Lombok Journal Of Urology

August 2022,1(2)

CASE REPORT

Large Bladder Stone in Sasak Young Teen Boy

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ABSTRACT

Background: The incidence of bladder stone in children approximately 1-2% of that in adults, and are common in the first 3 years old and more than 60 years old. Children in underdeveloped countries are more likely to have endemic bladder stones. Large bladder stones in children are not very common. The choice of treatment depends on the number, size, location, composition of the stones and the anatomy of the urinary tract.
Case Presentation: A Sasak young teen boy, 12 years old, complained pain on micturition in the last 5 years. The pain became worse in the last one week before admission. On abdominal ultrasound and plain abdominal x-ray, we found large bladder stone with diameter 4 cm. Then we performed open cystolithotomy on this patient. One day after surgery, patient discharged from hospital with urethral catheter still inserted.
Discussion: The incidence of endemic bladder stones is higher in developing nation mostly in families with low protein and phosphate diets, and recurrent diarrhea. The clinical presentation ranges from asymptomatic to the presence of urgency, frequency, incontinence, fever, hematuria, etc. In pediatric bladder stones, conventional open cystolithotomy has been considered the gold standard surgical procedure.
Conclusion: The incidence of bladder stones in children living in endemic areas is mostly caused by nutritional problems. Prevention, early diagnosis and management of bladder stones in the pediatric age group is very important to reduce morbidity and mortality.

Keywords: Large bladder stone, endemic bladder stone, young teen boy, open cystolithotomy

BACKGROUND

Bladder stones account for approximately 5% of all urinary stones.1,2 The incidence in children approximately 1-2% of that in adults.1 The age distribution has two peaks, the first at age 3 years old for children in developing countries and the second at age 60 years old.3,4 Children in underdeveloped countries are more likely to have endemic bladder stones than kidney stones.2,5 These areas include Eastern Europe, Southeast Asia, India, and the Middle East.5 However, recent epidemiological studies have shown that in the Western world, especially among girls, Caucasians, African-Americans, and older children, the prevalence of childhood calculi is also increasing.6

Bladder stone etiology is classified into primary and secondary, related to association with other diseases. Primary or endemic bladder stones occur in the absence of other urinary tract diseases. It usually occurs in children in areas of low animal protein intake, poor hydration, and recurrent diarrhea.1,7 Secondary bladder stones occur in the presence of other urinary tract abnormalities, including bladder outlet obstruction, chronic bacteriuria, neurogenic bladder dysfunction, bladder diverticula, bladder augmentation or urinary diversion, and foreign bodies including catheters.1

Children may be asymptomatic or have symptoms such as urgency, frequency, incontinence, dysuria, pyuria, difficulty in voiding,

small-caliber urinary stream, lower abdominal pain, and intermittent voiding. Fever also one of the symptoms of bladder stone in children age ≤ 5 years old, which were reported in approximately 20-50 % cases.2,4 From urine analysis, 33-90% show microscopic or macroscopic hematuria.2 The approximate frequency of kidney stone types in the pediatric age group is calcium with phosphate or oxalate (57%), struvite (24%), uric acid (8%), cystine (6%), endemic (2%), mixed (2%), and other types (1%).5 Most bladder stones consist of calcium oxalate (45-65%), followed by calcium phosphate (14-30%), most stones are around 0,6 cm to 1,27 cm in size.2,8 Large bladder stones in children are not very common and are usually related to nutritional factors.9

The choice of treatment depends on the number, size, location, composition of the stones and the anatomy of the urinary tract.6 In pediatric bladder stones, conventional open cystolithotomy has been considered the gold standard surgical procedure. However, recent advances in minimally invasive technology and endoscopic techniques have improved the urological armamentarium for the definitive treatment of bladder stones in children.10 In this report, we present a case of a large bladder stone with diameter larger than 4 cm in a Sasak young teen boy.

CASE PRESENTATION

A 12 years old Sasak young teen boy came to Mataram University Hospital with chief complain pain on micturition in the last 5 years. The pain became worsened in the last 7 days before admission to hospital. There was no fever. Patient was admitted to hospital and being treated with antibiotic, ceftriaxone 1 gr injection, by pediatrician for 5 days, then consulted to urologist after bladder stone was found on ultrasound.

On abdominal ultrasound, we found large bladder stone with diameter 3,5 cm and cystitis. Another abdominal organ, including both kidneys, were normal. On plain abdomen X ray, we found bladder stone with diameter 4,4 cm. There was many erythrocytes, positive bacteria, and leucocytes 5-8/HPF on urine examination.

Figure 1. Abdominal ultrasound confirmed the bladder stone about 3.5 cm in diameter and cystitis, and the other organs were normal.

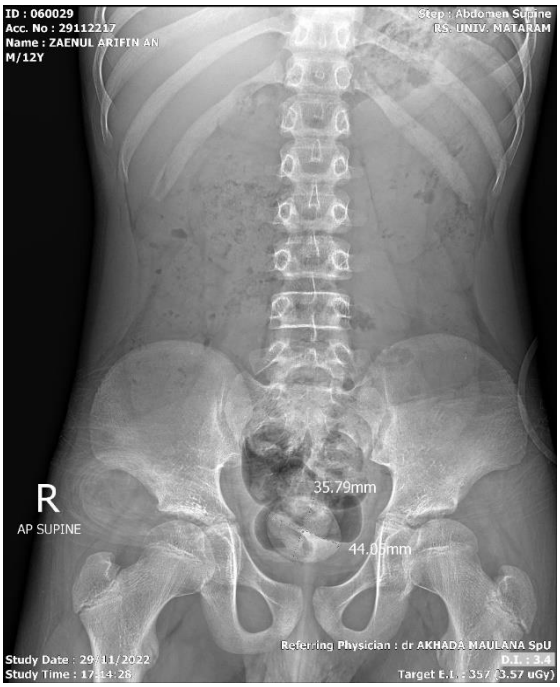

Figure 2. Plain abdominal X-ray revealed a large, round pelvic calculus measuring 4,4 x 3,6 cm.

Then we performed cystolithotomy (open bladder stone surgery) on Wednesday, November 30th. We made Pfannenstiel incision on suprapubic region, deepened to

rectus fascia. Fascia sharply opened; muscle then split. Bladder was incised, but before that, we instilled 200 ml saline liquid into it. After that, the stone was removed with stone tang. It was hard to remove the stone, because of its large size. Ater that, we wash the wound and bladder with saline liquid, until no more stone flakes and dirt. Then we close the bladder with one layer locking continuing suture, using absorbable 2-0 polyglactin thread. We close the surgical wound, without leaving drain into it. We continued intravenous antibiotic, ceftriaxone 1 gr, and paracetamol infusion for analgetic. One day after surgery, the patient condition was good, and the urine color was clear, so we let him discharged from hospital with urethral catheter still inserted.

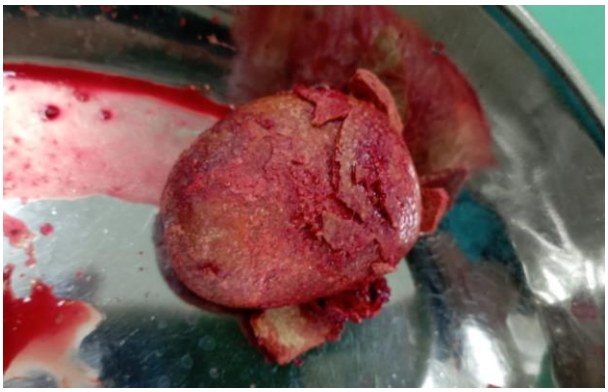

Figure 3. A bladder stone was extracted by open cystolithotomy in a young teen boy.

Six days after surgery, patient went to urology outpatient clinic. He just complained mild pain on his penis, no fever, and no hematuria seen in the catheter. The surgical wound was in good condition, no sign of inflammation. Then we removed the catheter, and patient could void spontaneously.

DISCUSSION

Urinary bladder stone contributes about 50% of urolithiasis in children.11 The incidence of endemic bladder stones is higher in developing nation, more common in males, with male-female ratios between 10:1 and 4:1 reported.4 In Indonesia, bladder stones are relatively common in children in West Sumatra, with an incidence of 8.3/100,000 population per year, and a peak age of 2-4 years, mostly seen in poor families with low protein and phosphate diets, and many children suffer from diarrhea. The climate is tropical, with an average summer temperature of 30 °C and 2,000 mm of rainfall.12 Our patient comes with complaints of pain on micturition or dysuria in the last 5 years. There's no obstruction to the flow of urine, and no evidence of pathological abnormalities in the organs based on our finding. Therefore, the etiology in this patient is primary or endemic bladder stone.

One of the underlying cause or precipitating event in the initiation of primary bladder stones, namely replacement feeding of newborns on a high-carbohydrate diet. The frequent use or exclusive dependence on carbohydrate foods in place of milk feeding leads to a relative dietary deficiency of phosphate and the formation of insoluble urinary salts.13 A cereal-based diet poor in animal protein and low in phosphate also causes hypophosphaturia and hyperamonuria, promoting deposition of calcium oxalate and ammonium uric acid. Coupled with low dietary intake of vitamins B1, B6, and magnesium, can cause hyperoxaluria. Deficiency of Vitamin A also causes urothelial degeneration which can increase stone formation.11 Girls have a shorter urethra than boys and are not convoluted and can pass most of the calculus debris without retaining nuclei in the bladder. In some males, a stone core forms and is maintained. Subsequent stone growth is determined by the net effect of storage and resorptive mechanisms operating over months or years.13

The clinical presentation of bladder stone ranges from a complete absence of

symptoms to the presence of suprapubic pain, dysuria, intermittency, frequency, hesitancy, nocturia, and urinary retention.4 Bladder stones can rarely cause kidney dysfunction. In general, they are mobile within the intravesical space. Therefore, they do not impair urine flow and barely cause bladder outlet obstruction.1 Large stones can be left without causing symptoms for a long time.13 However, if left untreated, infra-vesical obstructive uropathy can develop, as larger stones impact the bladder neck and exert mechanical pressure on the ureteral orifice.1

Our patient underwent a cystolithotomy (open bladder stone surgery) with stone size 4,4 x 3,6 cm. Open cystolithotomy, transurethral cysto-lithotripsy, shock wave lithotripsy (SWL), and percutaneous cysto-lithotripsy are several treatment methods available for the treatment of bladder stones.14 Open surgical removal may be necessary if the stones >2,5 cm in diameter.15 Safe and effective minimally invasive management of bladder stones in children, such as endourological procedures, was mainly indicated for smaller stones with a diameter less than 1.0 cm.3 SWL is the recommended treatment for stones smaller than 2.0 cm because it is the least invasive. The success rate of SWL is relatively high compared with (57% to 92% the long-term stone-free rate) in adults.16

In pediatric bladder stones, conventional open cystolithotomy has been considered the gold standard surgical procedure, due to the high stone-free rate and availability of published long-term data.10,11 In recent years, transurethral cysto-lithotripsy has become an alternative method to open cystolithotomy. However, the applicability of this approach is limited especially in boys, since urethral diameters are small and there are concerns about iatrogenic urethral restriction.3,14 Transurethral extraction using a cystoscopic instrument is the treatment of choice in small bladder stone. However, in other cases, a simple open cystolithotomy may provide the most effective treatment with minimal patient morbidity. In some developing countries, several advanced methods and equipment are not yet available, and many patients cannot afford the costs of less invasive procedures. Under these conditions, open surgery is safe, effective, with an acceptable length of stay, excellent patient acceptability, low cost, and low morbidity, and provides good stone-free rates.3

Our patient was discharged from the hospital one day after surgery with a urethral catheter in place. After six days, the catheter was removed and he was able to void spontaneously without any sign of inflammation. It is recommended to place a catheter in the bladder after surgery to allow good healing and to place a drain in the retropubic space for a few days to allow drainage of urine or hematoma if leakage occurs after surgery. However, there are side effects of catheter use that need to be monitored such as infection and stricture.17 These complications can be avoided by placement of indwelling urinary catheters for an approved indication only, aseptic technique during catheter insertion and removal, cleaning the urethral meatus with sterile water and maintenance of the drainage bag below bladder level, and prompt removal when indications are no longer present.18 Catheter duration should not exceed 8 days because shorter duration of catheterization and length of patient stay have a positive impact on reducing catheter-associated urinary tract infections.19

Conclusion

The incidence of bladder stones in children living in endemic areas is mostly caused by nutritional problems. Good prevention, early diagnosis and management of

bladder stones in the pediatric age group is very important to reduce morbidity and mortality.

REFERENCES

1. Husein A, Sigumonrong Y. Pediatric's giant bladder stone: A proposed new terminology. International Journal of Surgery Open. 2021;37:100409. DOI: https://doi.org/10.1016/j.ijso.2021.100409
2. Ali SS, Mukhopadhyay NN, Bhar P, Sarkar NN. Giant Bladder Stone in children. Journal of Pediatric Surgery Case Reports. 2022;77:102164. doi: https://doi.org/10.1016/j.epsc.2021.102164
3. Esposito C, Autorino G, Masieri L, Castagnetti M, Del Conte F, Coppola V, et al. Minimally invasive management of bladder stones in children. Frontiers in Pediatrics. 2021;8. doi: https://doi.org/10.3389/fped.2020.618756
4. Basler, Joseph. Bladder Stones [Internet]. Medscape; 2022. Available from: https://emedicine.medscape.com/article/2120102-overview
5. Fathallah-Shaykh, Sahar. Pediatric urolithiasis [Internet]. Medscape; 2021. Available from: https://emedicine.medscape.com/article/983884-overview
6. Radmayr C. EAU guidelines on paediatric urology [Internet]. 2022. Available from: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Paediatric-Urology-2022.pdf
7. Mohamed AH, Yasar A, Mohamud HA. Giant bladder stone of 152g in an 11-year child with recurrent urinary tract infections: A rare case report and review of the literature. Urology Case Report. 2021;38:101676. doi: 10.1016/j.eucr.2021.101676
8. Moreno, Megan A.. Kidney Stones in children and adolescents [Internet]. JAMA Pediatrics. JAMA Network; 2015. Available from: https://jamanetwork.com/journals/jamapediatrics/fullarticle/2442837
9. Aktoz, T., Kaplan, M., Atakan, I.H. and Inci, O. Giant bladder stone in children: case report. American Journal of Case Reports. 2008; 9, 1-3. Available from: https://amjcaserep.com/abstract/index/idArt/690767
10. Davis NF, Donaldson JF, Shepherd R, Neisius A, Petrik A, Seitz C, et al. Treatment outcomes of bladder stones in children with intact bladders in developing countries: A systematic review >1000 cases on behalf of the European Association of Urology Bladder Stones Guideline Panel. Journal of Pediatric Urology. 2022;18(2):132–40. doi: 10.1016/j.jpurol.2022.01.007
11. Zafar GM, Javed N, Humayun F, Iqbal A. Transurethral fragmentation of bladder stone in children: Our experience. Journal of Pediatric and Adolescent Surgery. 2020;1(1). doi: 10.46831/jpas.v1i1.24
12. Soliman NA, Rizvi SA. Endemic bladder calculi in children. Pediatric Nephrology. 2016;32(9):1489–99. doi: 10.1007/s00467-016-3492-4
13. Halstead, Scott B. Epidemiology of Bladder Stone of children: Precipitating events. Urolithiasis. 2015;44(2):101–8. doi: 10.1007/s00240-015-0835-8
14. Dahril, Ismy J, Asnafi A, Pratama R. Percutaneous cystolithotripsy of bladder stones in children: A case series, an experience from a tertiary hospital. Urol Ann. 2022 Jan-Mar;14(1):85-88. doi: 10.4103/UA.UA_177_20
15. Ozturk H, Dagistan E, Uyeturk U. A child with a large bladder stone: A case report. Pediatric Urology Case Reports. 2014;1(4):22-18. doi: 10.14534/pucr.2014446417
16. Bañuelos Marco B, Haid B, Radford A, Knoll T, Sultan S, Spinoit A-F, et al. Guideline adherence of paediatric urolithiasis: An EAU members' survey and expert panel roundtable discussion. Children. 2022;9(4):504. doi: https://doi.org/10.3390/children9040504
17. Rattan, K. N., Bhatia, V., Ratan, S. K., Sharma, M., & Rohilla, S. Catheterless and drainless open suprapubic cystolithotomy in children: a safe procedure. Pediatric Surgery International. 2006 ; 22(3), 255–258. doi:10.1007/s00383-005-1619-y
18. Araujo da Silva, A. R., Marques, A. F., Biscaia di Biase, C., Zingg, W., Dramowski, A., & Sharland, M. Interventions to prevent urinary catheter–associated infections in children and neonates: a systematic review. Journal of Pediatric Urology. 2018. doi:10.1016/j.jpurol.2018.07.011
19. Al-Hazmi, Hamdan. Role of duration of catheterization and length of hospital stay on the rate of catheter-related hospital-acquired urinary tract infections. Research and reports in urology. 2015 Mar 25;7:41-7. doi: 10.2147/RRU.S75419. PMID: 25848551; PMCID: PMC4378875.BALAWENDER, K.; CISEK, A.; CISEK, E. & ORKISZ, S. Anatomical and clinical aspects of horseshoe kidney: A review of the current literature. Int. J. Morphol., 37(1):12-16, 2019.

LITERATURE REVIEW

Kidney Transitional Cell Carcinoma (Upper Tract Urothelial Cancer)

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ABSTRACT

Kidney transitional cell carcinoma or upper tract urothelial cancer (UTUC) is a rare malignant tumour that affects approximately 5% of all urothelial carcinoma cases. Various risk factors for this disease have been identified, including genetic and environmental such as smoking, aromatic amines exposure, aristolochic acid-induced nephropathy, analgesic abuse, chemotherapy regimens, and chronic urinary tract infections. Gross haematuria is the most common symptom of UTUC and only a small percentage of patients is asymptomatic. Radio-imaging has become main modalities for diagnosis of UTUC, mostly computer tomography urography (CTU) because of visualization ability of the lesion. Resection are the most treatment for low grade tumour and combine with immunotherapy for high grade tumour. Grade and stage of the disease have the most significant influence factors on survival rate.

Keyword: Kidney, Transitional cell carcinoma, UTUC

INTRODUCTION

Kidney malignancies are diverse and originate from different cell types with distinctive morphology and clinical behavior.1 Urothelial carcinoma (UC) or transitional cell carcinoma is the most common malignancy of the urinary tract.2,3 UC can be located in upper urinary tract (renal pelvic, ureter) or lower urinary tract (bladder, urethra).3,4,5 The majority of UC occurs in the urinary bladder (UBUC).2,6 Upper tract urothelial cancer (UTUC) is a rare malignant tumor that affects only about 5% of all UC cases.2,5 UTUC or kidney transitional cell carcinoma or renal urothelial carcinoma is a malignant tumor arising from transitional (urothelial) epithelial cells that line the upper urinary tract from the calyx to the orifice of the ureter.1,5 Pelvicalyceal tumors are anatomically three times more common than those located in the ureter. Gross hematuria is the most common symptom of kidney transitional cell carcinoma, only a small percentage of patients is asymptomatic. UTUCs are classified according to tumor, nodule, and metastasis (TNM). The outcome of UTUC is strongly associated with the stage of the tumor. Tumor grades of endoscopic biopsy can be used to predict stage and advise patients on treatment options.5 The aim of this literature review was to summarize current progress in UTUC research by focusing on epidemiology, etiology, staging and risk factors as well as on diagnosis and treatment.

EPIDEMIOLOGY

Urothelial carcinoma is the fourth most common tumor in developed countries and the most common malignancy of the urinary tract.2,3 It accounts for 10 to 15% of all primary renal malignancies and more than 90% of renal pelvic tumors.1,7 The incidence of disease in the ureter over the past 30 years has increased from 0.69 cases per 100,000 person/years to 0.91 cases per 100,000 person/years, the incidence of renal pelvic

disease has decreased slightly from 1.19 cases per 100,000 person/years to 1.15 cases per 100,000 person/years, and the overall incidence is tumors. The number of upper urinary tract cases increased from 1.88-2.06 per 100,000 person/years.8 The highest incidence is found in the Balkans, where urothelial carcinoma accounts for 40% of all renal cancers.1,7 Bladder tumors account for 90-95% of urothelial carcinoma and are the most common malignant neoplasms of the urinary tract.2,3,6 Transitional cell carcinomas in upper urinary tract occurs in about 5% of all urothelial carcinomas and 7% of all primary renal malignancies.1,3,5 Upper tract urothelial carcinoma (UTUC) is rare, with an estimated annual incidence of nearly 2 cases per 100,000 people in Western countries.2,3,4

ETIOLOGY AND RISK FACTOR

The exact cause of renal transitional cell carcinoma is not known. On the other hand, various risk factors for the disease have been determined.1 It divided into genetic and environmental factors.3,9

Genetic About 10-20% of all UTUCs have a genetic background.2,10 Familial UTUCs are linked to Lynch Syndrome or hereditary non-polyposis colorectal carcinoma (HNPCC), which have mutation in the DNA mismatch repair genes MLH1 (MutL homolog 1), MSH2 (MutS protein homolog 2), MSH6 (MutS protein homolog 6), and PMS2 (mismatch repair endonuclease PMS2). People with this syndrome have higher chance to develop gastric, pancreatic, colonic, urothelial, sebaceous, uterine and ovarian carcinoma.9 UTUCs ranks third (5%) after colon cancer (63%) and endometrial cancer (9%) within the group of Lynch syndrome-associated tumors.5,10 In Lynch syndrome-related UTUCs, immunohistochemistry analysis showed loss of protein expression consistent with disease-predisposing mismatch repair (MMR) gene mutations in 98% of samples (46% microsatellite instability, 54% is microsatellite stable). The majority of tumors occur in MSH2 mutation carriers. Patients should undergo DNA sequencing and family counseling if they are identified as a high risk for Lynch syndrome. Screening of all patients under the age of 65 with UTUC and those with a family history of UTUC is important to reduce the incidence of undiagnosed hereditary disorders in urological cancer (figure 1).3

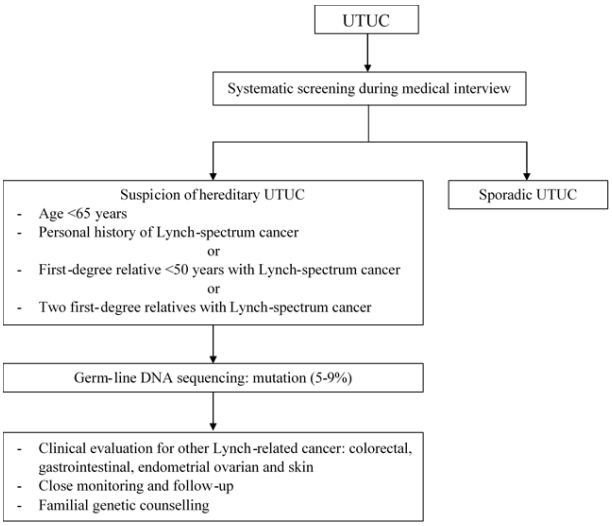

Figure 1. Selection of patients with UTUC (upper tract urothelial cancer) for hereditary screening during the first medical interview. (Adapted from European Association of Urology Guidelines on Upper Urinary Tract Urothelial Carcinoma 2020).3

Environment

Various environmental risk factors contribute to the development of renal transitional cell carcinoma or UTUC. Cigarette smoking is a modifiable risk factor and probably the most important one.9 70% of men and 40% of women with UTUC are exposed to cigarettes.5 Tobacco exposure increases the relative risk from 2.5 to 7.0.3 The mechanism of carcinogenesis in cigarette exposure is complex. Toxic substances inhaled during smoking, including aromatic amines with

arylamine, benzopyrene, and dimethylbenzanthracene. This aromatic amine is metabolized by the body in the carcinogenic N-hydroxylamine. Enzyme systems such as cytochrome P450s with CYP1A1, glutathione S-transferases, and N-acetyl transferases detoxify these derivatives. Genetic polymorphisms in enzymes that neutralize N-hydroxylamine may reflect susceptibility to the carcinogenic effects of smoking. Patients with a 20 pack-year smoking history had an odds ratio (OR) of 2.0. For heavy smokers such as 60 or more pack-years, the respective ORs are 6.2. A 60% to 70% reduction in UTUC risk occurred with smoking cessation for more than 10 years (OR 2.3 for former smokers vs. 4.4 current smokers).9

Occupational exposure to carcinogenic aromatic amines associated with UTUC "Amino tumor". These fragrances are still used in products such as paints, textiles, rubber, chemicals, petrochemicals and coal. The aromatic amines benzidine and beta naphthylane are involved in carcinogenesis.9

Aristolochic acid-induced nephropathy increases the risk of urothelial carcinoma. About half of those affected develop urothelial carcinoma and 90% of these are UTUC. Exposure to aristolochic acid results from ingestion of herbal medicine (Aristolochic acid is included in Mu Fang Ji medicine) or contaminated wheat in Balkans (Aristolichia clematis contaminates the flour supply and causes Balkans endemic nephropathy). Characteristics of nephropathy are proximal tubular damage, renal interstitial fibrosis and slow progression to renal failure.5

Chronic use or high dose analgesic abuse of the phenacetin has been considered a risk factor for UTUC since the 1960s.5,11 It causes a characteristic nephropathy called capillosclerosis.11 Its use has been restricted or replaced, and the number of UTUC cases due to phenacetin is decreasing.5 The incidence of UTUC is high in Taiwan and is also associated with blackfoot disease.3,5,11 Blackfoot disease is recognized as an endemic peripheral vascular disease and is associated with arsenic-rich groundwater.11 Chemotherapy regimens such as cyclophosphamide and ifosfomide which are alkylating agents have been shown to induce UTUC through acrolein metabolites.5,9 Other risk factors for UTUC are chronic urinary tract infections and urolithiasis.5

MOLECULAR CHARACTERISTIC

UTUC is a rare part of urothelial carcinoma and has not improved in recent decades because its biological mechanism is still unknown. Due to its rarity, there are few comprehensive studies on the molecular basis of UTUC.6 A high incidence of potentially actionable genomic changes including repetitive activating mutations in receptor tyrosine kinase (FGFR3, ERBB2), HRAS, PIK3CA and TSC1 currently have been identified in UTUC. However, these molecular profiling studies have also identified numerous genomic variants of unknown significance and significant genetic diversity among UTUC patients.12 Lee et al. found that the most common amplifications in UC were NOTCH1 (17,7%) and FGFR3 (14,5%). The molecular basis of NOTCH1 amplification in UC needs to be further clarified. In the recent study, the landscape of alterations in UTUC and UBUC was similar. TP53 was the most frequently mutated gene (68.5% of all UC cases). On the other hand, FGFR3 mutations (13.0%) occurred less frequently. FGFR3 mutation is associated with low-stage, low-grade tumors, and TP53 mutation is associated with high-stage, high-grade tumors.6

STAGING

UTUCs are classified according to the tumor, node, metastasis (TNM) classification (Table 1). The outcome of UTUC is strongly associated with the stage of the tumor.3,5

Table 1. TNM (Tumour, Node, Metastasis) classification 2017 for upper tract urothelial cell carcinoma.3

T - Primary tumour
TX Primary tumour cannot be assessed
T0 No Evidence of primary tumour
Ta Non-invasive papillary carcinoma
Tis Carcinoma *in situ*
T1 Tumour invades subepithelial connective tissue
T2 Tumour invades muscularis
T3 (Renal Pelvis) Tumor invades beyond muscularis into peripelvic fat or renal parenchyma
(Ureter) Tumour invades beyond muscularis into periureteric fat
T4 Tumour invades adjacent organs or through the kidney into perinephric fat
N - Regional lymph nodes
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in a single lymph node 2 cm or less in the greatest dimension
N2 Metastasis in a single lymph node more than 2 cm, or multiple lymph nodes
M - Distant metastatis
M0 No distant metastasis
M1 Distant metastasis

The American Joint Committee on Cancer (AJCC) further classified the staging of UTUC based on TNM classification.13 The staging classification is shown in table 2 below.

Table 2. The American Joint Committee on Cancer (AJCC) staging classification of UTUC.13

Stage	TNM
0a	Ta, N0, M0
0is	Tis, N0, M0
I	T1, N0, M0
II	T2, N0, M0
III	T3, N0, M0
IV	T4, N0, M0
	Any T, N1, M0
	Any T, N2, M0
	Any T, Any N,M1

DIAGNOSIS

Clinical Manifestation

Gross hematuria is the most common symptom of kidney transitional cell carcinoma, occurring in 75-95% of patients.1,3,11 Microscopic hematuria occurs in 3-11% of patients. Dull pain on flank is reported by about 14-37% of patients and is associated with gradual obstruction of the collecting system. Renal colic can also occur with the passage of a blood clot.1 Lateral abdominal pain occurs in about 20% of cases.3 Other symptoms that may occur include weight loss, lower extremity edema, fever, and fatigue.3,7 Only a small percentage (1-2%) of patients is asymptomatic. The patient's physical

examination is usually neither informative nor specific, especially in patients with early-stage disease. A palpable pelvic mass can be found in less than 20% of patients. The classic clinical triad of hematuria, pain, and mass is also rare (15%) and is usually an indicator of advanced disease.1

Imaging

Several studies had been conducted to improve the diagnosis of UTUC to be less invasive and easy to perform. The American Urological Association recommendation for standard work-up consists of urinalysis and cytologic analysis, cystoscopy, and excretory Urography. Recent studies shows that computer tomography urography (CTU) have been used as diagnostic tools with minimal invasive procedure, detection of urinary caliculi and renal parenchymal masses.14 However, a positive biopsy is required for a definitive diagnosis.2

Excretory Urography (EU)

Mostly used in investigation of hematuria. It is non-invasive method of imaging, offers detailed anatomy of pelvico-calyceal system and ureters.15,16 Transitional cell carcinoma (TCC) is characterized by a filling defect within contrast-enhanced, may be single or multiple and smooth, irregular, or stippled. Stipple sign refers to injection of contrast material into interstitial part of a papillary lesion (Figure 2).14

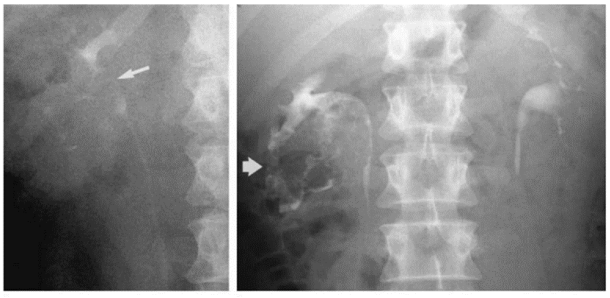

Figure 2. (small arrow) shows irregular filling defect in right pelvis and extending in to lower part of calices; (big arrow) shows a large stipple filling defect in collecting system of the right kidney.14

Retrograde Pyelography (RP)

RP is usually performed during cystoscopy to further analyze the abnormalities, in abnormal excreting ability of the kidney or in cases of allergy of contrast material. RP is an invasive procedure, yet it allows confirmation of diagnostic evaluation by providing biopsy or brushin and cytological examination of localized urine collections. In RP, renal TCC appears as intraluminal filling defect, may be smooth, irregular, or stippled. If TCC involves an infundibulum, there may be appearance of "amputated" calix with or without focal hydronephrosis and caliculi secondary to obstruction (Figure 3).14

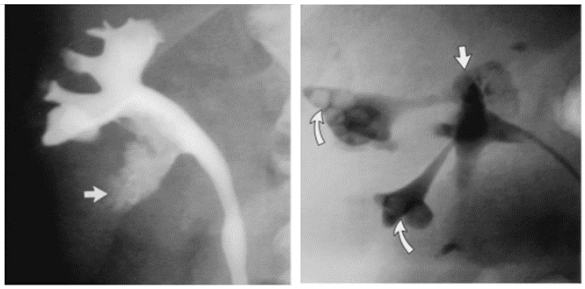

Figure 3. (Left) Diffuse infiltrating of TCC in right lower pole calix and irregular shape involves mucosa (arrow). (Right) Amputation of the upper pole of calix due to TCC (straight arrow) and multiple calliculi are seen in the lower pole and interpolar calices (Curved arrows).14

Computer tomography urography (CTU)

CTU has been shown to be more sensitive than EU in the detection of small renal mass lesions and urinary tract caliculi. The pre-enhanced scan is performed to exclude renal stone. CTU allows to evaluate mass, vascular abnormalities, and the extension of the masses

(Figure 4).14 CTU with at least one series of images during the excretory phase (10–15 min) after contrast injection is the standard imaging technique for detecting and staging UTUC.2

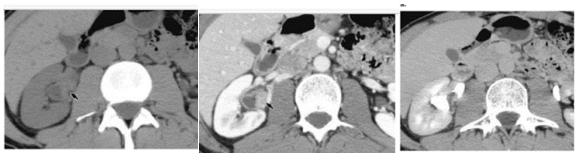

Figure 4. (left) axial non-enhanced CT-scan shows slightly hyperdense; (middle) axial nephrography shows an early enhancement of tumor and extension into situation of upper pole parenchym (arrow); (right) Axial excretory phase CT shows a mass within renal pelvis with surrounding excreted contrast medium.14

Magnetic resonance urography (MRU)

MRUs vary widely in the accuracy of UTUC classification. Therefore, it is recommended for patients who are not candidates for CTU, usually when radiation or iodinated contrast media are contraindicated.2,3 The sensitivity of MR urography is 75% after contrast injection for tumors < 2 cm.3

Ureteroscopy

Flexible ureteroscopy (URS) is used to visualize the ureter, renal pelvis, and collection system and to perform biopsy of suspicious lesions. The presence, appearance, and size of the tumor can be determined by URS. In addition, ureteroscopic biopsy can determine tumor grade in 90% of cases, regardless of sample size, and has a low false-negative rate.3

Cytologic

Primary upper urinary tract (UT) cytology and endoscopic biopsy play a central role in the UTUC treatment paradigm. UT urinary cytology is widely used and plays an essential role in the detection of UTUC. In the literature, the sensitivity of UT urine cytology in the detection of UTUC is widespread. Some studies have shown that high-grade UTUC is fairly reliably detected by UT cytology. On the other hand, the sensitivity of UT cytopathology to low-grade lesions is low. Some cytological features of low grade tumor (I and II) are nuclear hyperchromasia, lack nuclear pleomorphism. The characteristic of high grade (III and IV) tumor including nuclear hyperchromasia, nuclear enlargement, and irregular nuclear membrane.17

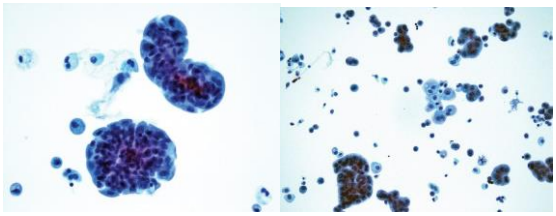

Figure 5. (left) Low-grade papillary urothelial carcinoma. Tight clusters of hyperchromatic urothelial cells show nuclear membrane irregularity. The cells lack nuclear pleomorphism. The concurrent histology revealed low-grade papillary urothelial carcinoma. (Right) Positive for high-grade urothelial carcinoma. Papillary clusters of malignant urothelial cells show nuclear hyperchromasia, nuclear enlargement, and irregular nuclear membrane.17

Histopathology

The spectrum of atypical morphology of UTUC resembles that of the bladder. Previous reports of resected specimens include UC with squamous cell differentiation, UC with glandular differentiation, microcystic UC, micropapillary UC, UC with reverse growth pattern, UC with choriocarcinoma or syncytiotrophoblastic giant cells (currently UC with trophoblastic differentiation), sarcomatoid UC (including cases with heterologous components present such as rhabdoid cells or chondrosarcoma), lymphoepithelioma-like UC, nested UC, plasmacytoid UC, signet ring cell (currently

included in plasmacytoid UC if no extracellular mucin component is present), , small cell carcinoma, clear cell UC, and lipid-rich UC, osteoclast-rich poorly undifferentiated carcinoma, and UC with pseudosarcomatous stromal changes.18

TREATMENT

The choice of treatment depends on clinical evaluation.19 Treatment for low-risk UTUC may include kidney-sparing surgery, flexible ureteroscopy or segmental resection or percutaneous approach. Meanwhile, for high-risk UTUC, RNU can be performed with or without peri-operative platinum-based combination chemotherapy and then a single post-operative dose of intravesical chemotherapy.3 The development of new therapeutical endourological intervention of kidney transitional cell carcinoma has provided new options for regional management of the cancer. Electrofulguration and resection or laser can be performed transuretrally or percutaneously and may reduce the primary cancer. The biopsy as treatment and diagnostic remain unclear.19

Nephroureterectomy (NU)

Nephroureterectomy (NU) is the gold standard approach for UTUC, but may be over-treatment for patients with distal or low-grade non muscle invasive ureteral tumors and may not be feasible in patients with a single upper urinary tract.5 Kidney-sparing surgery or partial nephrectomy for low-risk UTUC reduces the morbidity associated with radical surgery, without affecting cancer outcome. For low-risk cancers, this is the preferred approach because survival is similar to that after RNU.3 Radical nephroureterectomy (RNU) with excision of bladder cuff is the standard treatment for high-risk UTUC.5 Due to the high recurrence rate of ureteral stumps observed after simple nephroureterectomy, nephroureterectomy with bladder cuff resection was the main treatment.11 This can be done through several different open (ONU) approaches, such as a single midline incision, thoracoabdominal incision, or flank incision with Gibson or bladder incision to remove Gibson or bladder cuff, or laparoscopic (LNU) or robot-assisted laparoscopic technology.5 Electro-resection and fulguration or laser fulguration can be performed in superficial tumor. Segmental resection, ureterorenoscopic or percutaneous resection/ fulguration/ laser destruction can be performed if the renal unit is solitary or renal function is decreased.19 In low-grade non-invasive tumors that are too large for endoscopic treatment or in patients with high-grade tumors requiring nephron sparing, segmental ureterectomy can be performed.5

Ureteroscopy

Endoscopic ablation should be considered in low-risk clinical cancer patients.3 Some UTUCs such as low-grade noninvasive muscle tumors can be safely treated endoscopically, as long as it is accessible. Endoscopic management is recommended for patients with isolated upper airway (anatomy or function), those with bilateral UTUC, patients with poor baseline renal function, or patients with severe renal impairment, patients with a lot of comorbid to undergo RNU and for tumors that are low-grade non-muscle invasive lesions.5 Laser vaporization or coagulation can be done through endoscopy or percutaneous access. It depend on the accuracy of initial staging and the adequacy of visualization of the targeted lesion. The efficacy depend on staging at initial treatment and the monitoring after the procedure.19

Chemotherapy/immunotherapy and radiotherapy

The efficacy of thiotehpa, mitomycin, doxorubicin for superficial cancer therapy in the bladder may be used in UTUC. There may

be some consideration regarding the use of these therapies such as the extent of the disease in renal pelvis, the availability, patients' response to the treatment, and the accuracy and adequacy of initial tumor staging and monitoring.19 Topical immunotherapy or chemotherapy can be given retrogradely through a ureteral catheter or antegradely through a percutaneous nephrectomy. The agents used for adjuvant treatment of UTUC were mainly extrapolated from those used for bladder cancer. Several different agents have been described, including mitomycin C, thiotepa, bacille Calmette Guérin (BCG)/interferon, and BCG alone.5 Adjuvant radiation therapy has been suggested to control local disease after RNU. The data is still controversial and insufficient to draw conclusions.3

PROGNOSIS

UTUC is a rare subset of urothelial carcinoma which has a poor prognosis.6 Age was strongly correlated with overall survival. 5-year survival decreased from 75% of patients under 50 years to less than 20% of patients over 85 years. Race / ethnicity was associated with differences in overall survival, with Black non-Hispanic patients having a 30% higher mortality rate than Hispanic or White non-Hispanic patients. Genetic and biological differences, access to health care, and basic health, are hypothesized to be related to these differences.8 Tumor stage is the most important prognostic factor for urothelial carcinoma of the upper urinary tract. Survival is closely related to the stage of the tumor. Tumor size is prognostic and lies between the extremes of 3-12 cm in diameter, most in between. Tumor grade is another predictor of prognosis. Tumor malignancy usually follows the stage of the tumor, and patients with high-grade cancer have a more advanced stage. Stages and grades correlate up to 83% of the time, but stages are still a more accurate predictor of prognosis.1

CONCLUSION

Renal transitional cell carcinoma or upper tract urothelial carcinoma is a rare type of urothelial carcinoma. Various risk factors have been determined such as genetic and environmental factors. About 10-20% of all UTUCs have a genetic background. Cigarette smoking is a modifiable risk factor and probably the most important one. Due to its rarity, there are few comprehensive studies on the molecular basis of UTUC. TP53 was the most frequently mutated gene in urothelial carcinoma. Gross hematuria is the most common symptom (75-95%), and asymptomatic patients in only a small proportion (1-2%). CTU is the mainstay of diagnostic tools for UTUC because it's less invasive and convenient. However, a positive biopsy is required for a definitive diagnosis. The treatment mostly the resection of the mass and adjuvant with immunotherapy, but further studies need to be conducted for further evaluation of these treatments. The outcome of UTUC is strongly associated with the stage of the tumor.

REFERENCES

1.Enow, Orock G, Eyongeta, DE, Weledji, PE Renal.Transitional Cell Carcinoma: Case report from the Regional Hospital Buea, Cameroon and Review of Literature. International Journal of Surgery Research and Practice. (2014) Pract 1:007. DOI:10.23937/2378-3397/1410007

2.Szarvas, Tibor, Módos, Orsolya, Horváth, András, Nyirády, Péter. Why are upper tract urothelial carcinoma two different diseases?. Translational Andrology and Urology. 2016;5(5):636-647. DOI:http://dx.doi.org/10.21037/tau.2016.03.23

3.Rouprêt, M., et al. European Association of Urology Guideline on Urothelial Carcinomas of the Upper Urinary Tract. 2020

4.Lughezzani, Giovanni, et al. Prognostic Factors in Upper Urinary Tract Urothelial Carcinomas: Comprehensive Review of the Current Literature. European Urology. 2012; 62: 100-114. DOI:10.1016/j.eururo.2012.02.030

5.Linton, Kate D., Catto, James, WF. Upper Tract Urothelial Carcinoma. Journal of Clinical Urology. 2016; 6(5): 272–279. DOI:10.1177/2051415813502286
6.Lee, Ji Yun, et al. Molecular Characterization of Urothelial Carcinoma of the Bladder and Upper Urinary Tract. Translational Oncology. 2018; 11(1): 37-42. DOI:https://doi.org/10.1016/j.tranon.2017.10.008
7.Li, Mingyang, et al. Transitional cell carcinoma with extension of the renal vein and IVC tumor thrombus: report of three cases and literature review. World Journal of Surgical Oncology. 2016; 14:309. DOI: 10.1186/s12957-016-1041-z
8.Raman, Jay D., Messer, Jamie, Sielatycki, John A., Hollenbeak, Christopher S. Incidence and survival of patients with carcinoma of the ureter and renal pelvis in the USA, 1973–2005. British Journal of Urology International. 2010; 107, 1059 – 1064. DOI:10.1111/j.1464-410X.2010.09675.x
9.Partin, Alan W., Dmochowski, Roger G., Kavoussi, Louis R., Peters, Craig A. Campbell-Walsh-Wein Urology Twelfth Edition. 2021. Canada: Elsevier
10.Lindner, Andrea Katharina, et al. Lynch Syndrome: Its Impact on Urothelial Carcinoma. International Journal of Molecular Sciences. 2021, 22, 531. DOI:https://doi.org/10.3390/ijms22020531
11.Kirkali, Ziya, and Tuzel, Emre. Tansitional cell carcinoma of the ureter and renal pelvis. Critical Review in Oncology Hematology. 2003; 47: 155-169. DOI:10.1016/S1040-8428(03)00079-9
12.Kim, Kwanghee, et al. Modeling biological and genetic diversity in upper tract urothelial carcinoma with patient derived xenografts. Nature Communications. 2020; 11:1975. DOI:https://doi.org/10.1038/s41467-020-15885-7
13.Amin MB, Edge SB, Greene FL, et al., eds.: AJCC Cancer Staging Manual. 8th ed. New York, NY: Springer, 2017, pp. 749–55.
14.Browne RF, Meehan CP, Colville J, Power R, Torreggiani WC. Transitional cell carcinoma of the upper urinary tract: spectrum of imaging findings. Radiographics. 2005 Nov;25(6):1609-27. DOI: 10.1148/rg.256045517
15.Kawashima A, Glockner JF, King BF Jr. CT urography and MR urography. Radiol Clin North Am. 2003;41:945–961.
16.Maher, MM, Kalra, MK, Rizzo, S, Mueller, PR, Saini, S. Multidetector CT urography in imaging of the urinary tract in patients with hematuria. Korean J Radiol 2004;5:1–10.
17.Chen, L, He, H, Zarka, MA, Zhou, M, Magi-Galluzzi, C. Upper tract urinary cytology to detect upper tract urothelial carcinoma: Using the Johns Hopkins Hospital template and evaluation of its feasibility. Cytojournal. 2015; 12:17. DOI:10.4103/1742-6413.161608
18.Hayashi, Hiroyuki, Mann, Steven, Kao, Chia-sui, Grignon, David, T. Idrees, Muhammad. Variant morphology in upper urinary tract urothelial carcinoma: a 14-year case series of biopsy and resection specimens. Human Pathology. 2017; 65, pp 209-216. DOI: https://doi.org/10.1016/j.humpath.2017.05.001
19.PDQ® Adult Treatment Editorial Board. PDQ Transitional Cell Cancer of the Renal Pelvis and Ureter Treatment. Bethesda, MD: National Cancer Institute. Updated (01/20/2020). Available at: https://www.cancer.gov/types/kidney/hp/transitional-cell-treatment-pdq. Accessed (03/22/2022)

RESEARCH ARTICLE

RELATION OF NUTRITIONAL STATUS ON THE EVENT OF KIDNEY STONES IN WEST NUSA TENGGARA PROVINCE GENERAL HOSPITAL

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ABSTRACT

Background: Urinary tract stone disease is one of the diseases with a high rate of incidence in Indonesia based on the number of patients who come to Urology outpatient care center. One of the risk factors for urinary tract stones is a systemic disease, including hypertension and obesity. Based on previous research, there are studies who state that there was no relationship between body mass index and the incidence of urinary tract stones, other studies state that there was a relationship between body mass index and the incidence of urinary tract stones. The difference in the results of these studies prompted researchers to conduct research related to the relationship between body mass index and the incidence of urinary tract stones, especially in West Nusa Tenggara specifically in Mataram area.

Methods: The research method used was an analytic observational study. The research design used was cross-sectional. Study subjects were reqruited from medical record patient of urology outoatient department. In this research design, researchers conducted an analysis related to the relationship between variables.

Results: 69 kidney stone patients at the West Nusa Tenggara Province General Hospital were enrolled. Characteristics of respondents are based on age, most of them were aged of 56 years old and over, as many as 28 patients (40.58%), most of subjects were male, most of them did not finish primary school as many 29 patients (42.03), and ocupations mostly not working. While the nutritional status is mostly normal, as many as 46 respondents with a percentage of 66.67%.

Conclusion: This study shows that body mass index and age have a relationship with the incidence of kidney stones, while occupation and gender have no relationship with the said incidence.

Keyword: **Kidney stones, age, occupation, gender, nutritional status.**

Introduction

Urinary tract stone disease is one of the diseases with high rate of incidence in Indonesia based on the number of patients in the Urology outpatient care center. Urinary tract stones are conditions where urine calculus were formed in the urinary tract , ureters, bladder, and urethra. The main component of most urinary tract stone is calcium oxalate (50-70%) either in its pure form (30%) or a mixture with calcium phosphate (40%). Followed by stones of uric acid about 10-20% then struvite stones or ammonium magnesium phosphate stones as much as 5-10% and at least in the form of

cystine stones which are only 1-2% (Anhar and Widianto,2014).

One of the risk factor for urinary tract stones is a systemic disease, including hypertension and obesity. In individuals who are overweight, there is an increase in the incidence of urinary tract stones by more than 75%. In addition, there are also studies whose results state that a Body Mass Index (BMI) of more than 30 kg/m^2 is associated with an increased risk of kidney stone formation because urinary excretion of oxalate, uric acid, sodium and phosphate is higher than individuals with a normal BMI (Agustin,2019).

Body Mass Index (BMI) is a tool to monitor the nutritional status of adults. This index can be related to a person's excess weight or underweight. Inadequate or excessive nutritional condition can be a risk of certain diseases (Anhar and Widianto,2014).

Obesity and type 2 diabetes mellitus are both associated with urinary tract stones. As the epidemic of obesity and diabetes increases, the prevalence of urinary stones also increase. Anhar and Widianto (2014), stated that there was no relationship between body mass index (BMI) and the incidence of urinary tract stones, while Antonelli's research Wong, Cook, and Somani (2015) stated that there was an increase in the incidence of urinary tract stones of more than 75% in individuals who are overweight and obese.

The difference in opinion has prompted researchers to conduct further research related to the relationship between body mass index (BMI) and the incidence of urinary tract stones, in Mataram,area.

Material and Methods

Research design

This research conducted a cross-sectional research design, that was all research variables were collected at the same time. The dependent variables were BMI, age, gender, and occupation of the patients with renal stones, while the independent variable was the renal stone.

The research was conducted at the NTB Provincial General Hospital. The time of the study was carried out from December 2021-February 2022.

Research Subjects

The population in this study were all patients who suffered from urinary tract stones, especially kidney stone patients who were at the NTB Provincial General Hospital. The sample in this study was patients who met the inclusion criteria are patients diagnosed with kidney stones in January to December 2020. The research sample from this study were patients from the NTB provincial general hospital who had been diagnosed with kidney stones who met the inclusion criteria that had been determined and were taken based on total sampling recruitment.

Research Instruments

The instrument used for data collection was a data sheet which were filled out from medical record data of patients diagnosed with kidney stones in the NTB Provincial General Hospital and also data from patient interviews via telephone

Data analysis

Data analysis in this study used the software SPSS Statistical Package Social Service) version 21. Data were performed descriptively by using the frequencies table. The analysis of the relationship between variables used the Binomial test.

Results and Discussion

Characteristics of respondents

As many as 69 patients with kidney stone enrolled in this research. The characteristic of those patient demonstrated in table 1.

Table 1. Characteristics of respondents with kidney stones at the NTB Provincial Hospital.

Characteristics	Frequency	Percentage (%)	Binomial Test
Age			
Early adulthood 26-35 years	7	10.14	
Late adult 36-45 years	8	11.59	p = 0.002
Early elderly 46-55 years	26	37.68	
Late Elderly > 56 years	28	40.58	
Total	69	100	
Gender			
Female	30	43.48	p = 0.336
Male	39	56.52	
Total	69	100	
Education			
uneducated	29	42.03	
School Elementary	12	17.39	
Junior High School	5	7.25	
Senior High School	14	20.29	
Diploma-3	1	1.45	
Bachelor/Undergraduate	7	10.14	
Postgraduate	1	1.45	
Total	69	100	
Occupation			
unemployment	35	50.72	
Farmer	3	4.35	
Labor	5	7.25	
Entrepreneur	8	11.59	p = 0.057
Student	1	1.45	
Civil Servant	11	15.94	
Others	6	8.70	
Total	69	100	

According to Haerudin, Kusmiati and Budiman (2015), age is one of the factors that influence the occurrence of kidney stones, especially at the age of 55 years and over. This is also supported by research conducted by Fauzi and Putra (2016), that age above 40 years is the age with the most cases of nephrolithiasis, kidney stones that occur at a young age are usually due to family history or local medical conditions and gout. The results of this study are in line with the two opinions above where data is obtained that the age of the late elderly and the early elderly is the age with the most cases of kidney stones.

Age is one of the factors that are often associated with the incidence of kidney stones.

The results of this study indicate that the incidence of kidney stones has a relationship with a person's age with a value of p = 0.02 (p <0.05). In this study, it was found that patients who experienced kidney stones were in the elderly age, specifically 56 years and over. The results of this study are in accordance with research conducted by Nurfitriani and Oka (2019) that the incidence of urinary tract stones, which in this case includes kidney stones, has a significant relationship with the age of the patient.

Increasing age is in line with the increase in the work of stones in the kidneys and reaches a maximum level in adulthood. As we age, the capacity of the kidneys increases. If it is not balanced with appropriate metabolism, there will be a high deposition process in the Loop of Henle. In the elderly, some of the nephrons are no longer functioning properly, and are equally characterized by a decrease in proximal tubular volume or a Loop of Henle. This results in an increased chance of stone deposition occurrence (Ratu, Badji and Hardjoeno, 2006).

The results of this research on gender are in line with research conducted by David, Frederic and Orson (2008), that men are more progressive than women in kidney stone disease which were thought to be because the urinary tract in men is longer than the urinary tract in women.

The incidence of kidney stones from several studies states that male patients are more likely to experience kidney stones than female patients. The results of this study indicate a significant value of the relationship between gender and the incidence of kidney stones, the value of p = 0.336 (p>0.005), indicates that the incidence of kidney stones has no relationship with the gender of the patient. The sresults of this study are different from the research conducted by Muthia et al. (2015) wherein the incidence of urinary tract stones has a relationship with gender in which the male gender is more likely to be at risk of experiencing the disease. There is no relationship between gender and the incidence of kidney stones, it can also be caused by women's habits that can cause the disease, for example, holding back urination, sedentary life style and a high protein diet (Nurlina, 2008).

The occurrence of kidney stones can also be caused by hormones, one of which is testosterone. Testosterone has toxic properties on the kidneys, which can induce podocytes and TGF-β1 which is associated with accelerated processes of sclerosis and renal fibrosis. Testosterone also induces renin-angiotensin-aldosterone system (RAAS) which results in both glomerular and systemic hypertension. Unlike the hormone estrogen. Estrogen is protective due to the mechanism of inhibition of RAA, so that the incidence of kidney stones is more in men than women.

The results of this study stated that there was no significant relationship between occupation and the incidence of kidney stones where the p-value = 0.057 (p > 00.05). The results of this study are different from research conducted by Silalahi (2020) where sitting while working is one of the causes of urinary tract stones. On average, kidney stone patients at the West Nusa Tenggara Provincial Hospital are not work, some are retired employees and some choose to quit their jobs because they are no longer able to work due to old age. The incidence of kidney stones can be caused by excessive activity and bad habits of patients. Patients who have jobs cannot do activities such as sitting for an excessive period of time. Therefore, work does not affect the occurrence of kidney stones.

Nutritional status

Table 2. Nutritional status of kidney stone patients in NTB Provincial Hospital

No	Nutritional status (BMI)			Frequency	Percentage (%)	Binomial Test
1	Underweight	Heavy	(< 17.0 kg/m^2)	2	2.90	
		Light	(17.0-18.4 kg/m^2)	0	0	
2	Normoweight		(18.5-25.0 kg/m^2)	46	66.67	p = 0.00
3	Overweight	Light	(25.1-27.0 kg/m^2)	10	14.50	
	Obese	Heavy	(>27.0 kg/m^2)	11	15.95	
	Total			69	100	

Nutritional status is one of the most important factors in supporting human health. Susetyowati (2002), states that malnutrition in patients with kidney disease is usually caused by several factors including lack of food intake, increased catabolism, or the characteristics of the patient himself. The common method to assess nutritional status is by calculating the BMI.

The results of this study indicate that the highest number of patients suffering from kidney stones in the NTB Provincial Hospital was normoweight, that were 46 patients (66.67%). This means that most patients are not obese or malnourished. This is in accordance with research conducted by Haerudin, Kusmiati, and Budiman (2015) that the incidence of kidney stones in Majalengka Hospital in 2013 was experienced by most of the normoweight patients.

The incidence of kidney stones is caused by inadequate of water consumption, sleep patterns, hypertension, or the influence of other diseases. When the body lacks of water, the consequence is water reabsorption will occur in the kidney. Excessive consumption of minerals, vitamins, or other substances will be excreted through the urine. Excessive of minerals and vitamins cannot be excreted by the kidneys and then will affect the decline in kidney function and the excessive minerals and vitamins will precipitate and kidney stones (Han et al.,2015).

The Relationship between Nutritional Status (BMI) and the Incidence of Kidney

Kidney stones are a group of urinary tract stones. Kidney stones are defined as a condition in which there are stones containing crystalline components and organic matrix in the kidneys, which affects the function of these organs. Types of kidney stones consist of calcium stones, struvite stones, uric acid stones, and other types of stones such as cystine, xanthine, and brush (Fauzi and Putra, 2016).

Body Mass Index (BMI) is one method of nutritional assessment. BMI will categorize three categories, namely underweight, normal and obese. Body mass index is often associated with the incidence of urinary tract stones, especially in the obesity category. Obesity can cause various kinds of dangerous diseases such as hypertension, diabetes mellitus, and even urinary tract stones (Anhar and Widianto, 2014) .

The results of this study indicate that BMI has a significant relationship with p value = 0.000 (p>0.05) on the incidence of kidney stones in the Regional General Hospital (RSUD) of NTB Province. The results of this study are in accordance with research conducted by Nurfitriani and Oka (2019), that body mass index has a significant relationship with the incidence of urinary tract stones. Research conducted by Kim et al (2011) also states the same thing that one of the factors causing the occurrence of urinary tract stones is a person's Body Mass Index (BMI).

There is a significant relationship between BMI and the incidence of kidney stones because irregular food consumption can result in an increase in calcium, oxalate, and uric acid lithogenic substances that cause stone formation. This is in accordance with the opinion of Silalahi (2020) that the occurrence of kidney stones is caused by an excessive amount of calcium, oxalate, phosphate, and uric acid compounds in the body, compounds that are not used will precipitate and become kidney stones.

Conclusion

This study concluded that body mass index and age have a relationship with the incidence of kidney stones, while occupation and gender do not have relationship with the incidence of kidney stones.

REFERENCES

Agustin, O.A. (2019) "Hubungan Hipertensi dan Obesitas dengan Pasien Batu Saluran Kemih pada Pasien Poliklinik Urologi di RSUD Abdul Wahab Sjahranie Samarinda," *Health Science Journal*, 1(1), pp. 28–34.

Anhar, N.H. and Widianto, A. (2014) "Index Massa Tubuh Sebagai Faktor Resiko Terjadinya Batu Saluran Kemih di RS Muslimat Ponorogo Dalam Kurun Waktu Januari 2007 - Desember 2010," *Jurnal kedokteran dan kesehatan Indonesia*, 6(2), pp. 75–84. doi:10.20885/JKKI.Vol6.Iss2.Art4.

David, B.A., Frederic, C.L. and Orson, M.W. (2008) *Nephrolithiasis In Kidney*. 8th edn. Philadelphia: Saunders Elsevier.

Fauzi, A. dan M.M.A. Putra. (2016). Nefrolitiasis. Majority. Vol 5. No.2. 69-73.

Depkes RI (2009) *Sistem Kesehatan Nasional*.

Haerudin, H., Kusmiati, M. and Budiman (2015) *Hubungan Karakteristik Pasien dengan Kejadian Nefrolitiasis Di Rumah Sakit Umum Daerah Manjalengka Tahun 2013*. Universitas Islam Bandung.

Han, H., Segal, A. M., Seifter, J. L., & Dwyer, J. T. (2015). *Nutritional Management of Kidney Stones (Nephrolithiasis)*. Clinical Nutrition Research, 4(3), 137. https://doi.org/10.7762/cnr.2015.4.3.137. Diakses 20 Maret 2022.

Nurfitriani and Oka, A.A.G. (2019) "Usia dan Obesitas Berhubungan terhadap penyakit batu saluran kemih di RSUP Sanglah Denpasar Periode Januari 2014 sampai Desember 2014," *Jurnal Intisari Sains Medis*, 10(2), pp. 258–262.

Nurlina. (2008). *Faktor-faktor risiko kejadian batu saluran kemih pada laki-laki. (Studi kasus di RS. Dr. Kariadi, RS Roemani, dan RSI Sultan Agung Semarang*. Skripsi.

Ratu, G., Badji, A. and Hardjoeno (2006) "The Analysis of Urethral Stone Profile at The Clinical Pathology Laboratory," *Indonesian Journal of Clinical Pathology and Medical Laboratory*, 12(3), pp. 114–117.

Silalahi, M.K. (2020) "Faktor-Faktor yang Berhubungan Dengan Kejadian Penyakit Batu Saluran Kemih Pada di Poli Urologi RSAU dr . Esnawan Antariksa," *Jurnal Ilmiah Kesehatan*, 12(2), pp. 205–212.

Wong, Y. v., Cook, P. and Somani, B.K. (2015) "The Association of Metabolic Syndrome and Urolithiasis," *International Journal of Endocrinology*, 2015, pp. 1–9. doi:10.1155/2015/570674.

RESEARCH ARTICLE

CHARACTERISTICS OF VARICOCELE PATIENTS AFTER VARICOCELECTOMY IN BIOMEDIKA MATARAM HOSPITAL 2018-2020

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ABSTRACT

Background: Varicocele is an abnormal venous dilatation in the pampiniform plexus which affects 15% of the men population in all age groups. An understanding of the characteristics of varicocele patients can help determine the appropriate indication for therapy, so it is very important for the success of varicocele therapy. However, currently, it is still rare to find data that specifically discuss the characteristics of varicocele patients, especially those undergoing varicocelectomy in Mataram. This research is aimed to investigate the characteristic of varicocele patients who underwent varicocelectomy in Biomedika Mataram Hospital from 2018 through 2020.

Methods: This is retrospective descriptive research with a cross-sectional design. The sampling technique used in this research is total sampling which will collect secondary data in the form of medical records of all varicocele patients who underwent varicocelectomy in Biomedika Mataram Hospital from 2018 through 2020.

Results: This research found that varicocele patients who underwent varicocelectomy were mostly in the 26-45 years old age group with 26 patients (65%), with infertility disorder (26 patients; 72,5%). It was also found that 28 patients came with left unilateral varicocele (70%), 15 patients grade I varicocele, and 21 patients abnormal results in semen analysis (52,5%) with the most prevalent interpretation is azoospermia (6 patients; 28,6%). All patients underwent Ivanissevich varicocelectomy (40 patients; 100%), and the number of veins that were ligated during the procedure was 2-5 veins in 30 patients (75%).

Conclusion: Varicocele patients who underwent varicocelectomy were mainly in the 26-45 years old group, has an infertility disorder, left unilateral type, grade I, and an abnormal semen analysis with the interpretation of azoospermia. All of the patients underwent Ivannissevich varicocelectomy with the number of ligated veins was 2-5 veins in most patients.

Keyword: Varicocele, varicocelectomy, characteristics

Introduction

Varicocele is a condition caused by abnormally dilated pampiniform plexus in the spermatic funicle.[1,2] Currently, varicocele has become a common condition affecting around 15% of men population across all age groups.[3] The prevalence of varicocele in children, teens, and the adult population varies widely. Varicocele is more often found in the left testicles rather than the right. This tendency is thought to be caused by anatomical differences between the left and right spermatic veins.[4,5] Varicocele were commonly asymptomatic, but in some cases, clinical symptoms that may appear in varicocele

patients are pain or discomfort in the scrotum.[3,6] In men who are diagnosed with varicocele, the incidence of pain is predicted to be as high as 10%.[6] Besides that, varicocele can also cause infertility. A study in The United States of America (USA) showed that varicocele is the most etiology of infertility in men with a prevalence f 42,2%.[7]

Although some experts have different thoughts on the need for therapy for varicocele patients but based on some indications, therapy in varicocele patients is necessary.[5,8] Treatment options for varicocele are divided into two main categories which are percutaneous occlusion and ligation surgery. This surgical therapy consists of conventional open varicocelectomy (retroperitoneal ligation, inguinal ligation, and sub-inguinal ligation), laparoscopic varicocelectomy, and microsurgical varicocelectomy.[9]

A comprehensive understanding of varicocele patient's characteristics can help to decide a suitable treatment option, hence playing a significant role in the success of varicocele treatment.[10] However, specific data regarding varicocele patients' characteristics are still scarce, especially in Mataram, West Nusa Tenggara. Therefore, the author was interested in investigating the characteristic of varicocele patients who underwent varicocelectomy in Biomedika Mataram Hospital. This study aims to determine the characteristics of varicocele patients who underwent varicocelectomy at the Biomedika Mataram Hospital for the 2018-2020 period.

Research Methods

This research is a retrospective descriptive study with a cross-sectional design that uses secondary data from the medical records of varicocele patients who underwent varicocelectomy in Biomedika Mataram Hospital from 2018-2020. The research was carried out at the Biomedika Mataram Hospital in September-October 2021. The inclusion criteria were all patients diagnosed with varicocele and had underwent varicocelectomy, and also patients admitted within January 1st 2018 – December 31st 2020. While the exclusion criteria were medical records that were not able to be found. This study used a total sampling technique that all patients who met the criteria were included as the study sample. Collected medical records data were age, clinical manifestation, types of varicocele, severity grade of varicocele, pre-operation semen analysis, type of operation, and the number of the ligated vein during the operation. Collected data will then be analyzed using SPSS Statistics 28 Software and presented in the form of descriptive data. This research has been approved by The Research Ethical Committee of Faculty of Medicine, University of Mataram with No: 250/UN18.F7/ETIK/2021.

Results

Based on the inclusion and exclusion criteria, 40 samples were included in this study. As shown in **Table 1**, the included varicocele patients who underwent varicocelectomy in Mataram Biomedika Hospital in 2018-2020 were mostly in the age group of 26-45 years old with 26 patients (65%). The oldest patient was 50 years old while the youngest was 17 years old with an

average of 28,9 years old. Based on the clinical manifestations, most of the included patients showed a clinical manifestation in the form of infertility with 29 patients (72,5%). Based on the type of varicocele, most of the varicocele patients in this research suffer from left unilateral varicocele with 28 patients (70%).

Table 2, illustrates the most prevalent grade of varicocele found in this study were grade I with 15 patients, grade III with 12 patients, and grade II with 11 patients.

Based on the results of pre-operation semen analysis on varicocele patients who underwent varicocelectomy, most patients showed an abnormal result in the pre-operation semen analysis in 21 patients (52,5%). Out of 21 abnormal patients, most of the interpretations were azoospermia with 6 patients (28,6%) as shown in **Tabel 3**.

All varicocele patients in this study underwent Ivanissevich varicocelectomy surgery, with the number of veins ligated during the varicocelectomy surgical procedure mostly 2-5 veins in 30 patients (75%), >5 veins were ligated in 9 patients (22,5%), and 1 vein was ligated in 1 patient (2,5%). The average number of the ligated vein were 4,4 veins **(Table 4).**

Table 1. Overview of the characteristic of the patients based on age, clinical manifestation, and the type of varicocele

Characteristic	Frequency (n)	Percentage (%)
Age		
0-11 years old	0	0
12-25 years old	13	32,5
26-45 years old	26	65
46-65 years old	1	2,5
> 65 years old	0	0
Total	40	100
Clinical Manifestation		
Asymptomatic	4	10
Testicular pain or discomfort	7	17,5
Infertility	29	72,5
Total	40	100
Types of varicocele		
Unilateral (S)	28	70
Unilateral (D)	2	5
Bilateral	10	25
Total	40	100

Table 2. Overview of the characteristic of patients based on the degree of the varicocele

Type of varicocele		Frequency (n)			
		Grade I	Grade II	Grade III	No grading data is available
Unilateral	Unilateral (S)	11	6	6	5
	Unilateral (D)	1	0	0	1
	Left side	1	2	4	3
Bilateral	Right side	2	3	2	3
	Total	15	11	12	12

Table 3. Overview of the pre-operation semen analysis results in varicocele patients who underwent varicocelectomy

Semen Analysis Result	Frequency (n)	Percentage (5)
Pre-operation semen analysis		
Normal	0	0
Abnormal	21	52,5
No Data	19	47,5
Total	40	100
Abnormal Semen Analysis		
Oligozoospermia	0	0
Astenozoospermia	0	0
Teratozoospermia	5	23,8
Oligoastenozoospermia	0	0
Oligoteratozoospermia	3	14,3
Oligoastenoteratozoospermia	3	14,3
Azoospermia	6	28,6
Severe Oligospermia	1	4,8
Cryptozoospermia	2	9,5
Leukositospermia	1	4,8
Total	21	100

Table 4. Overview of characteristics based on the type of operation and the amount of ligated vein during the varicocelectomy operation

Characteristic	Frequency (n)	Percentage (5)
Type of Operation		
Palomo Varicocelectomy	0	0
Ivanissevic Varicocelectomy	40	100
Total	40	100
Ligated vein during operation		
1 vein	1	2,5
2-5 veins	30	75

>5 veins	9	22,5
Total	40	100

Discussion

Based on the presented result, it was found that most of the patients were in the age group of 26-45 years old with a percentage of 65%, which was categorized according to the Health Department of The Republic of Indonesia as an adult. A different result was obtained by Parusidha & Suwedagatha in 2019 which showed an average age of 20 years old with most of the patients were between the age of 15 and 24 years old with a percentage of 89,5%.[11] This difference is thought to be caused by the fact that most patients in the Parisudha & Suwedagatha were police candidates and police officers who underwent a medical checkup with lower average age and without any specific complaints while most of the participants of this research were admitted to the hospital because of their specific complain such as infertility. A study done by Mustika et al in 2014 showed the frequency of patients with left unilateral varicocele based on age. That study found that the highest incidence in the age of 16-20 years old with the percentage of 99,34% and the varicocele were mostly detected because of mandatory job requirement medical checkups.[12]

Most of the varicocele patients in this research showed a clinical manifestation in the form of infertility with 29 patients (72,5%). Results in this research were in line with a study published by Purnomo which concluded that in varicocele patients, they usually come to visit a doctor with a chief complaint related to infertility or haven't got any kids after years of marriage.[5] These results were in accordance with the indications of varicocelectomy according to Chan (2011) which were fertility especially if an abnormality in the semen or sperm analysis result was obtained.[9] Different results were obtained in the study by Parisudha & Suwedagatha which showed that most of the varicocele patients were asymptomatic with a percentage of 90,5%.[11] This difference is thought to be caused by the different characteristics of the population. In Parisudha & Suwedagatha's study, most of the research participants were police and police candidates who underwent a medical checkup and hence have no complaints or are asymptomatic. While the participants of this research were people with a specific complaint regarding varicocele which was infertility.

Based on the type of varicocele, most of the participants of this research were left unilateral varicocele with 28 patients (70%). This result is in accordance with the theory that left varicocele is more prevalent than right varicocele with 78-93% of the cases.[13] In theory, this is thought to be caused by the fact that the left internal spermatic vein ends up in the left renal vein with a perpendicular angle, while the right internal spermatic vein enters the vena cava with an oblique angle. Besides, the left internal spermatic vein is considerably longer than the right one with fewer and incompetent valves.[5] Research published by Dadhich & Meena and by Alkhamees et al in 2020 showed that most of the varicocele patients were left unilateral varicocele.[14,15] Different result was obtained by a study done by Gat et al in 2004 which showed the most prevalent type of varicocele were bilateral varicocele with the percentage of 80,8%.[16] This different result is thought to be caused by different diagnosis modalities which were used in both of those research. This research utilizes physical exam and

scrotal ultrasonography examination while in the research done by Gat et al, they used venography which has a higher sensitivity.

Grade I varicocele was the most prevalent severity of varicocele found in this research. Similar results were found in a research published by Soylemez et al in 2012 which showed that the most prevalent grade of varicocele was grade I.[17] Different results were obtained by Kwon & Lee in 2014 which showed that most of their participants were grade III varicocele with 87 patients and the percentage of 68%.[18] Inline with Kwon & Lee, Parisudha & Suwedagatha in 2019 also showed that the most prevalent severity of varicocele in their participants was grade III varicocele with 78 patients and the percentage of 82,1%.[11]

Based on the pre-operation semen analysis, 21 patients with varicocele who underwent varicocelectomy (52,5%) of the obtained data were abnormal while the rest of the participant's data cannot be retrieved. This result is in accordance with several literature which stated that dilatation of pampiniform plexus will cause an increase in temperature of the testis and eventually disturbed spermatogenesis. This indicates that varicocele can have a devastating effect on the function of the testis, hence men with varicocele will usually have a lower semen quality than those who don't have varicocele.[7,8] Similar results were obtained by Majzoub et al in 2016 which showed that most of the patients has an abnormal semen analysis result (332 patients; 87,7%).[19]

Out of 21 patients who showed an abnormal result in the pre-operation semen analysis, it was obtained a high variability of further analysis. Most of the results were azoospermia in 6 patients (28,6%). A different degree of variation was obtained by Rizaldi & Alif in 2013 which showed that the most prevalent result in the pre-operation semen analysis of varicocele patients was oligoastenozoospermia with a percentage of 23,2%.[20] This difference is thought to be related to the degree of damage in the testicle function caused by varicocele in individual patients. One of the factors affecting testicular function in varicocele was the degree of varicocele. According to research published by Ariyati et al in 2017, there was indeed a significant correlation between the degree of varicocele with sperm morphology, sperm concentration, and sperm motility in varicocele patients.[21]

All varicocele patients in this study underwent varicocelectomy surgery with an inguinal incision approach (Ivanissevich). A similar result was obtained in Parisudha & Suwedagatha in 2019 which showed that most of the patients underwent Ivanissevich varicocelectomy (72,8%). A different result was obtained in another research published by Mustika et al in 2014 and by Rizaldi & Alif in 2013 which showed that all patients that underwent a varicocelectomy procedure in their research utilize a Palomo technique.[12,20] According to Parisudha & Suwedagatha, the difference in the proportion of techniques used in the varicocelectomy procedure may be due to the preferences of each surgeon and different comorbidities.[11]

This study also collect data regarding the number of the ligated vein during the procedure. Results showed that 2-5 ligated veins were the most prevalent with 30 patients (75%). Similar results were obtained by research published by Pasqualotto et al in 2005 which showed that in most of their participant who underwent a varicocelectomy procedure, ≤5 veins (46%) were the most

prevalent.[22] Different results were obtained in research published by Majzoub et al in 2016. In that research, 5-10 veins were the most prevalent number in their patients which accounts for 48,7% of their participants.[19] The number of veins that were found during operation varies widely and has no correlation with the clinical degree of the varicocele.[23] The number of the spermatic vein which was ligated during the operation has a significant correlation with the pre-operation ultrasonography findings. Besides that, the number of veins that were found during the procedure was also affected by the location of the incision or the approach used by the operator, which means that the lower the incision, the more veins will be found.[19]

Conclusion

Based on the data analysis and discussion in this research, it can be concluded that the characteristic of varicocele patients who underwent varicocelectomy in Mataram Biomedika Hospital in 2018-2020 was dominated by patients in the age of 26-45 years old with an average age of 28,9 years old with mostly infertility-related chief complaints. While based on the type of varicocele, the most prevalent type was left unilateral varicocele, and based on the severity or grading of the varicocele, the most prevalent ones were grade I varicocele. In the current research, it was obtained that in the varicocele patients who underwent varicocelectomy, most of them has an abnormal result in the pre-operational semen analysis with a further analysis resulted in mostly azoospermia. All varicocele patients in this study underwent varicocelectomy surgery with an inguinal incision approach (Ivanissevich) and the number of veins ligated during the procedure was mostly 2-5 veins.

CONFLICT OF INTEREST

The authors state that there is no conflict of interest in this study.

REFERENCES

1. Duarsa GWK, Soebadi DM, Taher A, Purnomo BB, Rasyid N, Noegroho BS, et al. Panduan Penanganan Infertilitas Pria (Guidelines on Male Infertility). 2nd ed. Jakarta: Jakarta: Ikatan Ahli Urologi Indonesia; 2015. 32–35 p.
2. Walsh TJ, Smith JF. Male Infertility. In: Smith & Tanagho ' s General Urology. 18th ed. McAninch JW, Lue TF, editors. New York: New York: McGraw-Hill; 2013. 687–719 p.
3. Lomboy JR, Coward RM. The Varicocele: Clinical Presentation, Evaluation, and Surgical Management. Semin Intervent Radiol. 2016;33(3):163–9.
4. Clavijo RI, Carrasquillo R, Ramasamy R. Varicoceles : prevalence and pathogenesis in adult men. Fertil Steril [Internet]. 2017;108(3):364–9. Available from: http://dx.doi.org/10.1016/j.fertnstert.2017.06.036
5. Purnomo BB. Dasar-dasar Urologi. 3rd ed. Jakarta: Jakarta: CV. Sagung Seto Jakarta; 2012. 125–144 p.
6. Owen RC, Mccormick BJ, Figler BD, Coward RM. A review of varicocele repair for pain. Transl Androl Urol. 2017;6(Suppl 1):S20–9.
7. Magheli A. Male infertility. In: Handbook of Urology. 1st ed. Parsons JK, Eifler JB, Han M, editors. New Jersey: New Jersey: Wiley Blackwell; 2014. 43–54 p.
8. Barak S, Franzcog, Baker HWG. Clinical Management of Male Infertility [Internet]. Feingold K, Anawalt B, Boyce A, Al. E, editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-.; 2016. 1–67 p. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279160/
9. Chan P. Management options of varicoceles. Indian J Urol. 2011;27(1):65–73.
10. Baek SR, Park HJ, Park NC. Comparison of the clinical characteristics of patients with varicocele according to the presence or absence of scrotal pain. Andrologia. 2019;51(2):1–6.
11. Parisudha RD, Suwedagatha IG. High incidence of varicocele among young men in Public Police Hospital Denpasar, Bali, Indonesia: a descriptive study. Bali Med J. 2019;8(3):623–7.
12. Mustika N, Zuhirman, Suyanto. Gambaran Pasien Varikokel Kiri yang Menjalani Operasi Palomo Procedure

di Rumah Sakit Pekanbaru Medical Center Periode Januari 2009 – Desember 2013. J Online Mhs Univ Riau [Internet]. 2014;1(2):1–9. Available from: https://jom.unri.ac.id/index.php/JOMFDOK/article/view/2816

13. Cho CL, Esteves SC, Agarwal A. Novel insights into the pathophysiology of varicocele and its association with reactive oxygen species and sperm DNA fragmentation. Asian J Androl. 2016;18:186–93.

14. Dadhich AK, Meena R. AN EPIDEMIOLOGICAL STUDY OF VARICOCELE. Int J Med Biomed Stud. 2020;4(2):177–9.

15. Alkhamees M, Hamri S Bin, Alhumaid T, Alissa L, Al-Lishlish H, Abudalo R, et al. Factors Associated with Varicocele Recurrence After Microscopic Sub-Inguinal Varicocelectomy. Res Reports Urol - Dove Med Press. 2020;12:651–657.

16. Gat Y, Bachar GN, Zukerman Z, Belenky A, Gornish M. Varicocele : a bilateral disease. Fertil Steril. 2004;81(2):424–9.

17. Soylemez H, Atar M, Sancaktutar AA, Bozkurt Y, Penbegul N. Varıcocele among healthy young men in Turkey; prevalence and relationship wıth body mass index. Int Braz J Urol [Internet]. 2012;38(1):116–21. Available from: https://pubmed.ncbi.nlm.nih.gov/22397773/

18. Kwon CS, Lee JH. Is Semen Analysis Necessary for Varicocele Patients in Their Early 20s? World J Mens Health. 2014;32(1):50–5.

19. Majzoub A, Elbardisi H, Arafa M, Agarwal A, Said S Al, Rumaihi K Al. Does the number of veins ligated during varicococele surgery influence post-operative semen and hormone results ? Andrology. 2016;4(5):1–5.

20. Rizaldi F, Alif S. Pregnancy rate, semen analysis and varicocele profile in surabaya. J Urol Univ Airlangga [Internet]. 2013;1(2):1–7. Available from: http://journal.unair.ac.id/JUUA@pregnancy-rate,-semen-analysis-and-varicocele-profile-in-surabaya-article-8034-media-93-category-3.html

21. Ariyati I, Mulyadi R, Birowo P, Wiweko B, Prihartono J. Association between varicocele grade and semen analysis parameter. Med J Indones. 2017;26(4):270–6.

22. Pasqualotto FF, Lucon AM, Goes PM de, Sobreiro BP, Hallak J, Arap S, et al. Relationship between the number of veins ligated in a varicocelectomy with testicular volume, hormonal levels and semen parameters outcome. J Assist Reprod Genet. 2005;22(6):245–9.

23. Elbardisi H, Agarwal A, Majzoub A, Said S Al, Alnawasra H, Rumaihi K Al, et al. Does the number of veins ligated during microsurgical subinguinal varicocelectomy impact improvement in pain post-surgery? Transl Androl Urol. 2017;6(2):264–70.

RESEARCH ARTICLE

FACTORS ASSOCIATED WITH THE LENGTH OF STAY IN HOSPITAL OF BENIGN PROSTATIC HYPERPLASIA (BPH) PATIENT WHO UNDERGO TRANSURETHRAL RESECTION OF PROSTATE (TURP) SURGERY AT WEST NUSA TENGGARA PROVINCE GENERAL HOSPITAL MATARAM IN 2012-2017

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ABSTRACT

Background: Benign Prostatic Hyperplasia (BPH) is the most common benign tumor that occurs in elderly men. Complaints of BPH patients are mostly in the form of lower urinary tract symptoms (LUTS). TURP is the gold standard surgical procedure in BPH patients. LUTS that are suffered by patients is related to the high cost of personal and community medicine. Length of stay is one of the sources of treatment costs. It needs further investigation regarding the factors associated with the length of stay so that patient care can be more effective and efficient.

Method: This research is a descriptive-analytic study with a cross-sectional design. A total of 173 BPH patients who fulfilled the inclusion and exclusion criteria were examined based on age, prostate volume, length of stay, comorbidities, and complications of surgery. Analysis of bivariate correlation was performed using the Spearman and Contingency Coefficients correlation test according to variable data scales.

Results: From 173 patients, the average age was 65.55 years, the average prostate volume was 72.44 ml with the majority of patients in the grade III category (40.46%), and the average length of stay for 6.27 days. 80.9% of patients had concomitant diseases, 54.34% of patients had bleeding complications, and no patients had TUR syndrome. Correlation test showed no significant relationship between length of stay and age ($p = 0.663$); prostate volume ($p = 0.910$); hypertensive comorbidities ($p = 0.775$), CAD ($p = 0.459$), hypertension and DM ($p = 0.661$), hypertension and CAD ($p = 0.251$); and complications of surgical bleeding ($p = 0.715$).

Conclusions: There was no association between age, prostate volume, comorbidities, and surgical complications with the length of stay in BPH patients who underwent TURP surgery at West Nusa Tenggara Province General Hospital Mataram in 2012-2017.

Keyword: Length of stay, BPH, TURP

Introduction

Benign prostatic hyperplasia (BPH) is the most common benign tumor in the elderly. The incidence increases with age. The prevalence is 20% in the 41-50 age group, 50% in the 51-60 age group, and> 90% in the age group over 80 years old.1 The exact incidence

of BPH in Indonesia had never been studied. As a representation, 3,804 cases were found at Cipto Mangunkusumo Hospital, with average patient age of 66.61 years from 1994 to 2013. 2

Most complaints of BPH patients are lower urinary tract symptoms (LUTS), which can be divided into obstructive and irritable symptoms.1 The goal of treatment in patients with BPH is to relieve symptoms and improve the patient's quality of life.3 Treatment options depend on the severity, ranging from conservative treatment (watchful waiting) to medication and surgery.1,2,4 Transurethral Resection of the Prostate (TURP) is a gold standard surgery in patients with symptomatic BPH.5

The LUTS experienced by BPH patients is associated with the high cost of personal and community health care, because of the impact on their quality of life.6 Length of stay is one of the sources of expenditure for BPH treatment costs. The longer the patient's length of stay, the the greater the cost for treatment in the hospital.

West Nusa Tenggara Province General Hospital Mataram is the referral center for Lombok and Sumbawa Island. There is no data in the hospital showing factors related to the length of hospital stay of BPH patients who undergo TURP. Therefore, it is necessary to investigate the factors associated with the length of stay of BPH patients at West Nusa Tenggara Province General Hospital Mataram for better patient care and reduced treatment costs.

Methods

This research is a descriptive-analytic study with a cross-sectional design to determine the factors associated with the length of stay of BPH patients who underwent TURP surgery at the West Nusa Tenggara Province General Hospital Mataram from 2012 to 2017. The time of conducting the study is from September 2018 to February 2019.

The population of this study consisted of all BPH patients who underwent TURP surgery at West Nusa Tenggara Province General Hospital Mataram between the 1st of January 2012 and the 31st of December 2017. The sample for this study consisted of all members of the population with complete medical record information.

The independent variables of this study were age; prostate volume; comorbidities, namely hypertension, diabetes mellitus (DM), coronary heart disease (CHD); and surgical complications, namely bleeding and TUR syndrome, while the dependent variable of this study was the length of hospitalization.

This study used secondary data in the form of medical records of patients enrolled at the West Nusa Tenggara Province General Hospital Mataram. Data analysis was performed using univariate analysis for each variable and bivariate analysis for the relationship between variables. The correlation test used is the Spearman and the Contingency Coefficient, which is adjusted to the scale of the variable data.

Results

Research data collection on factors related to the length of stay of BPH patients who underwent TURP West Nusa Tenggara Province General Hospital Mataram was carried out from 19th January 2019 to 30th January 2019. The population in this study were all BPH patients who undergo TURP at the West Nusa Tenggara Province General Hospital Mataram from January 2012 to December 2017, totaling 216 patients. We got 173 cases as research samples, which met the inclusion and exclusion criteria.

Descriptive analysis showed that the mean age of the patients was 65.55 years old, the youngest was 47 years old and the oldest was 96 years old. The mean prostate volume of BPH patients was 72.44 ml, the smallest volume was 13.85 ml and the largest was 192.20 ml. The average hospital stay of BPH patients was 6.27 days, with the shortest hospital stay being three days and the longest being 16 days.

Table 1.1. Distribution of age, prostate volume, and length of stay

Variable	Frequency (n)	Percentage (%)
Age		
• **41-50**	7	4,05
• **51-60**	48	27,74
• **61-70**	67	38,73
• **71-80**	44	25,43
• **>80**	7	4,05
Total	173	100
Prostate volume		
• **≤20 ml**	2	1,16
• **Grade I**	2	1,16
• **Grade II**	45	26,01
• **Grade III**	70	40,46
• **Grade IV**	54	31,21
Total	173	100
Length of stay		
• **≤6 days**	112	64,74
• **>6 days**	61	35,26
Total	173	100

Table 1.1 shows that the most patients are in the 61-70 years age group (38.73%) and the lowest in the 41-50 years age group (4.05%) and >80 years (4.05%). Most of the patients had a prostate volume that was in grade III, which was 70 people (40.46%), and at least had a prostate volume of 20 ml and grade I, which were two people (1.16%) each. 64.74% of patients had a length of stay of 6 days, while the rest had a length of stay of >6 days.

Table 1.2. Characteristic of comorbidities

Comorbidities	Frequency (n)	Percentage (%)
• **Hypertension**	134	77,4
• **DM**	0	0
• **Coronary artery disease**	1	0,6
• **Hypertension dan DM**	2	1,2
• **Hypertension and CHD**	3	1,7
• **DM and CHD**	0	0
No comorbidities	33	19,1
Total	173	100

Table 1.2 shows that the most BPH patients who underwent TURP had comorbidities, as many as 140 patients (80.9%), while 33 patients (19.1%) did not have comorbidities. Of the 140 patients, most of them suffered from hypertension alone, namely 134 patients (77.4%), two patients with hypertension and DM (1.2%), and three people suffering from hypertension and CHD (1.7%). %), and only one person suffered from CHD (0.6%).

Table 1.3. Characteristic of surgical complication

	Frequency (n)	Perscentage (%)
Bleeding		
Bleeding	94	54,34
No bleeding	79	45,66
Total	173	100
TUR Syndrome		
TUR Syndrome	0	0
No TUR Syndrome	173	100
Total	173	100

Table 1.3 shows that 54.34% of patients had bleeding complications, whereas there were no patients with TUR syndrome (0%). Patients who did not experience surgical complications were 45.66%.

Table 1.4. Spearman analysis results between age and prostate volume with length of stay in hospital

Variable	Length of stay	
	Correlation coefficients (r)	Significance (p)
Age	0,033	0,663
Prostate Volume	-0,009	0,910

Table 1.4 shows that there is no significant relationship between age and length of stay in hospital and between prostate volume and length of stay with a p-value > 0.05.

Table 1.5. The results of the contingency coefficient analysis between comorbidities and bleeding complications with length of stay in hospital

Variable	Length of stay	
	Value	Significance (p)
Comorbidities		
Hypertension	0,022	0,775
CHD	0,056	0,459
Hypertension and DM	0,033	0,661
Hypertension and CHD	0,087	0,251
Surgical Complication		
Bleeding	0,028	0,715
TUR Syndrome	-	-

Table 1.5 shows that there is no significant relationship between comorbidities and length of stay and between TUR syndrome and length of stay with a p-value >0.05. Analysis of the relationship between complications of TUR Syndrome and length of stay could not be performed. This is because the variable is constant, and none of the patients experienced these complications.

Discussion

This study showed no significant association between age and length of stay of BPH patients who underwent TURP at West Nusa Tenggara Province General Hospital Mataram from 2012 to 2017. These findings were similar to research by Mahendrakrisna, Maulana, and Kresnoadi at Bhayangkara Hospital Mataram in 2014, specifically no association between age and length of stay in BPH patients who underwent TURP. The age characteristics of the patients in their study were similar to those in this study, in which the average age was 65.75 years.8 However, according to Wolverson et al., the patient's age was associated with the length of postoperative hospital stay, and being over 70 years of age was associated with an extension of six days or more of one postoperative hospital stay. In their study, there was a

significant difference between the mean age of all patients (74 years) and the mean age of patients staying ten days or longer (79 years).9 A study by Kirollos et al. showed similar results to Wolverson et al., who found a relationship between age and length of postoperative hospital stay. In their study, age contributed to the length of stay in four out of ten patients over the age of 80 years. In addition, some patients require multiple exercises and a trial of voiding due to axonal and muscle degeneration in old age, which may affect the length of stay.10

The difference in study results may be due to the characteristics of the samples used. In Wolverson et al., the age distribution of patients in their study is out of 100 patients, ten were under 60 years old, 36 were 60-70 years old and most were over 70 years old which counts 54 patients.9 In this study at West Nusa Tenggara Province General Hospital Mataram, the age distribution of patients was 173 patients, with 55 patients under 60 years old, 67 patients were 61-70 years old, and 51 patients over 70 years old. In addition, patients with a length of stay less than or equal to 6 days dominated with a total of 112 patients (64.7%).

A Study bt Wolverson et al. and Kirollos et al. found that there was an association between the weight of the TURP-resected prostate and the length of the patient's hospital stay.9,10 Prostate volume is related to surgical time and intraoperative bleeding risk.11 Surgical time is related to the length of hospital stay in patients with BPH.12 Compared with the two studies, this study assessed overall prostate volume before TURP and did not assess the weight of the resected prostate. Based on the results of this study, prostate volume did not have a significant relationship with the length of stay. This can occur with postoperative care that is carried out properly to avoid prolonging the patient's length of stay.

The comorbidities assessed in this study were hypertension, diabetes, and coronary artery disease, and it showed no significant association between comorbidities and hospital stay of BPH patients who underwent TURP at West Nusa Tenggara Province General Hospital Mataram. These results differ from Wolverson et al., which found a relationship between cardiovascular comorbidities and length of stay in patients with BPH.9 Based on this study, the presence of comorbidities in BPH patients was not a likely barrier to prolonging the treatment duration of BPH patients who underwent TURP at West Nusa Tenggara Province General Hospital Mataram. This may be due to the control of comorbidities before and after surgery to avoid prolonging the hospital stay.

The results of this study showed no significant association between bleeding complications and length of hospital stay. Bleeding risk is related to preoperative infection, urinary retention, prostate volume, and time to resection.11 The occurrence of bleeding requiring treatment may affect the time to hospital admission, such as the need for blood transfusion.12 According to Marszalek et al., blood loss during surgery can be reduced by careful surgery at a rational pace and paying attention to every detail.11 Technological advances in TURP implementation, such as the use of microprocessor-controlled units and video TUR can also reduce transfusion rates.13 In this study, bleeding complications that caused a decrease in postoperative hemoglobin levels could be overcome so as

not to cause an extension of the length of hospitalization.

There are no BPH patients who underwent TURP developed TUR syndrome between January 2012 and December 2017, so the relationship between TUR syndrome and length of hospital stay is not known. TUR syndrome is caused by the absorption of irrigating fluid during surgery which is hypoosmolar and causes delusional hyponatremia. Currently, TUR syndrome is rare, and the incidence of this syndrome has decreased significantly in the past decades from 3.5% to <1% .11 Theoretically, TUR syndrome can be eliminated by using isotonic irrigation fluids. Currently, some techniques can safely avoid TUR syndrome, including bipolar TURP (B-TURP).11,14

Limitations of this study are factors that can be related to the length of time a person undergoes hospitalization, in this case, BPH patients, are not only determined by age, prostate volume, comorbidities, and surgical complications. Other factors can affect the analysis of the relationship between these variables, which cannot be controlled by the researcher. In addition, this study used secondary data, therefore researchers have difficulty developing research due to limited data in medical records. More research is needed to pay more attention to other factors that may affect the length of hospital stays, such as admission procedures, treatment classes, medical action decisions, operating scheduling procedures, waiting time for surgery, length of operation, surgical operators, discharge procedures, the person in charge of costs, and reasons to discharge.

Conclusion

Based on the results of data analysis and discussion, it can be concluded that there is no significant relationship between age and length of stay, prostate volume and length of stay, comorbidities with the length of stay, and surgical complications with the length of stay in BPH patients undergoing TURP in West Nusa Tenggara Province General Hospital Mataram from 2012 to 2017. More research is needed to pay more attention to other factors that may affect the length of hospital stays.

REFERENCES

1.Cooperberg, Matthew R., Presti, Joseph C., Shinohara, Katsuto, Carroll, Peter R.. Neoplasm of The Prostate Gland. In: McAninch, Jack W., dan Lue, Tom F., eds. 2013. Smith & Tanagho's General Urology. New York: McGraw-Hill
2.Mochtar, Chaidir A., et al. Panduan Penatalaksanaan Klinis Pembesaran Prostat Jinak (Benign Prostatic Hyperplasia/BPH) Edisi 2. 2015. Jakarta: Ikatan Ahli Urologi Indonesia
3.Skinder, Danielle, Zacharia, Ilana, Studin, Jillian, Covino, Jean. Benign Prostatic Hyperplasia: A Clinical Review. Journal of the American Academy of Physician Assistants. 2016; 29(8), pp 19-23. doi: 10.1097/01.JAA.0000488689.58176.0a
4.Vuichoud, Camille, and Loughlin, Kevin R. Benign Prostatic Hyperplasia:
Epidemiology, Economics, and Evaluation. The Canadian Journal of Urology. 2015; 22(51), pp 1-6. PMID: 26497338
5.Gravas, S., et al.. Guidelines on the Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), include Benign Prostatic Obstruction (BPO). 2015. Netherlands: European Association of Urology.
6.Speakman, Mark, and Cheng, Xi. Management of the Complication of
BPH/BOO. Indian Journal of Urology. 2014; 30(2), pp 208-213. doi: 10.4103/0970-1591.127856
7.Wei, John T., Calhoun, Elizabeth, Jacobsen, Steven J. Urologic Disease in America Project: Benign Prostatic Hyperplasia. The Journal of Urology. 2006; 173, pp 1256-1261. doi: 10.1097/01.ju.0000155709.37840.fe
8.Mahendrakrisna, Daniel, Maulana, Akhada, Kresnoadi, Erwin. Faktor yang Berhubungan dengan Rawat Inap pada Pasien Pembesaran Prostat Jinak Di Rumah Sakit Bhayangkara Mataram. Duta Wacana Medical Journal. 2016; 1(2), 102-108. doi: http://dx.doi.org/10.21460/bikdw.v1i2.11
9.Wolverson, R.L., Blacklock, A.R.E., Geddes, J.R., O'Hagan, A. Factor
Influencing Postoperative Hospital Stay After Transurethral Resection of the

Prostate Gland. British Journal of Urology. 1986; vol 58, 161-163. doi:10.1111/j.1464-410X.1986.tb09018.x
10.Kirollos, Magdi M. Length of Postoperative Hospital Stay after Transurethral Resection of the Prostate. Annals of the Royal College of Surgeons of England. 1997; 97, pp 284-288. PMID: 9244074; PMCID: PMC2502823.
11.Marszalek, Martin, Ponholzer, Anton, Pusman, Marlies, Berger, Ingrid, Madersbacher, Stephan. Transurethral Resection of the Prostate. European Urology Supplement. 2009; 8(6), pp 504-512. doi: https://doi.org/10.1016/j.eursup.2009.02.003
12.Collins, Tracie C., Daley, Jennifer, Henderson, William H., Khuri, Shukri F.
Risk Factors for Prolonged Length of Stay After Major Elective Surgery.
Annals of Surgery. 1999; 230(2), pp 251-259. DOI: 10.1097/00000658-199908000-00016
13.Rassweiler, J., Teber, D., Kuntz, R., Hofmann, R. Complications of transurethral resection of the prostate (TURP)--incidence, management, and prevention. European Urology. 2006; 50(5), pp 969-980. DOI: 10.1016/j.eururo.2005.12.042
14.Welliver, Charles, dan McVary, Kevin T., 2016. Minimally Invasive and Endoscopic Management of Benign Prostatic Hyperplasia. In: Wein, Alan J., Kavoussi, Louis R., Partin Alan W., Peters, Craig A., eds., 2016. Campbell-Walsh Urology 11th edition. United States: Elsevier