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“TO STUDY THE RISK FACTORS FOR CHRONIC RENAL FAILURE IN CHILDREN WITH POSTERIOR URETHRAL VALVE”

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CERTIFICATE

This is to certify that the dissertation titled **"TO STUDY THE RISK FACTORS FOR CHRONIC RENAL FAILUREIN CHILDREN WITH POSTERIOR URETHRAL VALVE"** submitted by Dr.C.Santha Kumar to the Faculty of pediatrics, The Tamilnadu Dr. M.G.R. Medical university, Chennai in partial fulfillment of the requirement for the award of M.D. Degree(Paediatrics) is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

I, DR.C.SANTHAKUMAR **solemnly declare that the dissertation titled** "TO STUDY THE RISK FACTORS FOR CHRONIC RENAL FAILURE IN CHILDREN WITH POSTERIOR URETHRAL VALVE" **HAS BEEN PREPARED BY ME.**

This is submitted to **The Tamilnadu Dr. M.G.R. Medical University**, Chennai in partial fulfillment of the rules and regulations for the M.D. Degree Examination in Pediatrics.

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CONTENTS

INTRODUCTION

Background

The first description of posterior urethral valves (PUVs) was made by Hugh Hampton Young. PUVs represent a spectrum of severity, ranging from disease incompatible with postnatal life to disease that is minimal and may not manifest until later in life. Treatment of PUVs remains a clinical challenge, requiring active management from infancy into adulthood to avoid progressive dysfunction and deterioration of both the upper and lower urinary tracts.

Pathophysiology

During embryogenesis, the most caudal end of the Wolffian duct is absorbed into the primitive cloaca at the site of the future verumontanum in the posterior urethra. In healthy males, the remnants of this process are the posterior urethral folds, called plicae colliculi. Histological studies suggest that PUVs are formed at approximately 4 weeks' gestation, as the Wolffian duct fuses with the developing cloaca.

Young popularized a classification of PUV[1] Abnormally high insertion and fusion of these primitive folds were believed to be the origins of 95% of PUVs; this type was referred to as type I PUVs. Although Young described type II PUVs, most pediatric urologists believe that these are not obstructing valves but simply hypertrophy of

the plicae colliculi. Also described by Young, type III PUVs constitute a septum at the junction of the posterior and anterior urethra, instead of a sail-like valve. Type III PUVs are believed to originate from incomplete dissolution of the urogenital membrane. This classification has no clinical value and is now considered outdated.

Congenital obstructing posterior urethral membrane (COPUM) was first proposed by Dewan and Goh and was later supported by histological studies by Baskin [2] This concept proposes that, instead of a true valve, a persistent oblique membrane is ruptured by initial catheter placement and, secondary to rupture, forms a valvelike configuration.

PUV represents a spectrum of severity. The degree of obstruction caused by this abnormality widely varies depending on the configuration of the obstructive membrane within the urethra. The morbidity of PUVs is not merely limited to transient urethral obstruction; however, the congenital obstruction of the urinary tract at a critical time in organogenesis may have a profound and lifelong effect on kidney, ureteral and bladder function.

Renal insufficiency is caused by PUVs in approximately 10-15% of children undergoing renal transplant, and approximately one third of patients born with PUVs progress to ~~end-stage renal disease (ESRD)~~.

Moreover, children with PUVs develop thickened bladders because of increased collagen deposition and muscle hypertrophy within the

bladder wall. Hypertrophy and hyperplasia of the detrusor muscle and increases in connective tissue decrease bladder compliance during filling. Bladder emptying occurs with high intravesical pressures, which can be transmitted to the ureters and kidneys. These patients are susceptible to incontinence, infection and progressive renal damage.

Frequency

PUV is the most common cause of lower urinary tract obstruction in male neonates; the reported incidence is 1 per 8,000 to 1 per 25,000 live births.

Mortality/Morbidity

PUVs are the cause of renal insufficiency in approximately 10-15% of children undergoing renal transplant, and approximately one third of patients born with PUV progress to ESRD.

Sex

PUVs exclusively occur in males. The homolog to the male verumontanum from which the valves originate is the female hymen.

Age

Diagnosis is usually made before birth or at birth when a boy is evaluated for ~~antenatal hydronephrosis~~. Before the era of prenatal ultrasonography, PUVs were discovered during evaluation of ~~urinary tract~~

~~infection (UTI)~~, ~~voiding dysfunction~~, or renal failure. Although rare, adult presentation of PUVs has been described in case reports, with symptoms varying from obstructive voiding symptoms to postejaculatory dysuria. In the presonography era, late presentation of PUV was considered a good prognostic sign suggestive of a lesser degree of obstruction.

Clinical

History

- Prenatal diagnosis
    - The widespread use of antenatal ultrasonography and the sophisticated neonatal care available in most developed countries has enabled diagnosis of posterior urethral valves (PUVs) in many individuals in the prenatal timeframe.
    - Diagnosis is usually made before or at birth when a boy is evaluated for antenatal hydronephrosis.
    - In 1989, Thomas reported that 10% of patients with prenatal hydronephrosis detected by ultrasonography had PUV[3]
    - Despite widespread use of antenatal ultrasonography, some patients with PUVs present later in life.
    - In a 1993 report, Dinneen et al reported the sensitivity of antenatal ultrasonography to be only 45% in detecting PUVs

in 45 patients who presented when younger than 6 month[4]. With improvements in technology, the sensitivity has increased over the last 10 years.

- Those patients with PUVs not diagnosed on prenatal ultrasonography and who do not manifest overt urinary pathology are at risk of delayed presentation of PUVs.

- Delayed presentation
  - UTI, diurnal enuresis in boys older than 5 years, secondary diurnal enuresis, voiding pain or dysfunction, and decreased force of stream may indicate the presence of PUV[5]
  - PUVs are sometimes discovered during evaluation of abdominal mass or renal failure.
- Incidental diagnosis: Hydronephrosis or ~~proteinuria~~ found on examination for unrelated conditions may be the first sign of PUVs.

Physical

Most patients have normal findings upon physical examination. When present, abnormal physical findings are the result of severe renal insufficiency.

- Neonates may present with severe pulmonary distress due to underdevelopment of the lung caused by ~~oligohydramnios~~. An appropriate volume of amniotic fluid (produced by the kidneys) is necessary for complete and proper branching of the bronchial tree and alveoli. Physical findings can include the following:
    - Poor fetal breathing movements
    - Small chest cavity
    - Abdominal mass (ascites)
    - Potter facies
    - Limb deformities (skin dimpling)
    - Indentation of the knees and elbows due to compression within the uterus
- In older children, physical findings can include poor growth, ~~hypertension~~, and lethargy. An intermittent or weak urinary stream is a nonreliable sign.

Causes

PUV is a congenital obstruction caused by a malformation of the posterior urethra. The significance of this obstruction depends on the secondary effects on the bladder, ureters, and kidneys.

- Type I PUV: This type of obstruction is believed to be secondary to abnormal insertion and absorption of the most distal aspects of the Wolffian ducts during bladder development. In the healthy male, the remnants of these ducts are observed as the plicae colliculi.

- Type III PUV: These valves are observed as a membrane in the posterior urethra believed to originate from incomplete canalization between the anterior and posterior urethra.

- **RISK FACTORS**

I. Antenatal diagnosis <24wks of gestation

Antenatal USG features of PUV

1.Bilateral hydroureteronephrosis

2.Distended bladder

3.Dilated posterior urethra

4.Thickened bladder wall

5. “Keyhole” sign

6. Oligohydramnios

II. Age at diagnosis <1year

III. Bilateral VUR

IV.Urinary incontinence beyond 5years of age

V. Renal parenchymal damage detected by USG

- Hyperechoiec kidney
- No pyramids seen

VI. Serum creatinine >0.8mg/dl during Ist year of age.

VII. Persistence of dilated system after relief of obstruction

VIII. Recurrent UTI

IX. Timing of relief of obstruction >1year of age

X. Absent Pop – off Mechanisms

- unilateral VUR
- Urinary ascites
- Peri renal urinoma
- Large bladder diverticula

Other Problems to Be Considered

Anterior urethral valves

Urethral stricture disease

Detrusor sphincter dyssynergy

Diurnal urinary incontinence

Pediatric renal insufficiency

Workup

Laboratory Studies

- Immediately following birth, the infant's serum chemistries are the same as the mother's. Therefore, serum values for creatinine and BUN should be obtained at least 24 hours after birth. In utero, the placenta functions as the major blood filter for the fetus, with waste passed on to the mother. Observing serum chemistries for several days to weeks is important to determine the true status of the newborn's renal function.

- The normal newborn kidney is still undergoing maturation at birth, and infant glomerular filtration rate (GFR) continues to improve during the first several months of life. Because of renal immaturity at birth, the newborn is unable to concentrate urine and is susceptible to dehydration. This defect is exacerbated by renal dysplasia such as that found with posterior urethral valves (PUVs).

- As renal maturation continues, the serum creatinine clearance normally improves. If significant renal dysplasia or damage has occurred, the serum creatinine fails to reach a normal level during the first year of life. Serum creatinine levels greater than 0.8 mg/dL during the first year of life have been demonstrated to be associated with poor long-term renal function.

Imaging Studies

- Renal and bladder ultrasonography

    - Every child with antenatal hydronephrosis requires renal and bladder ultrasonography assessment in the immediate postnatal period. Focus should be directed towards appearance of the renal parenchyma, evidence of renal collecting system dilatation, bladder wall thickness, and presence of ascites.

    - Because newborns commonly have relative hypovolemia during the first few days of life, perform repeat ultrasonography after the first week of life if previous findings were normal in a child with previously diagnosed antenatal hydronephrosis before making a final determination that the hydronephrosis has resolved.

- Voiding cystourethrography
    - The key to the workup of any child with antenatal hydronephrosis is voiding cystourethrography (VCUG). Perform VCUG during voiding and under fluoroscopy, with imaging of the posterior urethra.
    - The diagnosis of PUV is indicated by visualization of the valve leaflets. Other clues to the diagnosis are a thickened trabeculated bladder, a dilated or elongated posterior urethra, and a hypertrophied bladder neck. Diverticula, cellules, vesicoureteral reflux, and reflux into the ejaculatory ducts secondary to elevated bladder and urethral pressures may also be present.
- Renal scintigraphy
    - Although not necessary in every child, renal scintigraphy may be helpful in some cases. It should not be performed in the neonatal period because renal immaturity does not allow for accurate estimation of renal function. If renal dysplasia is suspected, nuclear imaging can determine relative renal function. Some children may have secondary ureterovesical junction obstruction due to bladder hypertrophy.

- Tc-dimercaptosuccinic acid (DMSA), glucoheptonate, and mercaptoacetyl triglycine (MAG-3) renal scintigraphy are cortical imaging studies that provide information about relative renal function (each kidney relative to the other) and intrarenal function (eg, photopenic areas within the kidney indicate scarring or dysplasia). Additionally, the MAG-3 renal scan with furosemide (Lasix) provides information about renal drainage and possible obstruction.

Other Tests

- Urodynamic evaluation provides information about bladder storage and emptying. The mature bladder should store urine at a low pressure and then completely empty at appropriate pressures.

- The term "valve bladder" is used to describe patients with PUV and a fibrotic noncompliant bladder. These patients are at risk of developing hydroureteronephrosis, progressive renal deterioration, recurrent infections, and urinary incontinence.

- Patients with PUV require periodic urodynamic testing throughout childhood because bladder compliance may further deteriorate over time.

Procedures

- Cystoscopy serves both diagnostic and therapeutic functions in these infants. Appropriately-sized cystoscopes (<8F) are needed to avoid injury to the urethra.

    - Diagnostic cystoscopy: Confirmation with cystoscopy is required in every child in whom PUV is suggested after VCUG. In some, the filling defect observed on VCUG may represent only external sphincter contraction during voiding. In others, the valve leaflets are confirmed.

    - Therapeutic cystoscopy (ie, transurethral incision of the PUVs): Multiple techniques have been described for ablating the valves. Disruption of the obstructing membrane by blind passage of a valve hook is now only of historic interest. Currently, valves are disrupted under direct vision by cystoscopy using an endoscopic loop, Bugbee electrocauterization, or laser fulguration. The objective is to relieve the obstruction by cutting the valves at the 12-, 5-, and 7-o'clock positions. Perform this in the least traumatic fashion to avoid secondary urethral stricture or injury to the urethral sphincter mechanism.

- In some patients, the urethra may be too small for the available cystoscopic instrumentation. Fortunately, because of continued

advancements in pediatric endoscopic equipment, this is an uncommon occurrence. When this situation arises, a temporary vesicostomy is performed.

Treatment

Medical Care

The medical management of posterior urethral valves (PUVs) relates to the treatment of the secondary effects of the valves. Adequate care involves a team approach that includes a neonatologist, general pediatrician, pediatric urologist, and pediatric nephrologist. Short-term goals involve treating pulmonary distress, immediate relief of urethral obstruction (placement of 5F feeding tube), and fluid and electrolyte management. In children who survive the pulmonary distress, the long-term issues include treatment of bladder dysfunction and renal insufficiency.

- Renal treatment
    - Newborn period: Few patients present with bilateral renal dysplasia at birth. In the past, if patients did not die from associated pulmonary insufficiency, they died due to progressive renal insufficiency. With recent advances in peritoneal dialysis, some children may be treated successfully

from birth. If growth is adequate, renal transplantation is often possible after the first year of life.

- Delayed renal insufficiency: Approximately one third of patients with PUV progress to ESRD and the need for dialysis or transplantation. Progression of ESRD is accelerated at the time of puberty due to the increased metabolic workload placed on the kidneys. Growth in these children may be significantly below the reference range for the child's age. Adequate caloric intake and protein nutrition are essential to growth but may also accelerate the rise in serum creatinine levels. Renal dysfunction can be accelerated by recurrent infections and elevated bladder pressures. Treatment of the lower urinary tract may influence progression of upper tract disease.

- Bladder management

  - Newborn period: All male children with antenatal hydronephrosis require VCUG shortly after birth to exclude PUV. While awaiting this study, place a 5F or 8F urethral catheter to allow for bladder drainage. If valves are confirmed, they can be incised within the first few days of life. However, the newborn urethra may be too small to accommodate available equipment. In these individuals, a vesicostomy can be performed as a temporary solution until urethral growth has

been adequate to allow transurethral incision. Secondary ureterovesical junction obstruction from bladder hypertrophy is a controversial issue. Supravesical urinary diversion procedures (eg, cutaneous ureterostomies) are reserved for patients who appear to have ureterovesical junction obstruction. This is very infrequent.

- Delayed bladder management: Severe or prolonged urethral obstruction can lead to a fibrotic, poorly compliant bladder. This occurs when the developing bladder is exposed to high pressures from bladder outlet obstruction, leading to increases in bladder collagen deposition and detrusor muscle hypertrophy and hyperplasia. These bladders manifest poor compliance, leading to elevated storage pressures. This, in turn, leads to increased risk of reflux, hydroureteronephrosis, and urinary incontinence. Use of urodynamic testing to assess bladder compliance help identify patients at risk. Some patients may respond to anticholinergic medication, such as oxybutynin. Institution of intermittent clean catheterization may aid some patients achieve continence by preventing the bladder from overfilling. In patients who do not gain adequate bladder capacity and safe compliance despite optimal medical management, augmentation cystoplasty may be required.

Surgical Care

Surgical care of the patient with PUV varies according to age, bladder status, and renal status. Prenatal surgery has been reported in

patients diagnosed with PUV with the goal of improving postnatal outcomes. Antenatal hydronephrosis is detectable only after renal development has occurred and urine production has started. With improvement in prenatal ultrasonography, the hope was that earlier intervention with vesicoamniotic shunting would improve postnatal renal function. However, identification of those patients who may benefit form early intervention remains elusive. To date, improvement in renal function has been difficult to demonstrate and prenatal intervention remains experimental.

- Urinary drainage
    - Postnatal primary valve ablation
        - Ideal treatment involves transurethral incision of the PUV during the first few days of life.
        - Current infant resectoscopes are available in size 8F and smaller.
        - The valves can be incised at the 12-, 5-, and 7-o'clock positions, with either a cold knife or electrocautery.
        - Some surgeons prefer to leave a catheter in place for 2-3 days after the procedure.

- The timing of the postoperative VCUG varies and ranges from several days to several months.

- Comparison of posterior urethral diameter to anterior urethral diameter can provide an objective measure of valve ablation. In most patients, the posterior urethra is markedly dilated. Postincision diameter should decrease.

- The normal posterior-to-anterior urethral ratio is approximately 2.3. Approximately two thirds of patients have successful valve ablation with one procedure, manifested by a postincision ratio of 3.1 or less[6] One third of patients require a second incision to achieve this level of posterior urethral reduction.

- Vesicostomy: When urethral size precludes safe valve ablation, a communicating channel between the bladder and lower abdominal wall (ie, vesicostomy) can be created to provide bladder drainage. Generally, an 18-20F stoma is created approximately midway between the pubis and umbilicus in the midline. Take care to bring the dome of the bladder to the skin and to limit the stomal size to prevent prolapse of bladder urothelium through the vesicostomy. However, formation of too small a stoma results in stomal

stenosis and inadequate bladder emptying. Too large a stoma allows for bladder prolapse. Vesicostomy use has decreased because most patients can be safely drained and can undergo valve ablation.

- Cutaneous ureterostomies: Bilateral cutaneous ureterostomies can also be placed to provide for urinary drainage. Techniques for cutaneous ureterostomy include end stomal ureterostomy, loop ureterostomy, Y-ureterostomy (in which the ureter is divided and one end is brought to the skin and the other is reanastomosed in a uretero-ureterostomy), and ring ureterostomy techniques. Potential complications of cutaneous ureterostomies include ureteral devascularization, inadequate drainage, and stomal stenosis. These are rare.

- Secondary bladder surgery
    - Augmentation cystoplasty
        - Indications for bladder augmentation include inadequately low bladder storage volumes and high bladder pressures despite anticholinergic medication and clean intermittent catheterization.

- The ileum is most commonly used; however, large bowel, stomach, and ureter are also used, depending on clinical conditions and surgeon preference.

- Before undertaking the augmentation procedure, the implications of bladder augmentation should be carefully reviewed with parent and family. Augmentation should only be offered to patients willing to commit to lifelong intermittent catheterization.

- Potential complications include bladder rupture (approximately 10% of patients); electrolyte disturbances, which may be worsened by the placement of intestinal mucosa in contact with urine, especially in those with a serum creatinine greater than 2 mg/dL; and mucus production, which can be a source of catheter blockage and may be a nidus for stone formation.

- The future risk of neoplasia has not yet been defined in these patients, but several cases of malignant degeneration in augmented bladder have been reported. Despite these risks, augmentation can significantly improve patient lifestyle in those who have intractable incontinence due to poor compliance and bladder

overactivity. By lowering intravesical pressures, the upper urinary tract may also be protected.

- Continent appendicovesicostomy: Also called the Mitrofanoff technique, this procedure involves placement of a nonrefluxing tubular conduit for catheterization between the bladder and skin to provide an alternative channel for catheterization. In children with PUVs, institution of intermittent catheterization through a sensate urethra can be difficult. In addition, some patients may have a very dilated proximal urethra which may not be easily catheterized. The stoma often can be hidden in the umbilicus to provide acceptable cosmesis. The appendix, ureter, and tubularized bowel can be used for formation of this channel.

Consultations

The child with PUV is best cared for using a team approach.

- Pediatrics and neonatology
    - The most life-threatening problem in the newborn period is the potential pulmonary hypoplasia related to in utero renal dysfunction. This may be associated with oligohydramnios. At birth, pneumothoraces may be present, thus complicating the pulmonary management.

- Upon birth, new metabolic demands are made on the infant kidneys.
- Urinary stasis and elevated detrusor pressures are risk factors for urosepsis in the newborn.
- Generally, treatment is coordinated best by establishing a primary pediatrician or pediatric service to coordinate further referrals.
- Additional pediatric subspecialty consultations often include a neonatal intensivist, a pediatric nephrologist, and a pediatric urologist.

- Radiology
  - Establishing the diagnosis is a priority in the newborn period.
  - Obtain VCUG with proper views of the posterior urethra.
  - Other required studies include a renal sonography and, at times, renal scintigraphy.

- Urology
  - In the newborn period, the first treatment intervention is achieving bladder drainage. Catheterization may be difficult or

even impossible because of the thickness of the valves or dilation of the posterior urethra with a hypertrophied bladder neck. Cystoscopic visualization with incision of the valves should be accomplished in the first few days of life once the child is metabolically stable.

- After the initial newborn period and successful bladder drainage, either by valve incision or vesicostomy, long-term urologic care is needed. Renal deterioration secondary to progressive bladder dysfunction should be a primary goal and requires follow-up care with serial renal ultrasonographic and bladder urodynamic studies. Management is based on clinical findings, ranging from annual imaging to pharmaceutical management to bladder reconstruction.

Diet

Dietary restrictions depend on renal status.

- Avoiding progression of renal deterioration while supporting growth requires careful regulation of protein intake, which is best managed under the care of a pediatric nephrologist.
- In the absence of renal insufficiency, no modification of diet is needed.

Activity

Unless complications such as renal insufficiency occur, activity can generally remain unrestricted. Urinary incontinence may present a social barrier. This can often be managed with anticholinergic therapy with or without clean intermittent catheterization.

Medication

Posterior urethral valves (PUVs) initially represent a surgical condition. However, long-term treatment often comprises a combination of medical and surgical treatment, primarily directed at the bladder. The primary medications involved in bladder management are anticholinergic medications used to improve bladder compliance. Other medications that may be needed include prophylactic antibiotics and medications for management of renal insufficiency.

Anticholinergic agents

These agents are used to improve bladder capacity and compliance in the patient with elevated detrusor pressures leading to hydronephrosis, UTI, or incontinence.

Oxybutynin chloride

Inexpensive and effective, oxybutynin chloride long has been the first-line anticholinergic. By inhibiting muscarinic action of acetylcholine on smooth muscle, exerts antispasmodic effect on bladder muscle. Its nonselective anticholinergic action increases adverse effects; however, it may produce fewer adverse effects if dosing is gradually increased over >2 wk. Available in both 5-mg tab and 5-mg/5-mL elixir. A long-acting 10-mg tab with once-a-day dosing was recently introduced but is expensive and has been approved only for adults.

Hyoscyamine sulfate

Works by inhibiting postganglionic cholinergic receptors on smooth muscle cells. Rapidly absorbed and distributed throughout body, including across blood-brain barrier. Half-life is 3.5 h; excreted unchanged in urine. Available in PO, IV, and SL forms; tab generally used for treatment of PUV. Time-release formulation available. Elixir and drops available.

Tolterodine

A new antimuscarinic drug with more selective receptor profile targeted for detrusor smooth muscle. Used extensively in adults but not approved by FDA for children. In adults, demonstrated equal in efficacy to oxybutynin chloride with significantly fewer adverse effects. Available in 1- and 2-mg tab.

Antibiotics

Patients with history of recurrent UTI may benefit from antibiotic prophylaxis, especially in the presence of vesicoureteral reflux. The ideal antibiotic for urinary prophylaxis is safe, effective, inexpensive, and has no adverse effects. Although no antimicrobial is ideal, some are preferred in children. Prophylactic dosage is usually one quarter of the therapeutic dose administered once per day. Too high a dose increases adverse effects (eg, GI upset) and may alter fecal flora. More appropriate antibiotics in children include trimethoprim (TMP), sulfamethoxazole (SMZ), nitrofurantoin, and amoxicillin.

Trimethoprim and sulfamethoxazole

Inhibits bacterial growth by inhibiting synthesis of dihydrofolic acid. TMP alone or in combination with SMZ is the most commonly used antibiotic for both treatment and prophylaxis of UTI. Inexpensive and has minimal adverse effects on bowel and vaginal flora because excreted and

concentrated in urine. Pediatric susp (40 mg TMP and 200 mg SMZ per 5 mL) available.

Nitrofurantoin

Synthetic nitrofuran that interferes with bacterial carbohydrate metabolism by inhibiting acetylcoenzyme A. Bacteriostatic at low concentrations (5-10 mcg/mL) and bactericidal at higher concentrations. Another common prophylactic antimicrobial agent, which is also excreted in urine, allowing urinary levels to be high while having few effects on fecal flora. Inexpensive and comes in both liquid and tab preparations. Rarely, associated with peripheral neuropathy and pulmonary hypersensitivity. SR formulation available; liquid susp (25 mg/5 mL) also available.

Amoxicillin

Interferes with synthesis of cell wall mucopeptides during active multiplication, resulting in bactericidal activity against susceptible bacteria. Used as prophylaxis in certain PO, GI, or genitourinary procedure.

REVIEW OF LITERATURE

Kukreja RA et al in Nadiad (Muljibhai Patel Urological Hospital) studies retrospectively about 70 children with PUV over last 10yrs. Factors found to be statistically significant with a P value < 0.05 were age at intervention >2 years, recurrent urospesis, B/L high grade VUR, bilateral parenchymal damage as seen on USG and nadir serum creatinine of > 0.8mg percent.

Oliveira Eduardo A et al in Bresil studied 22 children with PUV to identify the prognostic factors; Oligohydramnios (p=0.02), ventilatory support (p=0.01), Bilateral VUR(p=0.02), urea>40mg/dl were identified as adverse factors.

Lopez Pereira P et al espagne studied 40 patients with PUV in retrospective study and B/L VUR, Creatinine levels, renal echo genicity associated with poor prognosis.

R Lal et al in AIIMS studied the long term prognosis of renal function in PUV found to have raised creatinine value in 53% patients at presentation and 22.5% eventually progressed to CRF . persistent high creatinine, B/L VUR, persistent upper tract dilatation after treatment, voiding dysfunction and delayed presentation are predictors of poor renal function.

B Duel et al found that increased cortical echogenicity & loss of corticomedullary differentiation are associated with poor renal outcome.

Rittenberg MH et al studied the protective factors(‘’pop-off’’ mechanism)found 1)VURD syndrome, 2)bladder diverticula, 3) urinary ascites are associated with better preservation of renal function.

Parkhouse HF et al found that bad outcome is associated with early presentation, B/L VUR and day time incontinence after 5 years.

De Foor W et al found that increased nadir creatinine level & bladder dysfunction are independent risk factors for ESRD(OR 71&8.9).

Elisa Ylinen et al found high nadir serum creatinine level during 1st yr($p<0.001$), B/L VUR($p<0.05$) and breakthrough UTIs($p<0.05$) are associated with poor outcome. Also found that no significant difference in outcome between AN & post natal detection of PUV.

Vincent C. Onuora et al studied high serum creatinine level after catheter drainage is associated with poor renal function($p<0.0001$)

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STUDY JUSTIFICATION

PUV present with various clinical manifestations. This study review to identify the prognostic factors and help in defining the end result and implicating the correct treatment protocol.

AIM OF THE STUDY

To study the risk factors for chronic renal failure in children with posterior urethral valve in a tertiary care hospital.

MATERIALS AND METHODS

Study Design: Case Control Study.

Place of study: Institute of child health & hospital for children, egmore, Chennai - 08.

Study Population: children diagnosed to have PUV are included in this study.

CASES: PUV patients with Chronic Renal Failure

CONTROLS: PUV patients without CRF

Sample Size: 72 patients (Sep 2007- Sep 2009).

MANOEUVRE :

This study is conducted in nephrology and urology departments. All patients with PUV are studied by using proforma. Noted about antenatal oligohydramnios and ultrasonogram report. History suggestive of PUV like stream disturbances, dribbling, dysuria, straining are asked and noted.

Weight and height of the child was noted. Clinical findings like pallor, bony abnormalities(genu valgum), palpable bladder, renal masses and ascites noted. Blood pressure is measured in all cases. Nutritional status of the child was assessed and noted.

Age at diagnosis was noted and classified as whether it was detected antenatal, newborn, infancy or more than 1 year. Timing of surgery(relief of obstruction) was noted and classified as < 1 year or > 1 year. Surgery details like type of surgery, complications are noted. Urinary tract infections if any number of episodes in 1 year noted. Recurrent UTI was considered when there are 3 or more episodes.

Investigations hemoglobin, urine routine, urine C/S, urea, creatinine and electrolytes, USG abdomen, MCU and cystoscopy done for all cases and details noted.

OBSERVATIONS

Total No. of study patients with PUV. 72 Patients with chronic renal failure 43 (59.7%) Patients without chronic renal failure 29 (40.3%).

Among patients presenting with PUV fever (76.4%) and dysuria (63.9%) are the common presentation.

Among patient with PUV CRF 43 patients in (59.7%), & 29 patients without CRF (40.3%). All are boys.

Other common presentation include stream disturbances in 32 patients (44.4%) dribbling in 30 patients (41.7%), refusal of feeds in 11 (15.3%) & vomiting in 24 (33.3%).

Other less common presentation include abdominal distention in 5 patients (6.9%), constipation in 7 patients (9.7%), hematuria in 5 patients (6.9%) hesitancy in 4 (5.6%).

Age of presentation ranging from 2 days to 12 years with a mean age of 5.9 year.

Earlier age of presentation usually associated with stream disturbances and later age usually associated with urinary infection & incontinence.

Among clinical features, pallor was present in 48 patients (66.7%) with PUV hypertension was present in 26 patients (36.1%).

Palpable bladder was present in 11 patients (15.3%), bony abnormalities was present in 15 patients with PUV (20.8%).

PUV was diagnosed in various ages. In this study, antenatal diagnosis was in 6 patients (8.3%) New born 17 patients (23.6%), infancy 36 patients (50%) more than 1 year 13 patients (18.1%).

Table. 1

Age of Diagnosis	Frequency	Percentage
Antenatal	6	8.3
New Born	17	23.6
Infancy	36	50.0
> 1 year	13	18.1

Children presented with PUV various surgical modalities done to relieve the obstruction. Among 72 children 30 children had fulguration (41.7%), 31 children had Diversion & fulguration of valves (43.1%), 11 patients diversion only (15.3%).

Table. 2

Surgery	Frequency	Percent
Fulguration	30	41.7
Diversion & fulguration	31	43.1
Diversion	11	15.3

All 72 patients with PUV 7 children didn't have UTI (9.7%) 18 patients had one episode of UTI (25%) similarly 2 episodes in 27 patients (37.5), 3 episodes 13 patients (18.1%) 4 episodes in 5 patients (6.9%), 5 episodes in 2 patients (2.8%).

Table. 3

UTI No. of episodes	Frequency	Percentage
0	7	9.7
1	18	25
2	27	37.5
3	13	18.1
4	5	6.9
5	2	2.8

Among72 patients 35 patients (48.6%) had bilateral vesico ureteric reflux (VUR), 23 (31.9%) patients had No VUR & 14 patients (19.4%) had unilateral VUR either right or left.

Table. 4

VUR	Frequency	Percentage
No VUR	23	31.9
Unilateral	14	15.4
Bilateral	35	48.6

Risk factors for CRF

1. Antenatel abnormal USG findings

Table. 5

AN USG FINDINGS	CRF n (%)	No CRF n (%)
Abnormal	2 (4.7)	10 (13.9)
Normal	41 (95.3)	19 (65.5)

AN USG findings were abnormal in 4.7% of patients with CRF & 13.9% of patients without CRF. AN diagnosis was associated with poor outcome with significant p value ($p < 0.001$).

2. Age at diagnosis

Table. 6

Age at diagnosis	CRF n (%)	No CRF n (%)
< 1 yr	30 (69.8)	29 (100)
> 1 yr	13 (30.2)	0 (0)

Age at diagnosis more than 1 year with associated with poor renal outcome with significant p value ($p < 0.0001$).

Table. 7

3. Bilateral VUR

VUR	CRF n (%)	No CRF n (%)
Bilateral VUR	29 (67.4%)	6 (20.6)
No or Uniltateral	14 (32.6)	23 (79.3)

Bilateral vesico ureteric reflux was present in 29 patients (67.4%) was important risk factor for chronic renal failure with odds ratio of 8 with p value ($p < 0.0001$).

4. Recurrent UTI

Table. 8

UTI	CRF n (%)	No. CRF n (%)
Recurrent UTI	20 (46.5)	0
No	23 (53.5)	29

Recurrent UTI is present is 20 patients (46.5%) with CRF, none of the patients in control groups had recurrent UTI with p value (<0.0001).

5. Renal parenchymal damage by USG abdomen

Table. 9

Renal parenchymal damage	CRF n (%)	No. CRF n (%)
Present	37 (86)	8 (38)
Absent	6 (14)	21 (62)

Renal parenchymal damage was present in 37 patients (82.2%) with CRF 8 patients without CRF (17.8%) among 43 patients with CRF 37 patients had renal parenchymal damage by USG with p value ($p < 0.0001$) (OR = 16).

6. Persistence of dilated system after relief of obstruction

Table. 10

Persistence	CRF n (%)	No. CRF n (%)
Present	31 (72.1)	1 (3.4)
Absent	12 (27.9)	28 (96.6)

Persistence of upper tract dilatation after relief of obstruction was seen in 32 patients. Among 43 patients with CRF 31 had a persistent upper tract dilation (72.1%) with p value ($p < 0.0001$) (OR = 72).

7. Timing of relief of obstruction

Table. 11

Timing of Relief of obstruction	CRF n (%)	No CRF n (%)
> 1 yr	31 (72.1)	3 (10.3)
< 1 yr	12 (27.9)	26 (89.7)

Relief of obstruction after 1 year of age was associated with poor renal outcome. Among 72 patients, 34 patients had surgery after 1 year. Among 43 patients with CRF 31 patients (72.1%) had surgery after 1 year with p value ($p < 0.0001$) (OR= 22).

8. Absent “pop – off” Mechanism

Table. 12

Absent “pop – off” Mechanism	CRF n (%)	No CRF n (%)
Yes	43 (100)	28 (96.6)
No	0 (0)	1 (3.4)

Among 72 patients 1 patient had peri renal urinoma. “Pop off” mechanism was absent in all 43 patients with CRF ($p < 0.22$).

9. Hypertension

Table. 13

Hypertension	CRF n (%)	No CRF n (%)
Present	23 (53.5)	3 (10.3)
Absent	20 (46.5)	26 (89.7)

Hypertension was present 26 patients among 72 patients with PUV among CRF patients 23 had hypertension (53.5%) with p value of ($p < 0.001$) (OR = 10).

DISCUSSION

Patients with PUV there are several risk factors associated with chronic renal failure. Factors important are antenatal diagnosis, B/L VUR, Recurrent UTI, renal parenchymal damage seen in ultra sound, age at diagnosis > 1 year, persistent dilatation after relief of obstruction absence of “pop-off” mechanism and hypertension.

Antenatal USG diagnosis was associated with significant of CRF with p value < 0.001. A similar observation was already been made oliveira Eduaurdo A et al[13].

Bilateral vesicoureteric reflux (VUR) was significantly associated with CRF with p value <0.0001. Similar observation was already been made by oliveira Eduaurdo A et al, lopez Pereira P et al and kukreja et al[7,12,13].

Recurrent UTI was important risk factor for CRF was significant p value less than 0.0001. Similar observation was made by kukreja et al and Elisa Ylinen et al[8,12].

Renal parenchymal damage by USG Abdomen was associated with significant risk factor for CRF with p value < 0.0001. Similar observation was made by kukreja et al and lopez Pereira et al[7,12].

Persistent dilated system after surgery was associated with poor renal function with p value < 0.0001. Similar observation was made by kukreja et al & B Duel et al[12].

Absent "pop – off" mechanism was associated with rapid progression of renal failure with p value < 0.22. Similarly Rittenberg MH et al[11] observed the protective factors like (1) VURD syndrome (2) bladder diverticula (3) urinary ascites associated with better preservation of renal function.

In the present study Hypertension was one of the significant risk factor for CRF with p value < 0.0001. No similar study was found in literature.

CONCLUSION AND SUMMARY

PUV was the most common cause lower urinary tract obstruction and important cause of chronic renal failure in boys.

Degree of obstruction, especially early in course of life adversely affect the renal function.

B/L VUR, Recurrent UTI, Hypertension and renal parenchymal damage by USG have a significant association with poor renal outcome.

Absent pop- off mechanism, age at diagnosis > 1 year are also cause for poor outcome need further study.

ABBREVIATION

PUV	-	Posterior urethral valve
CRF	-	Chronic Renal failure
VUR	-	Vesico ureteric reflux
UTI	-	Urinary Tract Infection
VCUG	-	Voiding cysto urethrogram
USG	-	ultra sonogram

ANNEXURE

PROFORMA

PROFORMA

Name

Age

Clinical Presentations

Non-urological:

Abd Distension /Fever/Vomoting

Constipation/Failure to thrive / Refusal of feeds

Others.

Urological:

Stream Disturbances / retention / Dribbling

Dysuria / Incontinence / Hematuria

Polyuria / Hesitancy

Examination :

Height & Weight

Pallor

Blood Pressure

Abdominal Finding (Loin mass/palpablebladder/urinaryAscites)

Bony abnormalities

Time of Ist Diagnosis : Antenatal / Newborn / Infant

Time of starting Treatment : <1year of age / >1 year of age

Type of Treatment

Fulguration / Diversion procedure / Diversion →fulguration

Valve ablation / Reimplantation

Complications

Due to Disease	**Due to Treatment**
UTI	Dribbling
VUR	Retention
Uremia	Extravasation
Hypertension	Hematuria
Hydronephrosis	Incontinence
CRF	False passage
ESRD	Fistula

LAB PARAMETERS

Urine

- Albumim
- Sugar
- Deposits

Urine C/S

RFT – Sugar

- Urea
- Creatinine
- Electrolytes

Hemoglobin
USG Abdomen
VCUG
Cystoscopy
Others

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