

URINARY TRACT INFECTION AFTER URODYNAMIC STUDY IN HUSM, KELANTAN

DR. SYAMILAH BT. MOKHTAR

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE
REQUIREMENT FOR THE DEGREE OF MASTER OF MEDICINE
(OBSTETRICS AND GYNAECOLOGY)



UNIVERSITI SAINS MALAYSIA

2018

ACKNOWLEDGEMENT

I would like to express my sincere appreciation and deepest gratitude to the following individuals, without whom my dissertation would not be at all possible:

- My most dedicated supervisor Dr Ahmad Amir Ismail, Senior Lecturer, Consultant Obstetrician and Gynecologist/ Urogynecologist, HUSM for their professional guidance and useful assistance to ensure the completion of this dissertation.
- Associate Professor Dr Mohd Pazudin Ismail, Head of Department of Obstetrics and Gynaecology, and to all lecturers and colleagues in Department of Obstetrics and Gynaecology, Hospital Universiti Sains Malaysia for their encouragement, guidance and assistance throughout the course of my trainingband preparation of this book
- Staff nurse Rosela Bharum Skedek who always in the clinic helping me in the data collection

The completion of this undertaking could not have been possible without the participation and assistance of so many people whose names may not all be enumerated. Their contributions are sincerely appreciated and gratefully acknowledged.

Last but not least, to my beloved parents, husband, family and colleagues who give their support and prayers for the completion of this book, thank you.

TABLE OF CONTENTS

CONTENTS	PAGE
ACKNOWLEDGEMENT	ii
TABLE OF CONTENTS	iii-v
LIST OF TABLES	vi
LIST OF FIGURES	vii
LIST OF ABBREVIATIONS	viii
ABSTRAK	ix
ABSTRACT	xi
1.0 INTRODUCTION	
1.1 The state of Kelantan	1
1.2 The HUSM	2
1.3 The Obstetrics and Gynecology Department HUSM	2
1.4 The Urogynaecology Unit, HUSM	2
1.5 Introduction to the study	3
2.0 LITERITURE REVIEW	
2.1 Diagnosis of Urinary Tract Infection	5
2.2 Pathogenesis of Urinary Tract Infection	5
2.3 Incidence and prevalence of urinary tract infection after urodynamic study and their risk factors	6
2.4 The use of antibiotic prophylaxis in urodynamic study	8
	ii

3.0	OBJECTIVES	
3.1	General Objectives	10
3.2	Specific Objective	10
3.3	Research Hypothesis	10
4.0	METHODOLOGY	
4.1	Study setting	12
4.2	Study design	12
4.3	Reference population	12
4.4	Source population and sampling frame	12
	Inclusion criteria	12
	Exclusion criteria	13
4.5	Operational Term Definition	14
4.6	Sample size calculation	17
4.7	Study period	20
4.8	Study Methode	20
4.9	Flow chart of the study	22
4.10	Statistical Analysis	23
4.11	Ethical Approval	23

5.0	RESULTS	24-39
6.0	DISCUSSION	40-45
7.0	CONCLUSION	46
8.0	LIMITATION OF STUDY	47
9.0	RECOMMENDATION	48
10.0	REFERENCES	49
11.0	APPENDIX	55
11.1	Ethical Approval	56-57
11.2	Patient's Performa/ Data Collection Sheet	58
11.3	Consent Form Malay Version	59-63
11.4	Consent Form English Version	64-67

List of Figures

<i>Figure</i>	<i>Content</i>	<i>Page</i>
Figure 1	Referral case distribution	24
Figure 2	Percentage of patients with bacteriuria after urodynamic study	25
Figure 3	Uropathogen post UDS	36
Figure 4	Antibiotic resistance profile E. Coli infection post UDS	37
Figure 5	Uropathogen pre UDS	38
Figure 6	The resistance profile of uropathogen before UDS	39

List of Tables

<i>Table</i>	<i>Content</i>	<i>Page</i>
Table 1	Clinical and demographic characteristic among 50 patients in the study population	26
Table 2	Clinical and demographic characteristic among 46 patients without bacteriuria after UDS	27
Table 3	Clinical and demographic characteristic among 4 patients with bacteriuria after UDS	28
Table 4	Urodynamic parameters: urodynamic diagnoses and post void residual volume among 50 patients in the study population	29
Table 5	Urodynamic parameters: urodynamic diagnoses and post void residual volume among 46 patients without bacteriuria after UDS	30
Table 6	Urodynamic parameters: urodynamic diagnoses and post void residual volume among 4patients with bacteriuria after UDS	31
Table 7	Association between clinical and demographic characteristic among 50 patients with or without bacteriuria after UDS	32
Table 8	Multiple regression analysis for significant risk factors	33
Table 9	Association between previous history of recurrent UTI and underlying neurological disorder	34
Table 10	Association between urodynamic parameters among patient with or without bacteriuria post UDS	35

Abbreviations

BOO	Bladder Outlet Obstruction
BS	Bladder scan
CFU	Colony Forming Unit
DO	Detrusor Overactivity
DSD	Detrusor Sphincter Dysynergia
ESBL	Extended Spectrum Beta Lactamase
GBS	Group B Streptococcus
HRPZ	Hospital Raja Perempuan Zainab
HUSM	Hospital Universiti Sains Malaysia
LUT	Lower Urinary Tract
O&G	Obstetrics and Gynecology
PVR	Post Void Residual
RCOG	Royal College of Obstetrics and Gynaecology
SBU	Significant Bacteriuria
SCI	Spinal Cord Injury
SUI	Stress Urinary Incontinence
UDS	Urodynamic Study
UTI	Urinary Tract Infection
WHO	World Health Organization

ABSTRAK

Jangkitan Kuman Pada Saluran Kencing Selepas Menjalani Ujian Urodinamik

Syamilah Mokhtar, Ahmad Amir Ismail

Objectif: Untuk menentukan insiden jangkitan kuman pada saluran kencing selepas menjalani ujian urodinamik serta mengenalpasti factor risiko yang menyebabkan jangkitan tersebut.

Kaedah: Satu kajian prospektif telah dijalankan di Hospital Universiti Sains Malaysia bermula daripada 1 Mac 2016 sehingga 29 Februrari 2017 (12 bulan). Kajian ini melibatkan 50 pesakit yang menjalani ujian urodinamik di unit urogininekologi HUSM. Sampel air kencing untuk kaji kuman dan sensitiviti diambil semasa memasukkan tiub kencing sebelum prosedur ujian urodinamik. Kemudian sampel kedua diambil 4 hingga 7 hari selepas prosedur ujian urodinamik. Insiden jangkitan kuman pada saluran kencing dikira dengan berlakunya kehadiran organism di dalam sampel air kencing yang sebelumnya tiada sebarang organism dikenal pasti sebelum ujian urodinamik. Untuk mengenalpasti faktor risiko berlakunya jangkitan kuman saluran kencing, latar belakang klinikal pesakit seperti umur, samada putus haid, bilangan anak, sejarah kencing manis, latar belakang penyakit saraf, sejarah jangkitan. Faktor risiko jangkitan kuman saluran kencing di periksa dengan menggunakan analisis statistic regresi mudah dan regresi berganda.

Keputusan: Seramai 50 pesakit telah diambil di dalam kajian ini. Insiden jangkitan kuman pada saluran kencing adalah sebanyak 8%. Jangkitan *E. Coli* adalah kuman terbanyak dikenalpasti (50%). Analisis oleh regresi mudah menunjukkan bahawa pesakit yang mempunyai latarbelakang penyakit saraf ($p=0.029$) dan pesakit yang mempunyai sejarah jangkitan kuman saluran kencing berulang ($p=0.037$) adalah antara faktor risiko yang menyebabkan berlakunya jangkitan kuman pada saluran kencing selepas ujian urodinamik. Analisis statistik daripada regresi logistik berganda menunjukkan tiada satu daripada faktor risiko tersebut yang secara tersendiri menyebabkan jangkitan kuman pada saluran kencing, iaitu ($p=0.098$) untuk pesakit yang mengalami penyakit saraf dan ($p=0.0259$) untuk pesakit yang mempunyai sejarah jangkitan kuman saluran kencing berulang. Isipadu air kencing yang tinggal selepas kencing berkait dengan risiko berlakunya jangkitan kuman pada saluran kencing ($p=0.022$). Bakteria terbanyak menyebabkan jangkitan kuman pada saluran kencing selepas urodinamik adalah *E. Coli* (50%), diikuti oleh *E. Coli ESBL* (25%) dan *Group B Streptococcus* (25%). Kuman *E. Coli* sensitif kepada antibiotik *cefuroxime*, namun tidak sensitif kepada *ampicilin* dan *bactrim*, serta separa sensitif terhadap *augmentin*. Manakala, kuman *E. Coli ESBL* tidak sensitive terhadap kesemua jenis antibiotik yang biasa digunakan. GBS pula sensitif terhadap *Penicilin G* dan *erythromycin*.

Kesimpulan: Kajian ini menunjukkan bahawa insiden jangkitan kuman pada saluran kencing selepas menjalani ujian urodinamik adalah sebanyak 8%. Faktor risiko yang signifikan terdiri daripada pesakit yang mengalami penyakit saraf, mempunyai sejarah jangkitan kuman pada saluran kencing yang berulang-ulang serta jumlah isipadu air kencing yang banyak selepas kencing.

Abstract

Urinary Tract Infection After Urodynamic Study

Syamilah Mokhtar, Ahmad Amir Ismail

Objective To determine the incidence of urinary tract infection after urodynamic study and to identify its risk factors

Method: A prospective cross sectional study in Hospital Universiti Sains Malaysia was conducted from 1st March 2016 until 29th February 2017 (12 months).The study included 50 female patients who presented or referred to urogynecology unit HUSM for urodynamic study. Urine culture and sensitivity was collected during catheterization before urodynamic study and repeat sample was collected after 4 to 7 days following procedure. The incidence of urinary tract infection was determined by the presence of growth in the urine culture post urodynamic study in the previously absence of growth in the urine culture before urodynamic study. To identify the risk factors for UTI, patient's clinical characteristics including age, menopausal state, parity, diabetic status, underlying neurological disorder, history of recurrent UTI and history of urological surgery were evaluated. The risk factors for UTI were analysed by using simple linear and multiple logistic regression.

Results: A total of 50 patients were recruited in this study. The incidence of urinary tract infection after UDS was 8% (n). E.Coli is the most common identified organism (50%). Simple linear regression analysis demonstrated that underlying neurological disorder ($p=0.029$) and history of recurrent UTI ($p=0.037$) were the significant predictors of urinary tract infection. On multiple logistic regression none of the covariate are significant independent risk factors. Neurological disorder ($p=0.098$) and previous history of recurrent UTI ($p=0.259$). Elevated post void residual volume was associated with higher risk of developing UTI ($p=0.022$). The commonest pathogen post UDS was E. Coli (50%), followed by E. Coli ESBL (25%) and Group B Streptococcus (25%). E. Coli had shown complete sensitive to cefuroxime, however complete resistance to ampicilin and bactrim and partial resistance to augmentin. Meanwhile E. Coli ESBL was resistant to all common antibiotic tested. GBS was found to be sensitive to Penicilin G and erythromycin.

Conclusion:

The rate of UTI following UDS was low at 8%. The significant risk factors include underlying neurological disorder, previous history of recurrent UTI and elevated volume in post void residual urine.

1.0 INTRODUCTION

1.1 The state of Kelantan

Kelantan is situated in the northeast part of peninsular Malaysia facing the South China Sea. It has a total area of 14,922 square kilometers. Based on the latest population census, Kelantan has a population of 1.6 million. The capital and royal seat of Kelantan is Kota Bharu. 95% of Kelantan's populations are Malay ethnic, and under the Malaysian's Constitution, all Malays are Muslims; therefore, Islam is the most influential religion in the state. There are 4 government hospitals with specialist in Kelantan, namely Hospital Raja Perempuan Zainab II (HRPZ II), Hospital Universiti Sains Malaysia HUSM, Hospital Kuala Krai and Hospital Tanah Merah.

1.2 The Hospital Universiti Sains Malaysia (HUSM)

The hospital was built in 1979 and started operation in 1983. It was built as part of the Health Center of Universiti Sains Malaysia. It is situated in Kubang Kerian which is 6.6 km from Kota Bharu. HUSM is a teaching referral hospital. HUSM receives patients coming from all over Kelantan and other and also north of Terengganu (Besut).

1.3 The Obstetrics and Gynecology Department, HUSM

The department started its operation alongside with the hospital. In 2016, the department of Obstetrics and Gynecology was staffed by 11 consultant/ specialist, 10 registrars and 22 medical officers. The post graduate programme was started

in 1991. The O&G clinic is situated on the ground floor. All of the clinics are conducted on a daily basis. The management unit was divided into four teams, A, B, C, D with each team having its own subspecialty – gynecology, urogynecology and adolescent gynecology, infertility and fetomaternal medicine respectively.

1.4 The Urogynecology Unit, HUSM

The subspecialty in urogynecology in this hospital started in December 2012. The clinic was headed by Urogynaecologist, Dr. Ahmad Amir B. Ismail. The clinic is conducted on a weekly basis, every Wednesday. This clinic offers urodynamic study as one of the modalities not only for the patient from urogynaecology unit HUSM, but also referral from Urogynaecology Unit Hospital Raja Perempuan Zainab II and urology department HUSM. In 2016 (January – December), 247 patients had attended urogynecological clinic – 167 for pelvic organ prolapse, 31 for stress urinary incontinence, 25 for overactive bladder, 8 for mixed urinary incontinence, 6 for urogenital tract abnormality/ vesicovaginal fistula, 10 following obstetric anal sphincter injury (OASIS) problems. This clinic provides ring and Gellhorn pessaries for conservative management of pelvic organ prolapse. OAB are mainly treated with lifestyle modification counseling and pharmacological treatment. Surgical options such as vaginal hysterectomy, perineal repair, continent surgery are also offered whenever necessary. This clinic is also equipped with endoanal ultrasound modality in the assessment of patients following OASIS, and referral to surgical unit for endoanal manometry.

1.5 Introduction to the study

‘Urinary tract infection’ is a term that is used to describe various infections involving the urinary tract. The spectrum ranges from asymptomatic bacteriuria to severe pyelonephritis. There are different classifications for UTI and these could be divided into lower urinary tract infection, i.e infection involving the urethra and bladder, or upper urinary tract infection, mainly involving the kidneys. UTI may also be classified as uncomplicated, when the infection happens without underlying structural or functional abnormalities, or complicated UTI, where several anatomical abnormalities predispose to UTI. One of the most common forms of complicated urinary tract infection is related to the use of urinary catheters (Robinson 2010)

Urodynamic studies (UDSs) involving catheterization of the lower urinary tract are required for investigation of patients with lower urinary tract dysfunction including female stress urinary incontinence (SUI). Urodynamic investigations are the only way to precisely define bladder and urethral function. In women with urinary incontinence, urodynamic investigations also allow characterization of the pathophysiological aspects of various symptoms, help to determine the prognosis and guide the choice of therapeutic strategies.(Choe, Lee et al. 2007)

Generally, clinical UDS use has been nicely summarized for the following situations: (1) to identify factors contributing to LUT dysfunction and assess their relevance, (2) to predict the consequences of LUT dysfunction on the upper tracts, (3) to predict the

consequences and outcomes of therapeutic intervention, (4) to confirm and/or understand the effects of interventional techniques and (5) to investigate the reasons for treatment failure. Clinicians who are making the diagnosis of urodynamic stress incontinence should assess urethral function. Surgeons considering invasive therapy in patients with SUI should assess PVR urine volume. An elevated PVR is suggestive of detrusor underactivity or bladder outlet obstruction or a combination of both. The exact clinical definition of an “elevated” PVR volume remains unclear. Nevertheless, patients with an elevated preoperative PVR may be at increased risk for transient or permanent postoperative voiding difficulties following urethral bulking injection therapy or SUI surgery.(Winters, Dmochowski et al. 2012)

However, the morbidity associated with this invasive procedure remains controversial. The reported prevalence of UTI, or significant bacteriuria after UDS, ranges from 1.1% to 28.3%. Several studies have also shown that despite screening and treatments before UDSs, a significant number of patients still harbor unsuspected asymptomatic bacteriuria at investigation(Choe, Lee et al. 2007)

In view of urodynamic study is commonly performed in the urogynae clinic, it is important to estimate the local infection rate in HUSM. Thus, this study is conducted to determine whether urodynamic study predisposes to significant bacteriuria and whether prophylactic antibiotic is needed prior to the procedure.

2.0 LITERATURE REVIEW

Diagnosis of Urinary Tract Infection

Quantitative studies have shown that the presence of a moderate number of bacteria on a stained smear is highly suggestive of significant bacteriuria (Jay P. Sanford MD 1956) This depends on the fact that the density of bacteria in infected urine is usually several orders of magnitude higher than the density of bacteria in contaminated urine. For the diagnosis of catheter-associated urinary tract infection, the criterion of 1×10^5 cfu/ml has been used most commonly, although a lower threshold may be appropriate.(MD 1983) Most screening tests for urinary tract infection have been evaluated using 10^5 bacteria/ml or greater for interpreting significant bacteriuria, whereas counts less than 10^5 bacteria/ml are considered to represent contamination (Helen M. Pollock 1983)

Pathogenesis

An indwelling catheter impairs normal host defenses both by promoting increased access of microorganisms to the bladder and by compromising complete voiding. Generally, infection is introduced via two routes after catheterization: the intraluminal route via the inside lumen of the catheter, or the trans-urethral route between the catheter and the urethra. The infections that arise with catheterization are caused by bacteria from patient's body or colonic flora and by bacteria found in the hospital setting. Bacteria can invade the lower urinary tract along the surface of the catheter or

by its lumen. Bacteriuria that occurs during short-term catheterization is usually caused by a single organism. The most commonly isolated pathogen is Escherichia-coli and enterococci, pseudomonas, enterobacter, staphylococcus aureus or epidermidis, klebsiella and serratia (S. Siracusano 2011)

Incidence and prevalence of urinary tract infection after uds and their risk factors

The incidence of bacteriuria associated with an indwelling urinary catheter is 3–10 per cent per day, and the duration of catheterization is the most important risk factor for developing UTI. They represent a huge reservoir of resistant bacteria in the hospital environment. (Robinson 2010)

The overall incidence of SBU after urodynamic study is 13.9% of whom 95.7% are asymptomatic. Symptoms occurring after UDS are mild, transient and rarely associated with infection. SBU after UDS is largely asymptomatic and self-resolving. (P Quek and 2004)

According to L. Bombieri 1999 the incidence of bacteriuria after urodynamic studies was 7.9% in which advancing age was the only variable associated with bacteriuria after urodynamic study. The incidence of UTI is even higher up to 20% in another study by (I. Okorochoa 2002) However, other study show invasive urodynamic studies are well tolerated by the patients and associated with a low risk of urinary tract infection; in which only only 4.1% had positive culture after urodynamic study. (Y.

Logadottir 2001) Similar finding was found in another study whereby the incidence of bacteriuria post UDS was 3.6%, in which 75% of the organism cultured originated from vaginal infection. (Dass, Lo et al. 2013) Another study determined the incidence of bacteremia after UDS which was on 7% (4 out of 55) (Onur, Ozden et al. 2004). However, according to [Tsai, Kung et al. 2013](#), higher prevalence of urinary tract infection after urodynamic examination was found which is 20%;. It implies that urodynamic examination, an invasive procedure, could indeed result in urinary tract infection.

According to (Yip, Fung et al. 2004) three independent risk factors for bacteriuria were identified: age >70 years (odds ratio, 1.99; 95% CI, 1.14-3.48), previous continence surgery (odds ratio, 1.90; 95% CI, 1.05-3.43), and urinary tract infection before urodynamic investigation (odds ratio, 3.13; 95% CI, 1.43-6.83).

Same findings found in another study by Choe, Lee et al. 2007 whereby univariate analysis also demonstrated that a history of recurrent urinary tract infection and urological surgery or procedure were significant predictors of significant bacteriuria. On multiple logistic regression analysis the past history of recurrent UTI was the only significant independent risk factor (OR ¼ 28.5, 95% CI ¼ 4.309–188.488, P ¼ 0.009) Therefore in patients with a previous history of recurrent UTI or urologic surgery the risk for significant bacteriuria is increased and use of prophylactic antibiotics should be considered.(Choe, Lee et al. 2007). In recent study in 2015, pelvic organ prolapse was

associated with significantly increased risk of bacteriuria. (Mônica Martins Nóbrega MDa 2015)

The use of antibiotic prophylaxis in urodynamic study

The use of prophylactic antibiotic is controversial. According to a systematic review of antibiotic prophylaxis in urologic procedures by Bootsma et al, the moderate to low evidence suggests no need for antibiotic prophylaxis in cystoscopy, urodynamic investigation, transurethral resection of bladder tumor, and extracorporeal shock-wave lithotripsy(Bootsma, Laguna Pes et al. 2008).

Antibiotic prophylaxis is not recommended for urodynamic studies in women at low risk, unless the incidence of urinary tract infection post-urodynamics is > 10% (1-E) (Nancy Van Eyk and Julie van Schalkwyk 2012). According to Gurbuz et al the prevalence of bacteriuria after UDS was relatively low in the study population. Therefore, for most patients, it may be unnecessary to use preventive prophylactic antibiotics. However, they suggest that in patients with a previous history of urologic surgery, the risk for significant bacteriuria is increased and the use of prophylaxis should be considered.(Gurbuz, Guner et al. 2013).

There was no statically significant difference (P=0.242) regarding UTI incidence rate between patients who received and those who did not received antibiotic prophylaxis.

In study among postmenopausal women undergoing urodynamic study by Siracusano found that the UTI incidence rate was not affected by administration of antibiotic prophylaxis at the desired level of efficacy.(Siracusano, Knez et al. 2008) In a single-blind prospective randomized study involving 94 women failed to provide data on the efficacy of routine antibiotic prophylaxis using cotrimoxazole administration after urodynamic testing.(U. M. Peschers 2001) :

One study try to determine the efficacy of prophylactic nitrofurantoin in preventing bacteriuria after urodynamics and cystourethroscopy, however, there was no significant difference, and they concluded bacteriuria after combined urodynamics and cystourethroscopy was not improved by a 1-day course of nitrofurantoin.(Geoffrey W. Cundiff 1999).

The use of antibiotic prophylaxis generates concern about the emergence of resistant organisms. Antibiotic resistance has serious implications as the level of resistance in a community increases. Concern over antibiotic resistance argues against the use of prophylaxis unless the benefits to the individual and the community clearly outweigh the risks. Therefore prophylactic antibiotics after urodynamics in low risk women should be administered only when the background rate of UTIs after urodynamics without prophylaxis is higher than 10%. (Lowder, Burrows et al. 2007)

The potential benefit of antimicrobial prophylaxis is determined by patient factors, procedure factors, and the potential morbidity of infection. Antimicrobial prophylaxis

is recommended only when the potential benefit outweighs the risks. For urodynamic study, antimicrobial prophylaxis is not necessary if urine culture shows no growth prior to the procedure. (Wolf, Bennett et al. 2008)

There is limited evidence available to guide clinicians in the use of prophylactic antibiotics in patients undergoing urodynamic studies. Prophylactic antibiotics can be used to reduce the risk of significant bacteriuria after urodynamics but their use in reducing symptomatic urinary tract infections and the clinical importance of reducing significant bacteriuria are still unclear. Amongst the various antibiotics used, there were very few side effects with an adverse reaction to the antibiotics in only two people (2%). However, only two trials reported adverse effects and hence there is limited information to base comments about adverse effects on. The number needed to treat with antibiotics to prevent bacteriuria was 10.9 (Foon R 2012)

Given the divergence in the rates of bacteriuria and UTI and possible predisposing factors associated with infectious complications after UDS, the present study aimed to determine the incidence of bacteriuria after UDS in women, as well as to identify the risk factors, most prevalent microorganisms, and antimicrobial susceptibility profile.

3.0 OBJECTIVES

3.1 GENERAL OBJECTIVES

To calculate the incidence of UTI after urodynamic study

3.2 SPECIFIC OBJECTIVES

3.2.1 To calculate incidence of UTI after urodynamic study

3.2.2 To identify the risk factors associated with increased risk of UTI following urodynamic study

3.2.3 To identify the common bacteria which UTI and its sensitivity in local setting

3.3 RESEARCH HYPOTHESIS

There is no significant incidence of UTI after urodynamic study in HUSM, and hence, prophylactic antibiotic unnecessary

4.0 METHODOLOGY

4.1 Study Setting

The study was conducted at Urogynecology Unit, HUSM, Kubang Kerian Kelantan

4.2 Study Design

This study was a prospective cross sectional study

4.3 Reference population

All female patients undergoing urodynamic procedure at urogynaecology unit Hospital Universiti Sains Malaysia from 1st March 2016 – 28th February 2017

4.4 Source population and sampling frame

All patients presented to HUSM or referred to HUSM for urodynamic study

Inclusion criteria:

All female patients presented or referred to Urogynae clinic HUSM for Urodynamics study from 1st March 2016 – 28th February 2017 were enrolled in this prospective study after obtaining informed consent.

Exclusion Criteria:

- a) Patients who are febrile
- b) On antibiotics for any reason,
- c) Those who are unwilling to comply with the study protocol
- d) Patient with positive urine culture on the day of urodynamic study
- e) Patient with anatomical abnormality of urinary tract i.e urethra vaginal fistula

4.5 Operational Term Definition

Term	Definition
Bacteriuria	Presence of small number of bacteria in the urine. In a clean-catch freshly voided sample, this represents 10 000 colony-forming units (CFU)/ml
Recurrent UTI	This is defined as three or more episodes of UTI during a 12-month period, or two infections in a six-month period. It is symptomatic infection that follows clinical resolution of an earlier UTI. (Robinson 2010)
Post Void Residual Volume	Volume of urine left in the bladder at the completion of micturition. In this study PVR was measured using bladder scan.
Urodynamic Stress Incontinence	Symptom, sign, and urodynamic investigations finding of involuntary leakage during filling cystometry, associated with increased intra-abdominal pressure, in the absence of a detrusor contraction

Term	Definition
Detrusor Overactivity	symptoms and urodynamic investigations is made in women with lower urinary tract symptoms (more commonly OAB-type symptoms—the Bladder Storage Symptoms when involuntary detrusor muscle contractions occur during filling cystometry
Voiding Dysfunction	Diagnosis by symptoms and urodynamic investigations, is defined as abnormally slow and/or incomplete micturition
Bladder Outlet Obstruction	This is the generic term for obstruction during voiding. It is a reduced urine flow rate and/or presence of a raised PVR and an increased detrusor pressure
Detrusor Sphincter Dysynergia	This is incoordination between detrusor and sphincter during voiding due to a neurological abnormality (i.e., detrusor contraction synchronous with contraction of the urethral and/or periurethral striated muscles).
Neurogenic detrusor overactivity	This is where there is detrusor overactivity and there is evidence of a relevant neurological disorder.(Haylen, Ridder et al. 2010)

Term	Definition
Neurological disorder	Neurological disorders are diseases of the central and peripheral nervous system. These disorders include epilepsy, Alzheimer disease and other dementias, cerebrovascular diseases including stroke, Parkinson's disease, neuroinfections, brain tumours, traumatic disorders of the nervous system due to head trauma, (WHO may 2016)
Urological Surgery	including urethral dilatation, ureteroscopic lithotripsy, cystoscopy or continence surgery.

4.6 Sample Size Calculation

Sample size calculation

Objective 1

The sample size was calculated using single proportion formula as below;

$$n = \left(\frac{Z\alpha}{\Delta}\right)^2 p(1-p)$$

Anticipated population proportion (p)= 13.9% (P Quek and 2004)

Absolute precision = 0.1

$$n = \left(\frac{1.96}{0.1}\right)^2 0.139(1-0.139)$$

$$= 46$$

For the risk factor, sample size is calculated using Power and Sample Size calculation program version 3.0.10as below; dichotomous for categorical and t test for continuous variables:

Risk factors (dichotomous)	α	power	P ₀	P ₁	m	Sample size
Diabetes mellitus	0.05	0.8	0.165	0.665	1	14
History of urologic surgery	0.05	0.8	0.08	0.58	1	13
History of UTI	0.05	0.8	0.165	0.665	1	14

Risk factors (t test)	α	power	m	δ	σ	Sample size
Age	0.05	0.8	1	10	9.5	15
Parity	0.05	0.8	1	1.0	1.2	24

With desired precision of 0.1, 46 subjects will be recruited into the study.

As 10% drop out rate was anticipated, therefore, a sample size of $46 + 4 = 50$ required at the analysis stage.

Table from literature review for each categorical risk factor to get P_0

Study	UTI	No	total	P_0	P_1
2013		UTI			
DM+	14	23	37		
No DM	37	187	224	37/224	+0.5
n	51	210	261	0.165	0.665

Study	UTI	No	total	P_0	P_1
2004		UTI			
h/o uro surgery	6	39	45		
No h/o uro surgery	61	689	750	61/750	+0.5
n	67	728	795	0.08	0.58

Study	UTI	No	total	P_0	P_1
2013		UTI			
h/o UTI	11	8	19		
No h/o UTI	40	202	242	40/242	+0.5
n	51	210	261	0.165	0.665

4.7 Study Period

The study was conducted at the Urogynecology Unit, HUSM for a period of 12 months duration from 1st March 2016 to 29th February 2017.

4.8 Study Method

All female patients who had undergone urodynamic study at urogynaecology clinic HUSM and fulfilling the entry criteria for this prospective study were enrolled after obtaining informed consent. Patient's clinical background such as underlying diabetes mellitus, neurological disease and history of urological surgery obtained. Those patients whom are febrile, or on antibiotics for any reason, or has underlying anatomical urinary tract abnormality or those who are unwilling to comply with the study protocol were excluded in the study

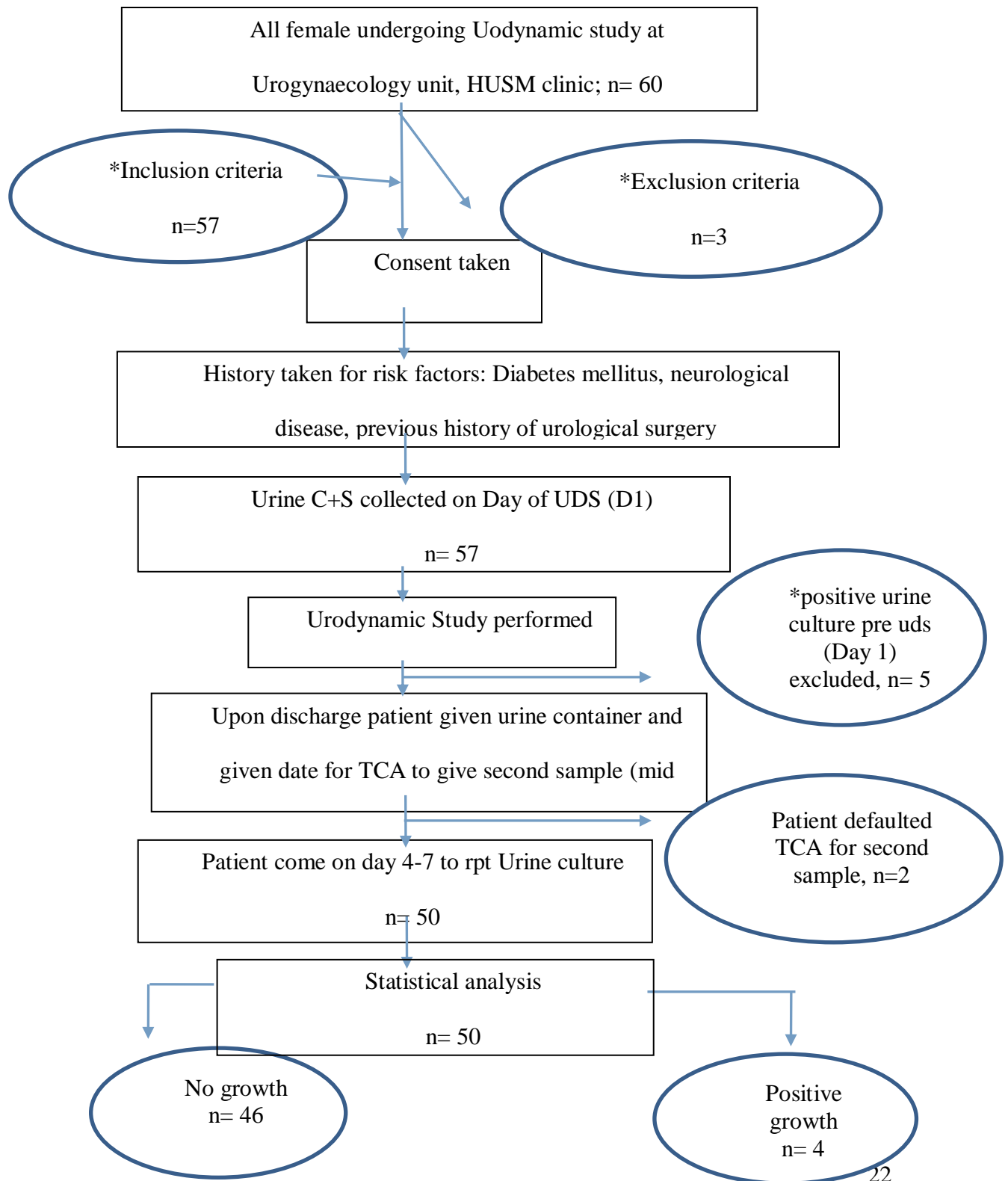
UDS was performed using sensic clinic urodynamic system. A rectal balloon catheter (4.5F) with a perforated latex sheath was introduced into the rectum to measure the intra-abdominal pressure. Patients were then cleansed and draped for urethral catheterisation utilising chlorhexidine gluconate 0.015% w/v and centrimide 0.15% w/v. An "Air-charged T-DOC[®]" Catheter was inserted through urethra into the bladder after lubrication with sterile lubricating gel and a urine culture specimen was collected at this point (Day 1 urine culture). The catheter was taped in place and connected to the pump and transducer respectively.

Multichannel urodynamics at medium fill was performed with sterile normal saline at room temperature. New connecting drip sets and a fresh bottle of normal saline were used for each case.

Upon discharge, all patients were given sterile urine container for the second sample. They were asked to come in for a midstream urine culture 4-7 days after their UDS. Patients subsequently found to have positive Day 1 urine cultures were excluded from further study.

The incidence and natural history of significant bacteriuria (SBU), defined as 10,000 CFU/mL of a single organism from a midstream urine specimen, and was determined on day 4-7. The organisms cultured and antibiotic sensitivity was tabulated. Age, sex, comorbid disorder, final UDS diagnosis, residual volume, history of UTI, history of urologic surgery were analysed as possible risk factors for SBU. Residual volume was determined by transabdominal ultrasonography bladder scan (sentic).

Flow Chart of The Study



4.9 Statistical Analysis

All the data collected were entered and analysed using SPSS version 22.0. The incidence of significant bacteriuria after urodynamic study was summarized with the use of descriptive statistics. The chi-square test was used to compare the categorical variables. Simple linear regression was used to determine the association between risk factors and the outcome. Multiple logistic regression analysis was used to adjust for covariates that were found to be significant in univariate analysis and to identify the risk factors that were independently associated with SBU after UDS. The level of statistical significance is defined as a $p < 0.05$.

4.10 Ethical approval

The ethical approval for the study was obtained on 16th June 2016 from Human Research Ethics Committee USM (HREC)

JEPeM Code: USM/ JEPeM/16020042 (Appendix)

5. RESULTS

Five subjects with bacteriuria before UDS, and 2 subjects who were on antibiotic at the time of UDS were excluded from the study. Another 1 subject was excluded due to underlying anatomical abnormality (urethrovaginal fistula). Those with negative urine culture before urodynamic study were followed up with second sample of urine culture, unfortunately, 2 out of 52 did not turn up (due to logistic reason). Finally, 50 patients were analyzed for the incidence of urinary tract infection following urodynamic study.

Out of 50 patients, 20 (40%) of them were from urogynaecology unit Hospital Universiti Sains Malaysia, another 19 (38%) were referred from urogynaecology unit Hospital Raja Perempuan Zainab II and 11 (22%) were referred from urology unit Hospital Universiti Sains Malaysia.(Figure 1)

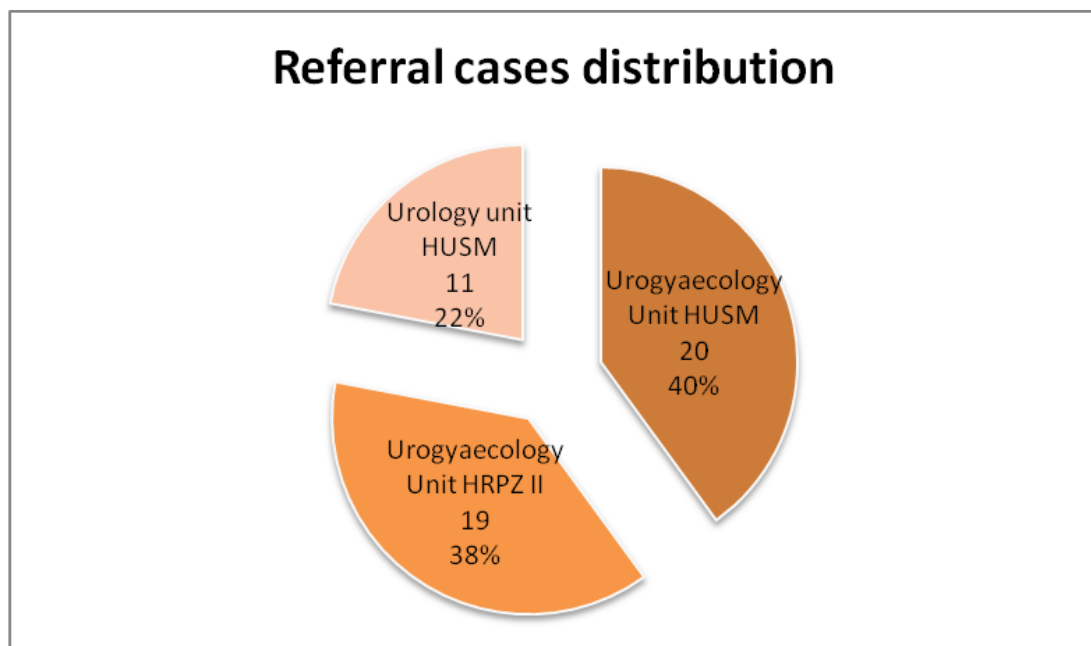


Figure 1: Referral cases distribution