CLINICAL PROFILE AND OUTCOME OF CHILDREN WHO UNDERWENT MICTURATING CYSTOURETHROGRAM: A TERTIARY HOSPITAL EXPERIENCE

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CLINICAL PROFILE AND OUTCOME OF CHILDREN WHO UNDERWENT MCUG: A TERTIARY HOSPITAL EXPERIENCE

yang telah dibuat pembetulan sepertimana yang diperlukan.

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Sekian, terima kasih.

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BAHAGIAN B (Untuk diisi oleh Penyelia)

Saya telah menyemak semua pembetulan/pindaan yang dilaksanakan oleh calon yang tersebut. Saya ingin mengesahkan bahawa :-

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ACKNOWLEDGEMENT

We must be willing to get rid of the life we have planned, so as to have the life that is waiting for us – Joseph Campbell

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LIST OF ABBREVIATION AND NOMENCLATURE

CKD	Chronic kidney disease
DMSA	dimercaptosuccinic acid
DTPA	diethylenetriamine pentaacetic acid
eGFR	Estimated glomerular filtration rate
Hospital USM	Hospital Universiti Sains Malaysia
MCUG	Micturating cystourethrogram
UTI	Urinary tract infection
VUR	Vesicoureteric reflux

ABSTRACT

Introduction: Micturating cystourethrogram (MCUG) is the gold standard test for the diagnosis of vesicoureteric reflux (VUR). The study aims to establish the association between the presence of VUR and renal outcomes.

Methods: A cross-sectional retrospective study was conducted in children who were referred for MCUG at a tertiary centre over a 10-year period. Baseline characteristic data and the results of renal ultrasound, MCUG, with renal function were compiled and analysed. Fisher Exact tests were used to compare between grade of VUR and renal outcomes. Simple and multiple logistic regressions were used to examine the risk factors that may contribute to the development of VUR.

Results: There were 136 children recruited in total of which forty-five were having VUR, (31 [68%] high-grade, 14 [32%] low-grade, respectively). One third (33.3%) were surgically treated, 29 (64.4%) developed chronic kidney disease (CKD), and 18 (40%) developed renal scarring. Children with urinary tract infection (UTI) and hydroureter have 4.19 and 3.40 times the odds of developing VUR respectively.

Conclusion: The presence of hydroureter from ultrasound is a strong indicator of underlying VUR and justifies the rationale of requesting for MCUG, especially for those with recurrent UTI. The study failed to demonstrate significant association between the presence of VUR and complication of renal scarring and CKD.

Keyword: paediatric, micturating cystourethrogram, vesicoureteric reflux, hydroureter, urinary tract infection

ABSTRAK

Latar belakang: *Micturating cystourethrogram* (MCUG) adalah ujian standard digunakan untuk mengesan refluks vesicoureteral (VUR). Kajian ini dilakukan untuk menyiasat perkaitan di antara VUR dan kesannya terhadap buah pinggang.

Kaedah: Ini merupakan kajian retrospektif keratan rentas, yang dijalankan terhadap pesakit kanak-kanak, yang dirujuk ke hospital rujukan berpakar untuk menjalani ujian MCUG, dari Januari 2010 sehingga Disember 2019. Data klinikal seperti keputusan ujian imbasan bunyi buah pinggang, MCUG dan fungsi buah pinggang direkodkan dan analisis regresi logistic mudah dan berganda digunakan untuk mengkaji faktor risiko untuk mendapat VUR.

Keputusan: Daripada 136 pesakit terlibat, 45 orang menghidapi VUR (31 [68%] gred tinggi, 14 [32%] gred rendah). Satu pertiga di kalangan mereka menjalani rawatan secara pembedahan, 29 (64.4%) menghidap penyakit buah pinggang kronik, dan 18 (40%) mengalami buah pinggang berparut. Kanak-kanak yang mempunyai jangkitan saluran kencing dan hidroureter masing masing mempunyai 4.19 dan 3.40 kali ganda kebarangkalian untuk mendapat VUR.

Kesimpulan: Ujian MCUG adalah disyorkan untuk mengesan kehadiran VUR terutama di kalangan kanak-kanak yang dikesan mempunyai hidroureter dari ujian imbasan bunyi dan sejarah jangkitan saluran kencing berulang. Namun, tidak terdapat perkadaran yang signifikan di antara kehadiran VUR dan komplikasi buah pinggang berparut dan penyakit buah pinggang kronik.

Kata kunci: pediatrik, *micturating cystourethrogram*, refluks vesicoureteral, hidroureter, jangkitan saluran kencing

CHAPTER II:

THE TEXT

Section A:

Introduction

INTRODUCTION

Micturating cystourethrogram (MCUG) is a fluoroscopic study of the urinary tract, in which contrast medium instilled into the bladder through urethral catheter. It offers a tremendous amount of information regarding the anatomic and functional status of the urinary tract, especially the identification of vesicoureteric reflux (VUR). It is one of the most performed fluoroscopic investigations among paediatric population.

Urinary tract infection (UTI) is one of the most common infections in children $\leq$ 2 years old, with international prevalence between 2.9 – 11.6% in infant $\leq$ 2 years and between 6.4 – 9% in children $\leq$ 19 years old. The incidence of UTI is higher in boys than girls in those $\leq$ 3 months of age. The overall recurrence rate during the neonatal period has been reported to be 25% and that for toilet trained children is 30 – 50%.

The natural course of UTI tends to be benign, however in certain patient it might progress into more serious problem such as renal scarring and chronic kidney disease. This problem is seen among those with others risk factor such as recurrent UTI or abnormal urinary tract anatomy. To date, most of the guidelines on how to manage UTI among paediatric population came from the Western countries. Fortunately, a recent Asian guideline has been developed, which is demographically more appropriate to our local population.

The investigations of UTI include the use of ultrasonography, fluoroscopy, and renal scintigraphy. The old practices focus on identifying and treating vigorously the VUR, thus MCUG being among the important investigation. However, with the advancement in evidence-based practice, the approach has been modified. The traditional approach of imaging study

starts with ultrasonography, and the subsequent investigation which include MCUG or renal scintigraphy, is dependent on the result and clinical presentation. Considering the disadvantages of MCUG exposing patient to radiation burden, discomfort due invasive procedure and iatrogenic infection, it is suggested to do it selectively. On the other hand, to perform renal scintigraphy, we may need to use sedation, more costly and less readily available as MCUG.

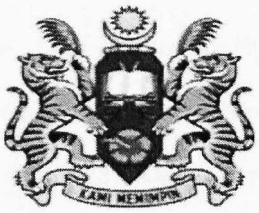
This purpose of this study is to identify the proportion of paediatric population who underwent MCUG, especially among those who has abnormal result, and to evaluate the urological pathology detected. The findings from this study will help in stratifying patients based on clinical presentation and reducing unnecessary referral for dimercaptosuccinic acid (DMSA) or diethylenetriamine pentaacetic acid (DTPA) scans, which are more expensive and not widely available. The finding of this study could also be used as a local reference for clinicians to counsel parents and plan treatment, especially in high-risk patients.

Section B:

Study Protocol

2.2.1 Documents submitted for ethical approval

Dissertation proposal



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Research Title: Micturating Cystourethrogram Finding and Outcome among Paediatric Population in a Tertiary Hospital

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1. Introduction

Micturating cystourethrogram (MCUG) is a radiographical examination of the bladder and urethra in which contrast medium instilled into the bladder through urethral catheter. It has the potential to provide a tremendous amount of information about the anatomic and functional status of the urinary tract, including identification of vesicoureteral reflux (VUR). It is one of the most commonly performed fluoroscopic investigations among paediatric patients.

Urinary tract infections are one of the most common infections in childhood, with international prevalence documented to be between 2.9 – 11.6% in infant less than 24 months and between 6.4 – 9% in children less than 19 years. The investigations of urinary tract infection included the use of ultrasonography of urinary tract, micturating cystourethrography and renal scintigraphy. The main reason to investigate urinary tract infection is to identify any urological pathology, which if left untreated can lead to renal scarring subsequently to end stage renal failure.

MCUG is indicated in the investigation of patients with a wide variety of clinical conditions including urinary tract infection. Other indications include:

- Children younger than 5 years with a febrile urinary tract infection
- Males of any age with a first urinary tract infection
- Females younger than 2 years with a febrile urinary tract infection
- Children with recurrent urinary tract infection
- Follow-up evaluation of vesico-ureteral reflux
- Hydronephrosis
- Enuresis
- Voiding dysfunction
- Incontinence
- Congenital conditions associated with genitourinary malformations

Undoubtedly, this examination is unpleasant experience to patients, parents and radiology staff performing the test. However, the importance of this study is unneglectable, as failed to identify urological pathology among paediatric patients may lead to detrimental effect.

2. Problem statement & Study rationale

Most physicians agreed that paediatric patients should be evaluated with imaging studies after a documented recurrent urinary tract infection. A comprehensive evaluation includes renal ultrasonography, renal scintigraphy and micturating cystourethrogram. Some studies suggested that patients with normal ultrasound and renal scintigraphy may not need invasive micturating cystourethrogram.

There are lack of study and data in Malaysia related to micturating cystourethrogram perform among paediatric population. Malaysian Paediatric Protocol 4th edition 2018, recommended routine radiological imaging for all children with urinary tract infection with renal ultrasonography being the first line. Subsequent will be renal scintigraphy and/or micturating cystourethrogram. However, it does not mention which study should be done first.

This aim of this study is to identify the proportion of paediatric population who underwent micturating cystourethrogram, especially among those who has abnormal result, and to evaluate the urological pathology detected. Later, these findings may help to stratify patient according to clinical presentation and reduce the unnecessary referral for imaging such as DTPA or DMSA scan, which will be more costly. Apart from that, micturating cystourethrogram is easily available throughout the country compared to renal scintigraphy. The result from this study also can be our local reference that can help clinician to counsel parents and plan management especially in those high-risk patients (recurrent UTI, high grade VUR).

3. Research Question(s)

1. What is the proportion of child who underwent micturating cystourethrogram has abnormal result?
2. What is the renal function at the point of time performing micturating cystourethrogram?
3. What is the common micturating cystourethrogram finding among paediatric population?
4. What is the association between vesicoureteric reflux and subsequent outcome?

4. Objective

General: To determine the proportion of paediatric patient who underwent micturating cystourethrogram with abnormal result and the outcome of vesicoureteric reflux.

Specific:

1. To determine the proportion of children who underwent micturating cystourethrogram with abnormal result
2. To determine the renal function at the point of time during performing micturating cystourethrogram
3. To identify the common abnormal finding of micturating cystourethrogram among children
4. To determine the association between vesicoureteric reflux and subsequent outcome

5. Literature Review

Urinary tract infection remains the important differential diagnosis among febrile children, it is more common in infant with male predominance. The evaluation of children with urinary tract infection might be differ depending on the local protocol but a thorough evaluation involves renal and bladder ultrasonography, renal scintigraphy and micturating cystourethrogram. It is important to get the correct diagnosis, timely wise planned appropriate assessment to provide the best management, subsequently improve the overall prognosis.

A complete report of micturating cystourethrogram is vital to aid with the management especially in those with urological abnormalities. A study to evaluate the completeness of MCUG reporting was done by Anthony et al[2] found that there was a substantial variation among radiologists, depending on the familiarities of procedure by the person in charged and centre. A standardized assessment tool was used to review 456 reports which include 26 variables; described the demographic, technical, anatomic and functional details. The mean percentage of items reported was 67+14%, 74+7% at free standing paediatric hospital (FSPH), 61+10% at paediatric 'hospital within hospital'(PHWH), and 48+11% in non-paediatric hospital (NPH). In multivariate analysis, the reports generated had 17% (95% CI: 14.5 – 19.7%, $p<0.0001$) and 9% (95% CI: 5.9 – 12.5%, $p<0.0001$) fewer item in NPH and PHWH respectively, compared to FSPH. Reports read by a paediatric radiologist had 12% more items included (95% CI: 9.1-15.3%, $p<0.0001$), compared to those read by a non-paediatric radiologist.

A retrospective study by Gomes N et al[1], to look at the pattern of urological pathology identified by MCUG among Jamaican children with UTI, yielded low incidence of VUR but detected presence of significant number of posterior urethral valves and other urethral abnormalities. The data were obtained from the electronic radiological records of Bustamante Hospital, from October 2008 until January 2012 involving 458 reports (11.8% abnormal report). Males outnumbered females both in number (male: female 2.5:1) and in the frequency of abnormalities (13% of males and 7% of females). The commonest pathologies were vesicoureteric reflux (29%, lower compared to international data) followed by bladder/urethral abnormalities (28%), posterior urethral valves were identified in 4 patients (1.2% in male patient). Epidemiologically, VUR is reported infrequently among black population, thus the results were understandable due to given population.

The incidence of VUR in healthy children is only 1 – 2%. A retrospective study in 2011 by Ji LN et al[3], involved 93 high risk children who were hospitalized in the Capital Institute of Paediatric from July 2007 to April 2010, found that children with UTI and fetal hydronephrosis posed significant risk at 34.5% and 17.1% respectively. The study also compared the usefulness of voiding sonography (VUS) in detecting VUR. The sensitivity of VUS in diagnosis of VUR was 100%, the specificity was 92.1%, the positive predictive value was 66.7% and the negative predictive value was 100%.

A prospective study done by Kuang YL et al[5], showed children with VUR were significantly more likely to develop pyelonephritis and renal scarring. This study involved 216 children admitted for febrile UTI and subsequently followed up for 6 months. The children were divided into three groups according to age, group I (< 1 year old), group II (1 – 5 years old), group III (5 – 17 years old). The incidences of VUR were 22%, 69% and 44%

respectively. The overall incidence of pyelonephritis was 70% with children had higher incidence ($p<0.05$). Of patient with pyelonephritis, 57% showed renal scar formation. In addition, children with high grade VUR were more susceptible to pyelonephritis and scar formation than those with low grade VUR ($p<0.05$).

A systematic review by Nader Shaikh et al[4] second to this finding. They reviewed 33 studies and among children with an initial episode of UTI, 57% (95% CI: 50-64) had changes consistent with acute pyelonephritis on acute phase DMSA scan and 15% (95% CI: 11 – 18) had evidence of renal scarring on follow up DMSA scan. Children with VUR were significantly more likely to develop pyelonephritis (RR: 1.5% [95% CI: 1.1 – 1.9]) and renal scarring (RR 2.6[95% CI: 1.7 – 3.9]) compared to children with no VUR. Children with VUR grade III or higher were more likely to develop scarring than children with lower grades of VUR (RR: 2.1 [95% CI: 1.4 – 3.2]). The development of renal scarring expose patient to hypertension, chronic kidney disease and end stage renal failure in later stage.

6. Conceptual Framework