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Research Article

Interstitial Fibrosis and Tubular Atrophy in Nephrectomy Patients with Unilateral Kidney Obstruction

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Abstract:

Background: Activation of interstitial myofibroblasts and extracellular matrix deposits in unilateral kidney obstruction results in hydronephrosis, there will be depletion of the renal parenchyma, tubular atrophy and the formation of interstitial fibrosis. The aim of the study was to assess the profile of interstitial fibrosis and tubulus atrophy in nephrectomy patients with unilateral obsruction.

Methodology: We reviewed medical records and histopathology examinations of patients with unilateral kidney obstruction underwent nephrectomy in Arifin Achmad Regional Hospital, Pekanbaru, Riau Province of Indonesia in 2012-2017. Statistic analysis used were univariate. Approval on the study was obtained from the Ethical Review Board for Medicine and Health Research, Medical Faculty, RiauUniversity.

Results: There were 77 unilateral kidney obstruction patients underwent nephrectomies in Arifin Achmad Regional General Hospital of Riau Province in which mostly 23 (29.9%) in age 50-59 years old patients. with males were in 55.8% patients and females were in 44.3% patients. Most blood ureum level <40 mg / dl was in 81.8% patients and most blood creatinine level was <1.5 mg / dl in 79.2% patients. The most etiology was miscellaneous in 15.6%. The results of histopathologic examination were interstitial fibrosis and tubular atrophy respectively in 51.8% patients.

Conclusion: Unilateral kidney obstruction underwent nephrectomy in our hospital was characterized by mostly in elderly age, half of the patients were male, blood ureum level <40 mg/dl, blood creatinin serum <1.5 mg/dl, miscellaneous was the most cause, interstitial fibrosis and tubulus atrophy in histopathology findings.

Keywords: Unilateral kidney obstruction, nephrectomy, interstitial fibrosis, tubular atrophy.

Introduction

Upper urinary tract obstruction is one of the problems in the field of urology in all phases of human life and the location can be along the upper urinary tract. As a result of this condition hidronephrosis might occur, namely the occurrence of pelvic dilatation or kidney calix [1]. Singh et al showed an outcome of 59,064 people with the incidence of obstruction in the urinary tract, in neonates until geriatrics was found 3.1% with hydronephrosis. In women, hydronephrosis was found in 20-60 years old group and associated to gynecological malignancy, and in men over the age of 60 years hydroneprosis was often associated to prostate enlargement both benign and malignant. Hydronephrosis might also be found in children with an incidence rate of 2-2.5% and is more common in boys [1]. During pregnancy hydronephrosis can also occur. This incidence is encountered in up to 90% of pregnancies in which was the result of a gravid uterine compression or because of the influence of progesterone resulted in smooth muscle relaxation. Usually a mild hydronephrosis often occurs in the right kidney. In the early phase the hydronephrosis might be treated intensively but if conservative therapy is not conducted it is necessary to do an operative procedure with the ureteric stent insertion. In late phase kidney failure might occur [2]. Of the total incidence of kidney failure, about 1.5% is caused by urological abnormalities. In 1999, in the United Kingdom, children's kidney transplant rate was 53.4 per 1 million children. Urinary tract obstruction is the leading cause of terminal kidney failure in children younger than one year with a transplant rate of 23% [1].

Obstructive urine is a functional blockage of the urinary tract functionally or anatomically due to various causes, so that there will be disruption of urine flow from proximal to distal. Various factors are expected to play a role in the process, among others; oxidative stress and inflammation. Increased hydrostatic pressure in kidney intra-tubules will lead to apoptosis, tubular necrosis and trauma that will lead to fibrosis.[3,4]. Interstitial fibrosis and decreased tubular function result in decreased reabsorption of solutes and water, loss of concentration of urine and impaired potassium hydrogen excretion [5]. Activation of the interstitial myofibroblasts and extracellular matrix deposits results in hydronephrosis which results in endothelial dysfunction of glomeruli and changes in the structure of the kidneys, such as depletion of kidney parenchyma due to atrophy and collecting

renal calyx [6,7]. Patients with urinary tract stones are at risk for chronic kidney disease (CKD) and if progressive this CKD will become terminal kidney disease (CKD) [5]. Histopathology examination showed the form of changes in interstitial tubular system and interstitial fibrosis, tubular atrophy, glomerulosklerotic and chronic or acute inflammation [8].

Based on the above descriptions we aimed at assessing description of interstitial fibrosis and tubular atrophy on histopathology examination in nephrectomy patients due to unilateral kidney obstruction.

Methodology

We reviewed medical records of unilateral renal obstruction patients underwent nephrectomies in Arifin Achmad Regional General Hospital, Pekanbaru, Riau Province, Indonesia in 2012-2017. The study variables were age, sex, blood ureum level, blood creatinine level, etiology, interstitial fibrosis and tubular atrophy. Statistical analysis used was univariat. Approval on the study was obtained from the Ethical Review Board for Medicine and Health Research, Medical Faculty, Riau University.

Results

There were 77 unilateral kidney obstructive patients in this study.

Table1. Characteristics of unilateral kidney obstruction patients

No	characteristics	N	F (%)
1	Sex		
	Male	43	55.8 %
	Female	34	44.2%
2	Age (Year)		
	<10	2	2.6%
	10-19	2	2.6%
	20-29	3	3.9%
	30-39	15	19.5%
	40-49	19	24.7%
	50-60	23	29.9%
	>60	13	16.9%
3	Blood ureum		
	<40 mg/dl	63	81.8%
	>41 mg/dl	14	18.2%
4	Blod creatinin		
	≤1.5 mg/dl	61	79.2%
	>1.5 mg/dl	16	20.8%

Table 2. Etiology of unilateral kidney obstruction

Etiology	N	F (%)
Kongenital	2	2.6
Neoplasia	8	10.4
Inflamation	4	5.2
Miscellaneous	63	81.8
Total	77	100

Table 3. Interstitial fibrosis

Interstitial fibrosis	N	F (%)
Yes	29	51.8
No	27	48.2
Total	56	100

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able 4. Tubular atrophy

Tubular atrophy	N	F (%)
Yes	29	51.8
No	27	48.2
Total	56	100

Discussion

There were 77 unilateral renal obstruction patients in this study. This study result showed male were mostly in 43 (55.8%) patients, and the least one in female group in 34 (44.3%) patients. This study result was similar to a study by Bell (2000) showed in 32,360 autopsies in 1995-2000 found 3.9% of male patients and 3.6% of female patients with unilateral kidney obstruction and hydronephrosis [9]. A study by María et al (2015) showed in fewer female patients suffering from unilateral kidney obstruction due to the role of estrogen hormone. In patients with high estrogen levels there were slow glomerular damage and fibrosis tissue formation [10].

A study by Mark (2012) showed men more (33%) often experienced unilateral kidney obstruction than in women (29%), especially in the age of 50-65 year [11]. This study showed 50-59 year age group were mostly in 23 (29.9%) patients, and the least one in <20 year age group in 2 (2.6%) patients.

This study result also suited a study by Raimund et al (2010) and the one by Navarrate (2012) showed in the age of 50-65 there was an increase in scar tissue formation in the glomerulus and renal tubules of patients. This happens because the aging process, which is a biological process that affects many organs and kidneys one of the main targets. Aging with reduced kidney function due to reduced number of nephrons. The fifth and sixth decades of men have reduced the stabilization systems, hemodynamic systems, and homeostasis [12]. This study result also suited a study by Mark (2012) showed in 4,869 patients suffering from unilateral kidney obstruction in the age group below 20 years there were 6.9% of patients, age group 21-30 years was in 35.7% patients and in the group age > 55 years was 57.4% [13]. A study by Richard (2014) showed the <20 years age group was the lowest group of unilateral kidney obstruction patients and in < 20 years old patients the main cause was ureteropelvic junction obstruction [14].

This study result showed blood ureum levels were mostly <40 mg/dl in 63 (81.8%) while blood ureum level > 41mg/dl in 14 (18.2%) patients. This study result suited a study by Klahr (1983) showed patients with unilateral kidney obstruction had blood ureum levels <40 mg after 12 days after nephrectomy. This was because if only one kidney was obstructed and in the nephrectomy, the normal contralateral kidney was able to compensate for the kidney function work that had been removed [15].

This study result suited a study by Shehab et al (2013) showed there were 138 patients with unilateral kidney obstruction and nephrectomies were performed in 56 (71.8%) patients with blood ureum level was <40 mg / dl [16].

Blood ureum levels depend on decreased glomerular filtration function. Decreased kidney function 15% (<15ml/min) indicates kidney failure and uremia. Kidney function among others regulate acid base balance, erythropoetin and excretion of metabolism waste such as ureum. When ureum is not removed in the body, uremia syndrome might occur. This uremia syndrome mainly occurs in patients with chronic kidney disease and will provide manifestations in other parts of the body such as gastrointestinal, skin, hematology, nerves and muscles, cardiovascular, endocrine and other system damages [17].

This study result showed blood creatinine were mostly <1.5 mg/ dl in 61 (79.2%) patients and > 1.5 mg / dl in 16 (20.8%) patients. This study result suited a study by Klahr (1983) showed patients with unilateral kidney obstruction had blood creatinine levels <1.5 mg/dl after 10 days of nephrectomy. This was because if one kidney was obstructed and underwent nephrectomy, the normal contralateral kidney was able to compensate the function of the removed kidney [18]. From the literature, unilateral kidney obstruction usually had nearly 50% of kidney degradation impairment accompanied by blood creatinine level increase. Kidney impairment phenomene in unilateral kidney obstruction was thought to be associated to compensatory hyperfiltration of the normal kidney. These kidney physiological disorders also depended on the degree and duration of the obstruction [10].

This study result showed the etiology unilateral renal obstructin patients were mostly miscellaneous (stones, peeling papillae, trauma, renal aneurysm) in 47 (15.6%) patients. This study result suited a study by Aristo (2016) showed the most etiology were stone disease in 50 (76%) patients while inflammatory disease was in 16 (24%) patients patients [19]. This study result suited a study by Edward David (2017) showed common etiologies of unilateral kidney obstruction were urinary stones, blood clots, tumors and puffy papillae [20].

From the literature, unilateral kidney obstruction may be caused by various causes such as congenital or acquired diseases, and diseases inside the lumen or outside the lumen. The obstruction resulted in damaging the affected side of kidney [20].

This study result showed interstitial fibrosis in histopathlogy examination of unilateral kidney obstruction patients were most in 29 (51.8%) patients. This study suited a study by Frederick (2012) showed most prominent interstitial changes in unilateral kidney obstruction were fibrosis, as well as accumulation of collagen and other extracellular matrix

components. It had been shown in various chronic kidney diseases that the present of interstitial fibrosis was a major determinant of glomerular filtration rate [21]. This study result suited a study by Oka (2014) showed 85 patients with unilateral kidney obstructions and after nephrectomies and histopathology examination results were interstitial fibrosis in 42 (49.4%) patients [22]. This study result suited a study by Yuan et al (2015) using 180-200g Sprague-Dawley Rat showed an increase in interstitial fibrosis was formed in week 3 following unilateral kidney obstruction. This experimental animal study mimics various obstructive stages and might lead to infiltration of inflammatory cells, tubular expansion and apoptosis, myofibroblast accumulation and differentiation from tubular epithelial, pericytes and perivascular fibroblasts, extracellular matrix deposition, and tubular atrophy [23].This study result showed the tubulus atrophy of unilateral kidney obstruction were mostly in 29 (51.8%) patients. This study result suited a study by Kevin (2009) showed 70 patients with unilateral kidney obstruction found tubular atrophy on histopathologic examination in 21 (30%) patients [24]. In microscopic examination, early lesions showed dilatation of the tubules, followed by atrophy and replacement of tubular epithelial cells with fibrosis tissue. The glomerulus was not affected, eventually in chronic cases, the glomerulus might also become atrophy and disappear. The whole kidney would turn into a thin shell of connective tissue [25]. Animal studies by Alvaro C Ucero et al (2018) using Sprague-Dawley Rats after 3 weeks after unilateral kidney obstruction showed histopathology picture of tubular atrophy. After 5-6 hours post nephrectomy found improvements in kidney function [26].

Untreated urinary obstruction might result in tubular atrophy, interstitial fibrosis and inflammation, loss of nephrons and eventually irreversible kidney injury [27,28]. Kidneys were obstructed or if they had only one kidney and were obstructed, an End Stage Renal Disease (ESRD) might occur. The kidney prognosis after the procedure of nephrectomy depends on the severity and duration of the obstruction. In fact, there was complete recovery of glomerular filtration rate (GFR) after recovery from total kidney obstruction after one week, whereas almost no recovery occurs after 12 weeks [28]. Fetal or neonatal obstructed unilateral kidney obstruction was more complicated by the effects of kidney maturity (kidney dysplasia, delayed nephron maturation and loss of nephrons) [29].

Conclusions

Unilateral kidney obstruction in our hospital characterized by mostly in male patient, elderly age, blood urea level <40 mg/dl, blood creatinin level >1.5 mg/dl, half of the etiology patients were miscellaneous (urinary stones, peeling papillae, trauma, kidney aneurysm) and interstitial fibrosis and tubulus atrophy in histopathology.

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