

**RENAL OUTCOME IN CHILDREN WITH
PELVIURETERIC JUNCTION OBSTRUCTION
(PUJO): A TERTIARY CENTRE EXPERIENCE**

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CHAPTER 1:
THE PRELIMINARIES

Acknowledgement

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LIST OF ABBREVIATION AND NOMENCLATURE

Hospital USM :	Hospital Universiti Sains Malaysia
HRPZII	Hospital Raja Perempuan Zainab II
PUJ	Pelvi-ureteric junction
VUJ	Vesico-ureteric junction
PUJO	Pelvi-ureteric junction obstruction
VUJO	Vesico-ureteric junction obstruction
DTPA	Diethylenetriamine pentaacetic acid
MAG3	Mercaptoacetyltryglycine
EDTA	Ethylenediaminetetraacetic Acid
VUR	Vesico-ureteric reflux
IVP	Intravenous pyelogram
DMSA	Dimercaptosuccinic Acid
EC	Ethylenedicysteine

ABSTRACT

Title

Renal Outcome in Children with Pelvi-Ureteric Junction Obstruction (PUJO): A Tertiary Centre Experience

Background: Antenatal hydronephrosis is a common findings during antenatal scan and pelvi-ureteric junction obstruction is the commonest cause. Dynamic study using radio-isotope scan has become the standard investigation for diagnostic purpose. We reviewed the outcome of children who underwent DTPA/MAG3 scan for suspected PUJO including their clinical presentation, indication for surgery, underlying causes and post-surgical outcome.

Methodology: This was a retrospective study looking at clinical data from 2008 until 2018 whom underwent DTPA/MAG3 imaging in a tertiary hospital. Baseline characteristic of the patient, age at the time of diagnosis, indication for undergoing radionuclide scan, type of surgery performed, and post-surgical follow-up investigations were recorded.

Result: A total patients of 151 were recruited into the study. Majority were males 101 (66.9%); and 50 of them were females (33.1%). Median age of the patient was four-year-old when the diagnosis was made. Antenatal hydronephrosis and abdominal pain were the commonest clinical presentation warranted for radionuclide scan to be performed. PUJO was confirm in 57 patients (37.7%) of which majority were found on the unilateral side involving left kidney 31 patients (53.1%). Pyeloplasty was performed as corrective surgery in seventy percent of them. Nevertheless, 7 patients (21%) showed persistent obstruction during follow up imaging after the surgery.

Conclusion: This study highlighted the importance of follow-up investigation in all antenatal hydronephrosis. Radionuclide scan is the diagnostic tool for PUJO and preferably should be arranged earlier to avoid delay in diagnosis and improve the renal outcome.

Potential residual hydronephrosis and obstruction may occur despite corrective pyeloplasty, hence the need for complement imaging as an imperative measure to prevent future risk of chronic kidney disease.

Keywords: obstructive uropathy, pelvi-ureteric junction obstruction, antenatal hydronephrosis

ABSTRAK

Tajuk

Kesan Kepada Buah Pinggang Bagi Kanak-kanak Yang Mengalami Halangan di Persimpangan Pelvi-ureterik: Pengalaman Pusat Rujukan Tertiar

Latar belakang: Antenatal hidronephrosis adalah penemuan yang biasa dijumpai semasa imbasan sewaktu mengandung dan halangan di persimpangan pelvi-ureterik adalah punca yang paling lazim ditemui. Kajian dinamik menggunakan imbasan radio-isotope telah menjadi penyiasatan standard bagi tujuan diagnostik. Kami mengkaji kesan kanak-kanak yang menjalani DTPA/MAG3 scan untuk kes yang disyaki mengalami PUJO termasuk presentasi klinikal, indikasi untuk pembedahan, punca penyakit dan kesan selepas pembedahan.

Kaedah: Ini merupakan kajian rentas yang melihat data klinikal dari 2008 hingga 2018 yang menjalani pengimejan DTPA/MAG3 di pusat rujukan tertiar. Ciri asas pesakit, umur pada masa diagnosis, indikasi untuk menjalani imbasan radionuklid, jenis pembedahan yang dilakukan, dan siasatan susulan selepas pembedahan direkodkan.

Keputusan: Seramai 151 pesakit menyertai kajian ini. Majoriti adalah pesakit lelaki, 101 (66.9%) dan 50 (33.1%) perempuan. Median umur pesakit merupakan empat tahun. Antenatal hydronephrosis dan sakit di bahagian abdomen merupakan sebab yang sering dirujuk bagi menjalani imbasan radionuklid. PUJO disahkan untuk 57 pesakit (37.7%) di mana majoriti melibatkan buah pinggang kiri 31 pesakit (53.1%). Tujuh puluh peratus (70%) menjalani 'pyeloplasty' sebagai pembedahan rawatan. Walau bagaimanapun, 21% menunjukkan halangan berterusan daripada pengimejan susulan selepas pembedahan.

Kesimpulan: Kajian ini menekankan kepentingan siasatan susulan dalam semua antenatal hydronephrosis, iaitu ultrasound dan imbasan radionuklid untuk mencapai diagnosis muktamad. Walaupun pesakit sudah menjalani pembedahan, terdapat kemungkinan

hidronephrosis dan halangan berterusan di dalam sesetengah pesakit. Oleh itu keperluan untuk mengulangi pengimejan adalah penting bagi mengelakkan risiko penyakit buah pinggang kronik.

Kata kunci: halangan uropati, halangan persimpangan pelvi-ureteric, pranatal hydronephrosis

CHAPTER II:
THE TEXT

2.1 Section A:

Introduction

Introduction

Urinary tract obstruction is referred to as restriction of urinary outflow that can lead to renal damage⁽¹⁾. Obstruction can occur at any point in the urinary tract, from the kidneys to the urethral meatus. Anatomical obstruction is divided into pelvi-ureteric junction (PUJO) and vesico-ureteric junction (VUJO) obstruction. PUJO has an incidence of 1 in 1000-1500 newborns and is the commonest cause of antenatal hydronephrosis⁽²⁾. It is defined as a partial or total blockage to urinary flow from the renal pelvis into the proximal ureter causing dilatation of collecting systems. Anatomical narrowing is the most common cause^(1,2).

Causes of urinary tract obstruction can be classified broadly into primary (congenital) and secondary^(2,3) with the former being the most common. The primary PUJO is resulted from the deposition of excess collagen secondary to the activation of inflammatory mediator with clockwise rotation of renal pelvis leading to hydronephrosis^(4,5). These congenital abnormalities may be seen in both children and adults but it is more common in children. Secondary causes are commonly due to acquired origin such as trauma, compression, calculi, inflammation or surgical procedure like endoscopy or lithotripsy^(1,4,5).

The resultant back pressure within the renal pelvis leads to progressive renal damage and deterioration. Delay in diagnosis and presentation had cause an increase in chances of developing renal damage. Thus, when the diagnosis of urinary tract obstruction was made, expected management is based on the cause, of which mostly been managed conservatively⁽⁶⁾. Surgical intervention will be required for the severe form of obstruction in about 20% of the patients⁽⁶⁾. Surgical procedure includes pyeloplasty, pigtail drainage or nephrectomy. These procedures are performed to relieve the obstruction and improve urinary drainage.

Establishing the distinction between urinary tract obstruction and urinary tract dilatation remains a challenging problem. Modalities such as Diethylenediamine Pentaacetate (DTPA), Mercaptoacetyltriglycine (MAG3) and Ethylenediaminetetraacetic Acid (EDTA) are the radionuclide imaging and dynamic study that clinically used to assess the obstruction and measure the glomerular filtration rate⁽⁷⁻⁹⁾. These radionuclide imaging can distinguish a true obstruction and other causes of pelvicalyceal dilatation such as vesicoureteric reflux (VUR)^(7,10). In the past, intravenous pyelogram (IVP) had been used to detect the obstruction. However, due to low sensitivity to detect obstruction especially in chronic renal obstruction and higher radiation dose exposure, its usage has been less popular compared to radionuclide scan⁽¹¹⁾. On the other hand, Dimercaptosuccinic Acid (DMSA) is a static parenchymal imaging used to assess relative renal function and detect renal scarring in patient with recurrent urinary tract infection but unable to delineate obstruction^(12,13).

A study in India by Pramod S et al demonstrated that PUJO is the most common ureteric obstruction with mean age of presentation of 6 year-old and the most common symptoms at presentation was abdomen pain⁽⁴⁾. The retrospective study designed to evaluate the outcome of urinary tract obstruction involving all children with hydronephrosis with obstruction. This was assessed by using diuretic renogram include DTPA and ethylenedicysteine (EC) scan. In the same study, almost 50% of the patients underwent pyeloplasty and 10% underwent nephrectomy. Post pyeloplasty imaging showed improvement of drainage and renal function on DMSA scan.

However, Prabha et al showed only 28% of their cohort were subjected to surgical intervention even though almost similar number of patients were recruited⁽¹⁴⁾.

Another study in Africa population by Atim et al also reviewed the outcome and management of patient with ureteric obstruction⁽¹⁵⁾. The study found a total 41 children

with obstruction of which 18 were congenital, 21 with renal calculi and 2 strictures. These patients were subjected to surgical intervention. Interestingly, 50% of their cohort had renal calculi and requiring pyelolithotomy.

Suliman et al demonstrated that MAG3 was more sensitive in detecting obstruction as the half time of radionuclide clearance was faster compared to DTPA⁽¹⁶⁾. However, DTPA is more sensitive to diagnosed kidney dysfunction as the perfusion is greater than MAG3. Based on same study, both DTPA and MAG3 improved the diagnosis accuracy of obstruction in children compared to other type of imaging. Thus, usage of both imaging to detect obstruction and assess renal function in children is the best modes of imaging.

This study aimed to determine on the proportion, clinical presentations and outcomes of obstructive uropathy among children in tertiary centre.

2.2 Section B:

Study protocol

2.2.1 Documents submitted for ethical approval

Dissertation proposal



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**THE PROFILE AND OUTCOME OF OBSTRUCTIVE UROPATHY IN CHILDREN OF TERTIARY
CENTRE IN KELANTAN**

Protocol v2.0 (19 JULY 2020)

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Research title: THE PROFILE AND OUTCOME OF OBSTRUCTIVE UROPATHY IN CHILDREN OF TERTIARY CENTRE IN KELANTAN

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Introduction

Urinary tract obstruction refers to as restriction of urinary outflow. The resultant back pressure within the renal pelvis may lead to progressive renal damage and deterioration. Obstruction occur at any point in the urinary tract, from the kidneys to the urethral meatus. It can present at any time from neonatal period to old age. Children present with symptoms such as abdominal pain, urinary tract infection, uremia or abdominal mass before the diagnosis of obstruction been made. Obstruction can be divided into either anatomical or causes.

Causes of urinary tract obstruction classified broadly into primary and secondary. Primary result from congenital. These congenital abnormalities may be seen in children and adults but more in children. Secondary caused by acquired such as trauma, calculi, inflammation or surgical procedure. The pelviureteric junction (PUJ) is the most common site of obstruction along the upper urinary tract. Pelviureteric junction obstruction defined as a partial or total blockage to urinary flow from the renal pelvis into the proximal ureter causing dilatation of collecting systems. PUJ obstruction has an incidence of 1 in 1000-1500 newborns and is the common cause of antenatal hydronephrosis.

Delay in diagnosis or presentation leads to increase chances of renal damage or loss. Thus, when the diagnosis of urinary tract obstruction was made, expected management is based on the cause of the obstruction. Mostly obstruction with dilatation is managed by conservatively. Surgical intervention will be required for the most severe form of obstruction in about 20% of the patients. Surgical procedure include pyeloplasty, pigtail drainage or nephrectomy are used to relieve the obstruction and improvement of urinary drainage, thus will improved the renal function.

Despite the increase incidence of diagnosed urinary tract abnormalities, the distinction between urinary tract obstruction and urinary tract dilatation remain a challenging problem.

Dynamic study (DTPA and MAG3) are clinically used to assess the obstruction and also can be used to assess the renal function. These radionuclide imaging can be used to distinguish between a true obstruction and other cause of pelvicalyceal dilatation.

Problem statement & Study rationale

There are lack of study and data in Malaysia related to obstructive uropathy (including pelviureteric junction and vesicoureteric junction). Therefore, the purpose of this study is to determine the prevalence of obstructive uropathy detected from DTPA/MAG3 scan in Kelantan. Later, these findings may help for stratification of patients according to clinical presentation and reduce the unnecessary referral for imaging.

Research Question(s)

- 1) What is the proportion of children with obstructive uropathy
- 2) What are the clinical presentations of obstructive uropathy in infant and children
- 3) What are the outcomes of obstructive uropathy in infant and children

Objective

General:

To determine the proportion, clinical presentations and outcomes of obstructive uropathy among children in tertiary centre of Kelantan

Specific:

- 1) To determine the proportion of children with obstructive uropathy
- 2) To describe clinical presentation of obstructive uropathy in children
- 3) To describe the outcome of obstructive uropathy in children

Literature review

From the study of Assessment of paediatric hydronephrosis using output efficiency in which published by Saunders et al in the Journal of nuclear medicine 1997 stated that 22 subjects out of 91 hydronephrosis kidney were noted to have obstruction⁽⁸⁾. From this study, it showed that ureteric obstruction is leading cause of hydronephrosis. This study also conclude that output efficiency imaging improved the diagnostic accuracy of obstruction. Therefore, DTPA and MAG3 imaging are the best way to detect obstruction in children.

According to Clinical Profile and Outcome of pelvi-ureteric junction obstruction in children presenting above than 1 year old in which published by Pramod S et al in International Surgery Journal, pelviureteric junction obstruction is the most common ureteric obstruction⁽⁴⁾. The mean age of presentation was 6 years and most common presentation was abdomen pain. More number of male affected were affected compared to female. Out of 26 children, 5 children had a split renal function of less than 10% in affected kidney. All the participant underwent surgical procedure, 22 underwent pyeloplasty and 4 underwent nephrectomy. 3 children presented with calculi with PUJ obstruction. In these children, pyelolithotomy with pyeloplasty were performed. Post pyeloplasty imaging showed improvement of drainage with improvement of renal function

Based on Profile and outcome of pelviureteric junction obstruction in The Open Urology &

Nephrology Journal 2014 by Prabha et al, pelviureteric junction obstruction was common abnormality of upper urinary tract⁽¹⁴⁾. Renal pelvic stone is common cause followed by congenital causes. From this study, 44 patients having urinary tract obstruction. 32 were treated conservatively with regular follow up and 12 underwent pyeloplasty in which 4 of them later needed for nephrectomy in view of non-functioning kidney.

Based on pelvi-ureteric junction obstruction - a ten year single centre review in North Central Nigeria in Medico research chronicle 2017 by Atim T et al, the study reviewed the outcome of management of patient with ureteric obstruction⁽¹⁵⁾. 41 patient with ureteric obstruction were seen. Out of 41, 18 were congenital, 21 with renal calculi and 2 strictures. 97% of patient with obstruction come with abdominal/loin pain while 61% come with nausea and vomiting. The age range was 3 years - 67 years of age. All patient underwent surgical intervention. 17 underwent pyeloplasty, 3 underwent simple nephrectomies and 21 underwent pyelolithotomy.

Research design

This involved a ten-year retrospective study from 2008 until 2018 which based on data of patients underwent DTPA/MAG3 imaging through data from Nuclear Medicine Department Hospital USM. All the patient's DTPA/MAG3 imaging findings and reasons for each imaging done will be traced. From the data, the patient's record will be traced through Record Office Hospital USM. The record will be reviewed to know the outcome of each patient underwent imaging in which include the renal function and need for surgical treatment.

Study area

Tertiary centre in Kelantan

- 1) Hospital Universiti Sains Malaysia Kubang Kerian
- 2) Hospital Raja Perempuan Zainab II, Kota Bharu

Study population

Reference population

Children with obstructive uropathy_of tertiary centre in Kelantan.

Source population / sampling pool

Children referred for DTPA/MAG3 for suspecting obstructive uropathy in tertiary centre in Kelantan (database obtained from nuclear medicine department)

Subject criteria**Inclusion criteria**

Infant and children (1month to 18 years age) (paediatric age) suspected obstructive uropathy underwent 99mTc labelled mercaptoacetyltryglycine (MAG3) or diethylenetriamine pentaacetic acid (DTPA) scan from 1 January 2008 until 31 December 2018

Exclusion criteria

Records with inadequate crucial data include missing data and lack of follow up records

Sample size estimation

$$n = \frac{Z^2 p(1 - p)}{d^2}$$

n= min. required sample

Z = value of standard normal distribution = 1.96

d= precision = 6%

p= 21% (obstruction and the minimally dilated renal collecting sample, genitourinary systems: US studies, 1999)

n= 171

Considering 10% non-response, minimum required sample is 187

Sampling method and subject recruitment

All eligible children that fulfilled inclusion criteria will be included and recruited in this study

Research tool

Data will be collected using sociodemographic porforma and medical record

Operational definition

Urinary tract obstruction - presence of obstruction (delay in excretion) detected from 99mTc labelled mercaptoacetyltryglycine (MAG3) or diethylenetriamine pentaacetic acid (DTPA) dynamic scan. Time to half maximum activity (T1/2 was calculated from the time of maximum counts to the time when the imaging decreased to half of the maximum counts) more than 20 minutes of excretion. (Evaluation of hydronephrosis in children, Carlos J. R. Simal)

^{99m}Tc MAG3 - Tracer exclusively excreted by secretion in the proximal tubules with higher extraction fraction, expressed as the effective renal plasma flow (Interpretation of the Renogram: problem and pitfalls in hydronephrosis in children, paediatric Urology)

^{99m}Tc DTPA - Tracer with a small molecule that is exclusively filtered by glomeruli, with an extraction efficiency of 20% in mature kidney, excreted by filtration (Interpretation of the Renogram: problem and pitfalls in hydronephrosis in children, paediatric Urology)

Data collection method

Data will be collected using data collection sheet containing desired patient's information and through medical record.

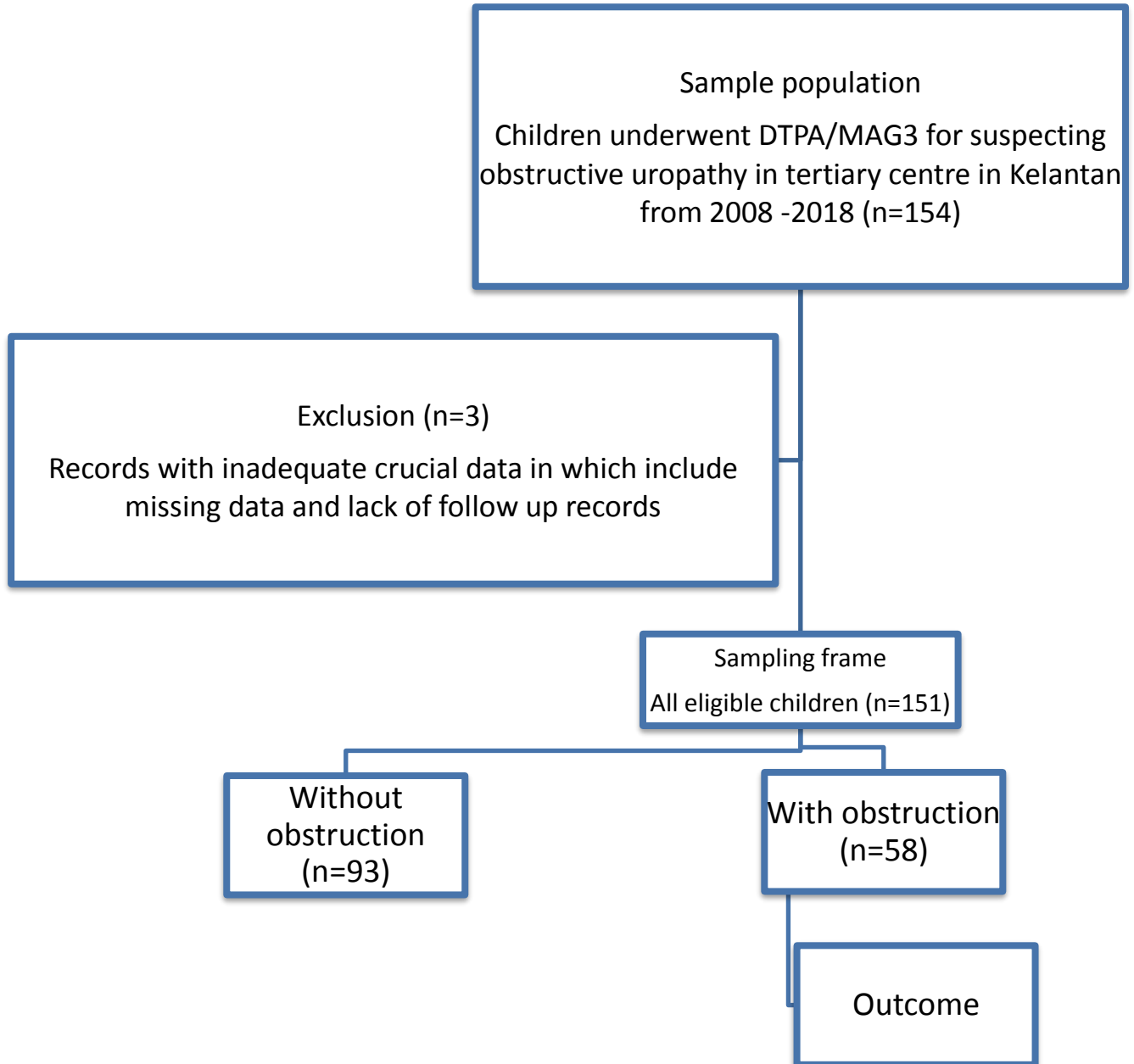
Patient will be identified during sampling frame from Jabatan Radiologi dan Radionuklear, Hospital USM.

All patient underwent MAG3 and DTPA scan only in Hospital USM and medical record of patient will be traced and reviewed from Hospital USM and Hospital Raja Perempuan Zainab II (HRPZII) and only those who fulfilled inclusion will be included in the study.

All relevant data were obtained, included:

- Baseline demographic characteristics: age, gender, family income status
- Baseline clinical examinations : weight, height, blood pressure, renal function, ultrasound findings
- Clinical presentations before the imaging was made
- Diagnosis of the patient
- Findings of radionuclide scan DTPA and MAG3
- Outcome of the patient after findings of obstruction – surgical or conservative treatment

Study flowchart



Data analysis

Data will be entered and analysed using SPSS version 24. Descriptive statistics will be used to summarise the socio-demographic characteristics of subjects. Numerical data will be presented as mean (SD) or median (IQR) based on their normality distribution. Categorical data will be presented as frequency (percentage).

Expected result(s)*Dummy tables*

1) Demographic Details

Variables	n (%)
Sex	
● Male	
● Female	
Age	Mean (SD)
Race	
● Malay	
● Chinese	
● Indian	
Total Family Income	

2) Proportion of obstructive uropathy among patient underwent MAG3/DTPA scan

Variables	n (%)
Detected	
Not detected	

3) **Types of obstructive uropathy**

Variables	n (%)
Pelvic ureteric junction obstruction	
Vesicoureteric junction obstruction	