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Research Article

Hematuria and Proteinuria in Nephropathy Patients before Neprectomy and Histopatolgy Findings after Nephrectomy

Zuhirman Zamzami,

M.D, Urologist, Ph.D

Urology Division,Surgery Department, Medical Faculty, Riau University.

Abstract:

Background: Nephropathy is a major cause of end stage kidney failure patients caused by glomerular and non glomerular diseases. The study aimed at assessing the description of nephropathy after nephrectomy by the age, gender, clinical syndrome, cause, urinalysis findings, and histopathology findings.

Materials and Methods: We reviewed medical records of nephropathy after nephrectomy patients by age, gender, clinical syndrome, cause, urinalysis findings, and histopathology findings in Arifin Achmad Regional General Hospital, Pekanbaru, Riau Province, Indonesia in January 2011 – Desember 2017. Statistical analysis of univariate was used. Approval on the study was obtained from the Ethical Review Board for Medicine and Health Research, Medical Faculty, University of Riau.

Results: There were 58 patients in this study. The result showed that nephropathy after nephrectomy patients were mostly (58.6%) in 40-59 year old age group and most frequent (53.4%) in males. The most frequent (48.3%) clinical syndromes were chronic glomerulonephritis. The most (63.8%) causes were non-glomerular diseases. Most frequent urinalysis findings were microscopic haematuria in 39.7% patients and proteinuria (+2) in 31.7% patients. The most frequent histopathologic finding was interstitial fibrosis in 66.7% patients.

Conclusions: Microscopic haematuria and proteinuria (+2) were the most frequent urinalysis findings while interstitial fibrosis was the most frequent histopathology findings in nephropathy patients.

Keywords: nephropathy post nephrectomy, hematuria, proteinuria

INTRODUCTION

Nephropathy is an inflammatory process in the glomeruli with aetiology, pathogenesis and pathophysiology, various histopathological changes in the kidneys but with almost uniform clinical features[1]. Primary nephropathy can be caused by an autoimmune process whereas secondary nephropathy is caused by systemic disease, infection, malignancy or metabolic disease causing abnormalities associated with the renal system [1.2].

Clinical epidemiological studies had shown that nephropathy was a major cause of terminal kidney failure patients [1]. A study by Costa et al (2016) showed that nephropathy was the third leading cause of chronic kidney disease in haemodialysis patients after hypertension and diabetes mellitus [3]. The Eighth Indonesian Kidney Registry (2015) found that the sequence of causes of kidney failure in patients receiving haemodialysis were hypertensive renal disease (44%), diabetic nephropathy (22%), primary nephropathy (8%), chronic pyelonephritis (7%), obstructive nephropathy (5%), lupus nephropathy (1%), polycystic kidney (1%), uric acid nephropathy (1%), others (8%), and unknown (3%) [4].

Grogan (2010) studied glomerulonephritis or primary nephropathy found in adult cases with the highest incidence rates of IgA 2.5 / 100000 nephropathy per year [5]. Alawi (2017) conducted the most common secondary nephropathy study found the causes were diabetic nephropathy (46%), hypertensive nephropathy (19 %), and glomerulonephritis (15%) [6]. In Indonesia, hypertensive renal disease was the leading cause of secondary nephropathy in 44% cases and diabetic nephropathy in second position in 22% patients [4].

Nephropathy occurs due to glomerular damage with various pathogenesis both in primary and secondary or due to changes in anatomical structure and decreased kidney physiology caused by disturbances in other urological organs such as the presence of blockage of the urinary tract. Clinical features of nephropathy might occur without complaints and discovered incidentally from routine urine examinations, mild complaints to medical emergencies requiring kidney replacement therapy [1].

Clinical manifestations might occur in asymptomatic urinary abnormalities, macroscopic haematuria, nephritic syndrome, nephritic syndrome, rapidly progressive glomerulonephritis and chronic glomerulonephritis [2]. Laboratory finding results of nephropathy disease that might occur including hematuria, proteinuria, and diminished glomerular filtration rate (GFR) [7]. Haematuria might occur in glomerular and non glomerular diseases[4]. Histopathology structures in nephropathy diseases include interstitial fibrosis, tubular atrophy, glomerulosclerosis, accompanied by chronic inflammatory processes of the kidney parenchyma [9].

Based on the above description, we aimed to conduct a study on the hematuria and proteinuria of urinalisis findings in nephropathy before nephrectomy in Arifin Achmad Regional General Hospital, Pekanbaru, Riau Province, Indonesia.

METHOD

We reviewed medical records of nephropathy after nephrectomy patients by age, gender, clinical syndrome, cause, urinalysis findings, and histopathology findings in Arifin Achmad Regional General Hospital, Pekanbaru, Riau Province, Indonesia in January 2011 – Desember 2017. Statistical analysis of univariate was used. Approval on the study was obtained from the Ethical Review Board for Medicine and Health Research, Medical Faculty, University of Riau.

RESULTS

In this study there were 58 patients with nephropathies disease underwent nephrectomies

Table 1. Age and gender frequency distributions of nephropathy patients underwent nephrectomies

Age (year)	Gender				Frequency N	Percentage (%)
	Male		Female			
	N	(%)	N	(%)		
0-19	1	1.7	1	1.7	2	3.4
20-39	9	15.5	6	10.3	15	25.9
40-59	17	29.3	17	29.3	34	5.6
≥60	4	6.9	3	5.3	7	12.1
Total	31	53.4	27	46.6	58	100

Table 1 showed most patients was in 40 - 59 year old age group 34 (58.6%) patients, and the lowest was in 0-19 year old age group in 2 people (3.4%). Male (53.4%) was more frequent than female (46.6%).

Table 2. Clinical syndrome frequency distribution of nephropathy patients underwent nephrectomies

Clinical syndrome	0-19		20-39		40-59		≥60		Total	
	(N)=2 (3.4%)		(N)=15 (25.9%)		(N)=34 (5.,6%)		(N)=7 (12.1%)			
	M	F	M	F	M	F	M	F	N	(%)
Chronic glomerulo-nephritis	-	-	6	2	6	10	2	2	28	48.3
Nephrotic syndrome	1	-	-	1	3	4	-	1	10	17.2
Macros-copic hematuria	-	1	-	1	3	2	-	-	7	12.1
Rapidly progressive glomerulo nephritis	-	-	2	1	3	-	1	-	7	12.1
Nephritic syndrome	-	-	1	1	2	1	1	-	6	10.3
									58	100

Table 2 showed the most clinical syndrome was chronic glomerulonephritis in 28 (48.3%) patients while the least one was nephritic syndrome in 6 (10.3%) patients. The age group 40-59 years was more common in women in 10 (17.2%) patients.

Table 3. The cause frequency distribution of nephropathy patients underwent nephrectomies

Causes of nephropathy	0-19		20-39		40-59		≥60		Total	
	N=2 (3.4%)		N=15 (25.9%)		N=34 (5.6%)		N=7 (1.1%)			
	M	F	M	F	M	F	M	F	(N)	(%)

Glomerular	1	-	6	1	5	7	-	1	21	36.2
Non glomerular	-	1	2	6	12	10	4	2	37	63.8
									58	100

Table 3 showed the most common cause of nephropathy after nephrectomy was non-glomerular disease in 37 (63.8%) patients in the age of 40-59 years and more frequently in males in 12 (20.7%) and the least cause was glomerular disease in 21 (36.2%) patients in which also often in the age of 40-59 years and occurred in women 7 (12%) patients.

Table 4. Hematuria finding frequency distribution of nephropathy patients before underwent nephrectomies

Hematuria finding	0-19		20-39		40-59		≥60		Total	
	(N)=2 (3.4%)		(N)=15 (25.9%)		(N)=34 (58.6%)		(N)=7 (12.1%)			
	M	F	M	F	M	F	M	F	(N)	(%)
Negative	1	-	2	1	2	6	-	1	13	22.4
Micro scopic	-	1	3	4	8	5	1	1	23	39.7
Macro scopic	-	-	3	2	7	6	3	1	22	37.9
									58	100

Table 4 showed in nephropathy patients before underwent nephrectomies, microscopic hematuria was the most frequent in 23 (39.7%) patients, in the age group 40-59 years and in men in 8 (13.8%) while the macroscopic hematuria was in 22 (37.9%) patients.

Table 5. Proteinuria finding frequency distribution of nephropathy patients before underwent nephrectomies

Proteinuria level	0-19		20-39		40-59		≥60		Total	
	(N)=2 (3.4%)		(N)=15 (2.,9%)		(N)=34 (58.6%)		(N)=7 (12.1%)			
	L	P	L	P	L	P	L	P	(N)	(%)
Negative	-	1	-	-	4	2	-	-	7	12.1
(+1)	-	-	2	1	4	4	2	1	14	24.1
(+2)	-	-	4	4	7	4	1	-	20	34.5
(+3)	1	-	2	1	2	7	1	1	15	25.9
(+4)	-	-	1	-	-	-	-	1	2	3.4
									58	100

Table 5 showed in nephropathy patients before underwent nephrectomies, proteinuria +2 was the most frequent in 20 (34.5%) patients, mostly in 40-59 year old age group and in male (12%) while the least proteinuria +4 was in 2 (3.4%) patients in 20-39 year old age group and in ≥60 year old age group in 1 (1.7%) patients.Table 6. The histopathology findings frequency distribution of nephropathy patients underwent nephrectomies

Histopathology	Frequency (N)	Percentage (%)
Chronic inflammation	21	36.2
Glomerulosclerosis	14	24.1
Tubular atrophy	34	58.6
Interstitial fibrosis	42	72.4

Other	9	15.5

Table 6 showed the histopathology findings in nephropathy patients underwent nephrectomies was mostly (66.7%) interstitial fibrosis and least (25%) was glomerulosclerosis.

DISCUSSION

This study result showed the most frequent patients was in 40-59 age year old group in 34 (58.6%) patients, and the least in the age group 0-19 years as many as 2 people (3.4%). Male patients were more (31.4%) than the female in 27 (46.6%). There were no gender-based differences in nephropathy after nephrectomy in the most age groups and in the least. The characteristics of patients by age in this study suited a study by Jain (2017) found the most nephropathy patients was in 25-50 year old age group in 32 (72.72%) patients [10]. This study result also suited a study by Wirta (2007) found 2567 kidney histopathology findings in 40-59 year old age group 546 (23.1%) patients, while the least one was in ≤20 year old age group in 26 (10.2%) patients [11].

Several literatures stated nephropathy diseases might occur in all age groups [1]. In this study age group of 40-59 was the age most frequently affected. This condition might be caused by the functions of organs of the body decreased with age, including the function of kidney organs. Kidney function is determined by the number of nephrons that are still functioning. The decrease in the number of nephrons might occur due to the aging process, or damage to the nephrons caused by certain causes such as trauma, infection and other causes, while the kidneys do not have the ability to regenerate new nephrons so that when nephron damage occurs the kidney function might not be maintained. In addition, risk factors for kidney disease according to the National Kidney Foundation (2013) include clinical and socio-demographic factors. Clinical factors include history of diabetes mellitus, hypertension, autoimmune diseases, urinary tract infections, urinary tract stones, low birth weight, and sociodemographic factors, then age, race, lifestyle and economy[12].

Characteristics of patients by gender in this study was similar other studies. O'Shaughnessy (2017) surveyed 29 nephropathology laboratories on four continents showed 42,603 patients diagnosed with glomerular disease in 2012-2013 were predominantly male compared to female, USA / Canada 12,004 (52.3%) patients, Europe 7169 (56.4%) patients, Asia 1609 (49.5%) patients and Latin America 930 (36.4%) patients [13]. The same previous study by Crensiglova (2015) on 131 kidney biopsy samples from January 1, 2008 - December 2012 at Universidade Federal do Paraná, more than women, 59 (46.5%) patients [14]. Similar studies conducted by Tavares (2012) found that more male patients than women were in 80 (54%) and 67 (46%) [15]. Based on the literatures these were due to the influence of different reproductive hormones and lifestyles between male and female such as the pattern of protein, salt, cigarette and alcohol consumption [16]. Female might have a lower incidence during fertile period when compared to men of the same age. The estrogen hormone has a big role as nephron-protective. The estrogen hormone works on nephron component cells. The estrogen -α receptor (ER) is expressed in the kidney as a sodium regulator, potassium homeostasis and renin angiotensin pathway, whereas ER is expressed primarily in henle and distal contrast tubules. Estrogens prevent glomerulosclerosis and tubulo-interstitial fibrosis. 17-β estradiol can prevent the growth of β-1 transformation (TGF-β-1) in induced glomerulopathy. However, when entering premenopausal periods estrogen levels tend to decrease and kidney protection against various disease risks will be reduced, so in this study obtained age group 40-59 years to get the same risk of kidney disease between women and men [17].

The study result found the most common clinical syndrome in patients with nephropathy after nephrectomy was chronic glomerulonephritis in 28 (48.3%) patients 40-59 year old group and mostly in women in 10 (17.2%) patients. The least clinical syndrome was nephritic syndrome 6 (10.3%) patients, occurred in the age 40-59 year old age group in 2 (3.4%) patients. This study result suited a study by Sugiyama (2011) found 2400 patients underwent kidney biopsy in which the most common clinical syndrome was a chronic glomerulonephritis 1156 (48.2%) patients and the least clinical syndrome was in 35 (1.5%) patients [18]. Costa (2017) showed the most rare clinical syndrome was nephritic syndrome in 18 (3%) of 670 research samples[3] The chronic glomerulonephritis criteria are persistent proteinuria > 3 grams / day, hematuria with decreased renal function, edema and hypertension. Most chronic glomerulonephritis might be caused by sustained kidney damage that eventually went into the condition of chronic kidney disease (CKD). Most patients experienced the disease at young ages and manifested as in adults [2]. In this study nephropathies most commonly occurred in older adults, 40-59 years of age. The likelihood of kidney disease that was experienced had been going on at a young age and was progressive in adulthood.

The acute nephritic syndrome or glomerulonephritis has a proteinuria criteria of 150 mg-3 g daily, hematuria > 2 High Powerful Field (HPF), or erythrocytes > $10x10^6$ cells / liter were usually dysmorphic without impaired kidney function, edema or hypertension. Acute glomerulonephritis was more common in streptococcus post-infection in children than in adult patients [2]. However, in this study the nephritic syndrome was more prevalent 40-59 year old age group as the number of adult patients were higher than those of the children.

This study result showed that nephropathy patients were most commonly caused by non-glomerular diseases 37 (63.8%) patients, mostly in 40-59 year old age group and more often in males in 12 (20.7%) patients. The least cause was glomerular disease in 21 (36.2%) patients, also commonly in 40-59 year

old age group and occurred mostly in women in 7 (12%) patients. We had not yet found other same published studies for comparing this result study of nephropathies caused by glomerular and non-glomerular abnormalities. Glomerulopathy is a decrease in kidney function caused by glomerular damage without known causes and results in various clinical manifestations. Clinical manifestations of nephropathy might occur without complaints and might discovered incidentally from routine urine examinations, mild complaints to medical emergencies requiring renal replacement therapy. So glomerular diseases are difficult to recognize rapidly and require specific histopathology examination [1]. Non-glomerulopathy is a decrease in renal function caused by extra-glomerular causes leading to decreased kidney function such as obstruction of the stone or obstruction of the urinary tract, infection known urinary tract microorganisms such as kidney tuberculosis. Clinical manifestations can be identified with the patient's perceived complaints according to the non-glomerular cause. [2]

Non-glomerular causes of the study consisted of urinary tract stones, pelvic uretero junction obstruction (PUJO), specific infections of kidney tuberculosis and polycystic kidney disease. In this study result showed 28 cases of nephropathy after nephrectomies caused by urinary tract stones. Blockages by stones in the kidneys and urinary tract might cause impaired kidney function. Long-lasting blockages might result in urine back flow up (reflux), so the kidneys dilated (hydronephrosis) or dilatation of the urinary tract over the blockage, causing malfunction and damage to permanent renal structure. Urinary tract stones were commonly found in 30-50 year old age group and were more common in men [19].This was consistent with the results of this study in which most patients were men in 40-59 year old age group.

This study results showed in nephropathy before nephrectomy, the most common were urinalysis finding was microscopic hematuria in 23 (39.7%) patients, mostly in 40-59 year old age group and often occurred in men 8 (13.8%) patients while macroscopic haematuria in 37.9% patients. A study by Yuste (2016) compared gross hematuria and microscopic hematuria in glomerulonephritis in 19,895 patients found microscopic hematuria was more common in 10.962 (55.1%) patients than gross hematuria in 1.710 (8.6%) patients [20]. This study result a study by Santangelo (2018) showed macroscopic haematuria occurred in less than 5% of the nephropathy patients underwent kidney biopsies, while the rest patients had a history of unconscious microscopic hematuria [21].

Microscopic haematuria is characterized by the discovery of three or more erythrocytes/HPF without known cause and is known only by microscopic urine examination. The causes might be associated to both urological and nephrology diseases [19]. In glomerulonephritis, microscopic hematuria is associated with a glomerular filtrate barrier (GFB) dysfunction. In kidney diseases associated to abnormalities in the GFB component or in inflammatory diseases in which proteolytic enzymes released by inflammatory cells might decrease the GFB component, resulting in more fragile GFBs that are more susceptible to rupture, such as primary glomerulonephritis, autoimmune disease, or infection. Microscopic haematuria might occur persistently due to impaired kidney filtration function [20].

Macroscopic haematuria is often caused by common urological causes including urinary tract infections, urinary tract stones or urological malignancies. In addition, microscopic and macroscopic haematurias might also be caused by partial obstruction of the urinary tract or may also be caused by other unilateral renal abnormalities that also cause erythrocytes in urine sediments. Therefore, the causes of haematuria should be known quickly to estimate the origin of urinary tract abnormalities in patients. Negative hematuria in nephropathy disease occurs due to changes in the membrane of glomerular filtration in the form of sclerosis or interstitial fibrosis that causes urine disturbed so that the absence of erythrocytes in the urine sediment or even anuria might occur [21].

This study showed positive protenuria +2 as was mostly in 20 (34.5%) patients, mostly occurred 40-59 year old age group and occurred in12% of men patients. The least was positive proteinuria +4 in 2 (3.4%) patients, occurred in 20-39 year old age group and ≥60 each in 1 (1.7%) patients. This study result suited a study by Kunitoshi (2011) showed that 450 end stage renal disease (ESRD) patients had proteinuria +2 in 16% patients and proteinuria +4 in less than 1 % [22]. Proteinuria is a major determinant of renal outcome. The progression of the protein obtained in the examination of the urine describes the condition of renal filtration function. The more severe the damage to the kidney components the more proteins to be released [23]. The difference in this study in patients with nephropathy was mostly in proteinuria +2. This was due to decreased kidney function and the presence of other symptoms occurred worsening the condition of the patient.

This study result showed interstitial fibrosis were mostly 66.7% patients and at least was glomerulosclerosis in 25% patients. A study by Leal (2017) found the most common histopathologic features of patients with nephropathy were atrophy of the interstitial tubules and fibrosis in 78% patients [24]. Another study classified nephropathy disease based on kidney biopsy and immunohistochemistry examination. Kidney and immunohistochemistry biopsy tests were not done in this study so that the histopathology features of nephropathy after nephrectomy only describe microscopic tissue structures only. The irreversible rate of irreversible kidney parenchyma was most easily assessed by the number of tubular atrophy and interstitial fibrosis following histopathology examination.

Persistent glomerulonephritis that aggravates kidney function was always accompanied by interstitial nephritis, kidney fibrosis, and tubular atrophy. The flow of urine was inhibited by tubular obstruction as a result of interstitial inflammation and fibrosis. Interstitial changes, including interstitial edema or fibrosis, alter tubular and vascular morphology that might interfere the normal tubular transport. The soluble and water from the tubular lumen moves into the vascular space. In addition, vascular resistance affects renal function through two

mechanisms. First, tubular cells are highly metabolically active, resulting in a decrease in renal perfusion leading to ischemic injury. Second, arterial glomerular outflow interference causes intra glomerular hypertension to increase intra glomerular exacerbations and prolong the mesangial sclerosis and glomerulosclerosis [15].

CONCLUSIONS

Microscopic haematuria and proteinuria (+2) were the most frequent urinalysis findings while interstitial fibrosis was the most frequent histopathology findings in nephropathy patients.

REFERENCES

[1]. Sukandar, E. Glomerulopati primer. Dalam: Nefrologi klinik. Bandung: ITB; 2006. p. 110-22.

[2]. Floege J, Feehally J. Introduction to glomerular disease: clinical presentation in comprehensive clinical nephrology. 5th ed. Philadelphia:Elsevier; 2015. p.184-97.

[3]. Costa DM, Lucila MV, Pedro AD, Filipe WS, Gisele VF, Maria AG, et al. Comparative analysis if primary and secondary glomerulopathies in the Northest Brazil. J Bras Nefrol. 2017;39(1). p.29-35.

[4]. 8th Report of Indonesian renal registry, Kementrian Kesehatan Republik Indonesia. http://www.depkes.go.id

[5]. Grogan AM, Casper FM, Franssen, Corinne SV. The incidence of primary glomerulonephritis worldwide: a systematic review of the literature. Nephrol Dial Transplant. 2010. p.1-17.

[6]. Alawi IA, Issa AS, Adhra AW,4 Yacoub AM, John AS. End-stage kidney failure in oman: An analysis of registry data with an emphasis on congenital and inherited renal diseases. J Nephrol. 2017 . p. 1-7.

[7]. National institute of diabetes and digestive and kidney disease. Glomerular disease. NIH. Publ. No.14-4358. 2014. *Available from https://www.kidney.org/sites/default/files/12-10-6139_glomerulardisease.pdfp*

[8]. Gerber SG, Brendler CB. Evaluation of the urologic patient: history, physical examination, and urinalysis. In: *C*ampbell Walsh Urology. 10th ed. Philadelphia: Elsevier; 2012. p. 75-92.

[9]. Kremers WK, Denic A, Lieske JC, Alexander MP, Kaushik V, Elsherbiny HE, et al. Distinguishing age-related from disease-related glomerulosclerosis on kidney biopsy: the Aging Kidney Anatomy study. Nephrol Dial Transplant. 2015;30. p. 2034–9.

[10]. Jain S, Jain SK, Kaza RC, Singh Y. This challenging procedure has successful outcomes: Laparoscopic nephrectomy in inflammatory renal diseases. Department of Urology, Gauwhati. India;2017. p. 35-40.

[11]. Wirta O, Mustonen J, Helin H, Pasternack A. Incidence of biopsy-proven glomerulonephritis. Nephrol Dial Transplant. 2008.23; p.193–200.

[12]. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Inter. Suppl. 2013; p. 3-5.

[13]. O'Shaughnessy MM, Susan LH, Bawana DT, Rosanna C, Agnes BF, Charles J. Glomerular disease frequencies by race, sex and region: results from the International kidney biopsy survey. USA;Nephrol Dial Transplant. 2017. p.1–9.

[14]. Crensiglova C, Rehme BB, Kinasz LR, Chula DC, Nascimento MM, Soares MF. Frequency and clinical histological analysis of glomerular diseases in a tertiary hospital in southern Brazil. Universidade Federal do Paraná. 2015. p. 42-8

[15]. Tavares MB, Almeida MC, Martins RT, Sousa AC, Martinelli R and Santos DS. Acute tubular necrosis and renal failure in patients with glomerular disease. Informa Healthcare USA, Inc. 2012; 34(10): 1252–57.

[16]. Sulistiowati E, Idaiani S. Faktor risiko penyakit ginjal kronik berdasarkan analisis cross-sectional data awal studi Kohort penyakit tidak menular penduduk usia 25-65 tahun di Kelurahan Kebon Kalapa, Bogor. Buletin Penelitian Kesehatan. 2015:43(3) p.163-72.

[17]. Gluhovschi GH, Gluhovschi A, Anastasiu D, petrica L, gluhovschi C, silvia V. Chronic kidney disease and the involvement of estrogen hormones in its pathogenesis and progression. Rom. J. Intern. Med. 2012:50(2) p. 135–44.

[18]. Sugiyama H, Yokoyama H, Sato H, Saito T, Kohda Y, Nishi S, et al. Japan Renal Biopsy Registry: the first nationwide, web-based, and prospective registry system of renal biopsies in Japan. Clin Exp Nephrol. 2011. p. 493–503.

[19]. Purnomo, BB. Dasar-dasar urologi. Jakarta:Sagung Seto; 2011. p.6-9;27-50.

[20]. Yuste C, Rivera R, Moreno JA, Gomez JM. Haematuria on the Spanish Registry of Glomerulonephritis. Scientific reports. 2016. p.1-9.

[21]. Santangelo L, Netti GS, Giordano P, Carbone V, Torres DD, Rossini M, et al. Indications and results of renal biopsy in children: a 36-year experience. World J Pediatr. 2018. p. 145-7.

[22]. Iseki K. Role of urinalysis in the diagnosis of Chronic Kidney Disease (CKD). JMAJ. 2011. 54(1). p. 27–30.

[23]. Kee YK, Yoon CY, Kim SJ, Moon SJ, Kim CH, Park JT, et al. Determination of the optimal target level of proteinuria in the management of patients with glomerular diseases by using different definitions of proteinuria. Medicine (Baltimore). 2017. 96(44). p. 1-9.

[24]. Leal R, Pinto H, Galvao A, Santos L, Romaozinho C, Macario F, et al. Nephrotic range proteinuria in renal transplantation: Clinical and histologic correlates in a 10 year retrospective study. Elsevier Inc. 2017. p. 792-9.