699-707.
7. Imtiaz S, Nasir K, Drohlia MF, et al. Frequency of kidney diseases and clinical indications of pediatric renal biopsy: A single center experience. Indian J Nephrol 2016;26:199-205.
8. Hussain F, Mallik M, Marks SD, et al. Renal biopsies in children: current practice and audit of outcomes. Nephrol Dial Transplant 2010;25:485-9.
9. Kamitsuji H, Yoshioka K, Ito H, et al. Percutaneous renal biopsy in children: survey of pediatric nephrologists in Japan. Pediatr Nephrol 1999;13:693-6.
10. Hussain F, Watson AR, Hayes J, et al. Standards for renal biopsies: comparison of inpatient and day care procedures. Pediatr Nephrol 2003;18:53-6.
11. White RHR, Poole C. Day care renal biopsy. Pediatr Nephrol 1996;10:408-11.
12. Chesney DS, Brouhard BH, Cunningham RJ. Safety and cost effectiveness of pediatric percutaneous renal biopsy. Pediatr Nephrol 1996;10:493-5.
13. Simckes AM, Blowey DL, Gyves KM, et al. Success and safety of same-day kidney biopsy in children and adolescents. Pediatr Nephrol 2000;14:946-52.
14. Davis ID, Oehlenschlager W, O'Riordan MA, et al. Pediatric renal biopsy: should this procedure be performed in an outpatient setting? Pediatr Nephrol 1998;12:96-100.
15. Hogan JJ, Mocanu M, Berns JS. The Native Kidney Biopsy: Update and Evidence for Best Practice. Clinical journal of the American Society of Nephrology : CJASN 2016;11:354-62.
16. Stone H, Magella B, Bennett MR. The Search for Biomarkers to Aid in Diagnosis, Differentiation, and Prognosis of Childhood Idiopathic Nephrotic Syndrome. Front Pediatr 2019;7:404.
17. Noone DG, Iijima K, Parekh R. Idiopathic nephrotic syndrome in children. Lancet 2018;392:61-74.
18. Demircin G, Delibas A, Bek K, et al. A one-center experience with pediatric percutaneous renal biopsy and histopathology in Ankara, Turkey. Int Urol Nephrol 2009;41:933-9.
19. Yavascan O, Aksu N, Erdogan H, et al. Evaluation of Percutaneous Renal Biopsy Results in Children: An Eleven-Year Survey. The Turkish Nephrology Dialysis and Transplantation J (TNDT) 2005;14:195-201.
20. Cakmakci E, Caliskan KC, Turkoglu OK, et al. A modified technique for real time ultrasound guided pediatric percutaneous renal biopsy: the angled tangential approach. Quant Imaging Med Surg 2014;4:190-4.
21. Paripovic D, Kostic M, Kruscic D, et al. Indications and results of renal biopsy in children: a 10-year review from a single center in Serbia. J Nephrol 2012;25:1054-9.
22. Santangelo L, Netti GS, Giordano P, et al. Indications and results of renal biopsy in children: a 36-year experience. World J Pediatr 2018;14:127-33.
23. Banh TH, Hussain-Shamsy N, Patel V, et al. Ethnic Differences in Incidence and Outcomes of Childhood Nephrotic Syndrome. Clin J Am Soc Nephrol 2016;11:1760-8.
24. Chanchlani R, Parekh RS. Ethnic Differences in Childhood Nephrotic Syndrome. Front Pediatr 2016;4:39.
25. Varner JD, Matory A, Gbadegesin RA. Genetic Basis of Health Disparity in Childhood Nephrotic Syndrome. Am J Kidney Dis 2018;72:22-5.
26. Bittles A. Consanguinity and its relevance to clinical genetics. Clin Genet 2001;60:89-98.
27. Takano T, Bareke E, Takeda N, et al. Recessive mutation in CD2AP causes focal segmental glomerulosclerosis in humans and mice. Kidney Int 2019;95:57-61.
28. Kaplan S, Pinar G, Kaplan B, et al. The prevalence of consanguineous marriages and affecting factors in Turkey: a national survey. J Biosoc Sci 2016;48:616-30.
29. Shawky RM, Elsayed SM, Zaki ME, et al. Consanguinity and its relevance to clinical genetics. Egyptian J of Medical Human Genetics 2013;14:157-64.