OBSTRUCTIVE UROPATHY: CAUSES AND OUTCOME IN PEDIATRIC PATIENTS

Sahar Zaman Khan[1], Fraz Fahim[2], Khaula Mansoor[3]

ABSTRACT

Objective: *To pinpoint the major causes of obstructive uropathy in children and determine the outcome in terms of renal impairment and mortality.*

Methodology: *This observational study included pediatric patients presenting with obstructive kidney disease. All consecutive pediatric patients (< 12 years) presenting with signs and symptoms of obstructive uropathy ± chronic kidney disease (CKD) for the duration of 3 months or more represented by a GFR of < 52 ml/min/m^2 were included while patients with co-morbidities representing independent mortality risk like congenital heart diseases and with non-obstructive causes of renal failure and patients with no evidence of urinary tract obstruction on either ultra sonogram or renal scan were excluded. They were categorized into five segments and the outcome of the treatment at the end of follow up period of 2 years was recorded and categorized similarly to eliminate any bias.*

Results: *Forty three patients were recruited initially but 3 were excluded. The mean age was 5.3 years and there were 33 (82.5%) males. Majority had severe growth retardation. Posterior urethral valve (45%) and nephrolithiasis (35%) were commonest causes. The mean serum creatinine on admission was 6.35 (1.2–22) mg/d and at the end of follow up had reduced to 1.6 (0.4–3.2) mg/dl. (p= 0.0017). Post treatment 27 (67.5%) patients had no residual renal impairment while only 5 patients (12.5%) patients developed ESRD and were referred for transplant.*

Conclusion: *We conclude that obstructive uropathy is an important cause of preventable renal failure in children.*

Key Words*: Obstructive Uropathy, Renal Failure, End Stage Renal Disease, Pediatric Uropathy.*

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INTRODUCTION

Obstruction of the urinary tract can occur at any level from uretheral meatus to the calyceal infundibula. The term obstructive uropathy refers to the pathophysiolocial effects secondary to this obstruction leading to renal dysfunction[1]. It is a potentially lethal disease[1] and it represents a significant financial burden. As a major cause of end stage renal disease (ESRD) it accounts for 16.5% of all pediatric renal transplants in the United States[2]. Children comprise ~ 10% of all dialysis and transplant population and this costs a staggering $1.5 billion annually[2].

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The causes of this disease include congenital anatomic obstruction like posterior uretheral valves and ureteropelvic stenosis; as well as acquired causes such as to trauma, neoplasia, inflammation, calculi or surgical procedures. Most of these causes are correctible. Multipule treatment options are available ranging from temporary diversion by percutaneous nephrostomy, hemodialysis and sepsis control in case of infection to definitive surgical correction of obstruction. Hence, early definitive treatment of this correctable clinical entity is imperative. The morbidity adds up with time, ultimately leading to the death of the kidney and eventually the death of the patient[3]. If detected early enough, it may be entirely reversible, leaving no sequelae. But untreated, this disease leads to End Stage Renal Disease (ESRD)[4]. There has been a significant drop in infant mortality from obstructive uropathy in recent decades, attributable to prenatal diagnosis

with renal ultrasonography and coordinated surgical and medical care[5,6]. Hence there is a need to examine the reasons and assess the result of the treatment offered specially in a setting like ours.

The objectives of our study were to determine the major causes of obstructive uropathy in children and determine their outcome in terms of renal impairment and mortality.

METHODOLOGY

This was an observational study carried out at Pediatrics Department, Mayo Hospital, Lahore from March 2003 to February 2004. All consecutive pediatric patients (< 12 years) presenting with signs and symptoms of obstructive uropathy ± chronic kidney disease (CKD) for the duration of 3 months or more represented by a GFR of < 52 ml/min/m^2 were included in the study. Patients with co-morbidities representing independent mortality risk like congenital heart disease and with non-obstructive causes of renal failure and patients with no evidence of urinary tract obstruction on either ultra sonogram or renal scan were excluded from the study.

A thorough history and physical examination followed admission. The patients underwent a comprehensive protocol of investigations. These included complete blood count, ESR and urine complete examination. Renal function was assessed with serum creatinine, blood urea, serum electrolytes including calcium and phosphate. Ultrasonography and DTPA (Diethylene Triamine Penta Acetic Acid) Scan was used to assess differential renal function and scarring. Intravenous urogram (IVU) and voiding cystourethrography (VCUG) to rule out vesicoureteric reflux (VUR) were also done selectively. The treatment was then tailored according to the diagnosis. Management included percutaneous nephrostomy (PCN), emergency dialysis, sepsis control with antibiotics and finally surgery to relieve the obstruction, where required. The patients were divided according to pre defined criteria into five categories. (Table 1) They were as follows:

1. No renal impairment
2. Chronic Renal Insufficiency
3. Chronic Renal Failure
4. End-stage renal disease (ESRD)
5. Death

The outcome of the treatment at the end of follow up period 2 years was recorded. The parameters used to determine the status of the renal function were the same which were used to categorize the patients initially (Table 1). Hence any possible bias in determining improvement was removed. This data was then analyzed using SPSS 11.0.

RESULTS

Forty three patients were recruited initially but 3 were excluded because they did not complete treatment or could not be followed up leaving 40 patients. The mean age was 5.3 years (1 day to 11 years). Males 33 (82.5%) were in a clear preponderance. The mean duration of symptoms was 1.2 years. The clinical presentation by the order of frequency has been given in Table 2.

The growth parameters indicated a trend towards growth retardation. The mean weight at presentation was 14.25 kg (2.8 kg - 32 kg). The weight of 23 (57.5%) children fell within the 5th and 25th Centile, while 15 (37.5%) were less than 5th Centile. (Figure 1: Weight Distribution). The mean height was 93.3 cm (57 cm - 130 cm). Twenty two (56.25%) patients were below the 5th Centile. (Figure 2: Height Distribution) These parameters represent a failure to thrive associated with obstructive uropathy.

Posterior urethral valve in 18 (45%) patients and nephrolithiasis in 14 (35%) patients

Table 1:

	Symptoms	GFR*	Renal Scan	Electrolyte Imbalance
No Renal Impairment	Asymptomatic	Normal	Normal	Normal
Chronic Renal Insufficiency	Mild	25-50%	Decreased GFR	Mild electrolyte imbalance. Hypocalcemia Hyperphosphatemia
Chronic Renal Failure	Moderate Anemia± HTN	10-25%	± Scarring	Metabolic Acidosis Renal Osteodystrophy
ESRD	Severe Anemia± HTN	< 10%	± Scarring	Severe Metabolic Acidosis

*Glomerular Filtration Rate

Table 2: Clinical Presentation

S. No.	Presentation	N	Percentage
1	Failure to thrive	33	82.5
2	Abdominal / Flank Pain	29	72.5
3	Fever	23	57.5
4	Dysuria	19	47.5
5	Poor Urinary Stream / Retention	15	37.5
6	Vomitting	11	27.5
7	Hematuria	5	12.5

Figure 1: Weight Distribution

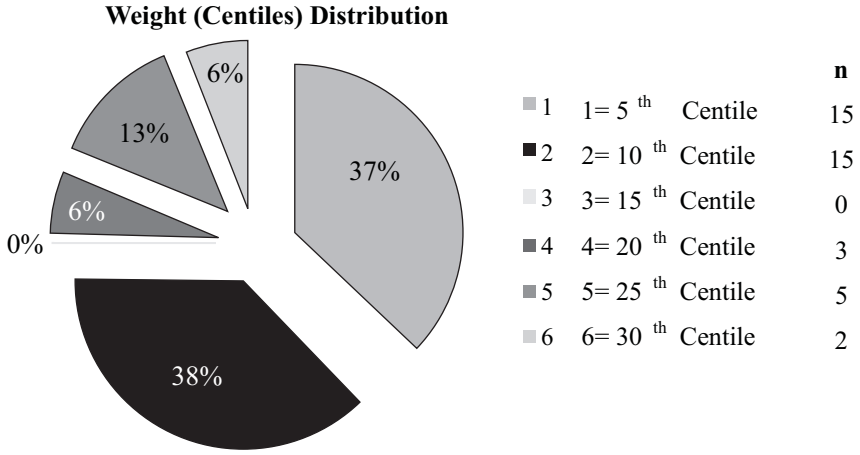
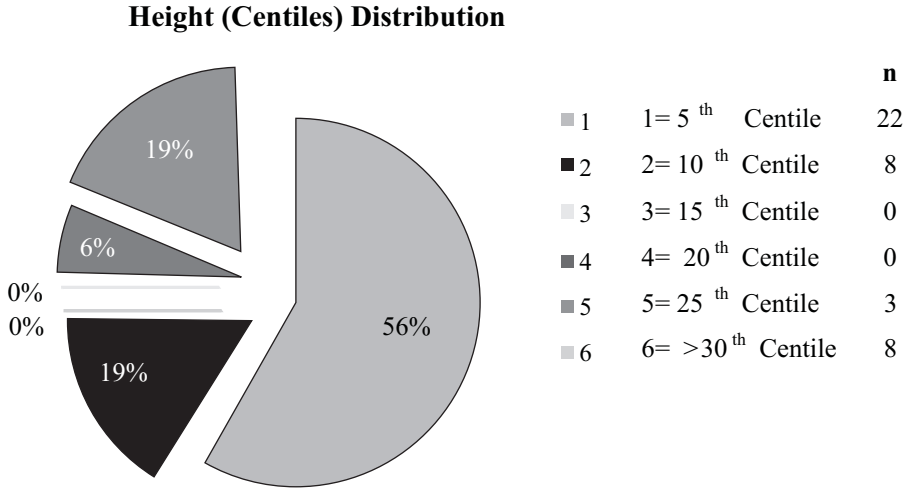


Figure 2: Height Distribution



were the most common causes of obstructive uropathy in our series. Other causes have been enumerated (Table 2: Etiology of Obstructive Uropathy).

The mean Hemoglobin of 8.3 G/dl reflected a tendency towards anemia. Thirty one (77.5%) patients had severe anemia, defined as Hb < 6 G/dl. Thirteen (32.5%) patients had evidence of urinary tract infection on urinalysis. Seven (17.5%) had bactriuria and pyuria but no elevation of white cell count.

Twenty one (52.5%) patients had urinary sepsis on admission and required antibiotics with or without urinary drainage. Hemodialysis was required in 17.5% of the patients. The definitive treatment offered to the patients has been detailed in Table 3.

The mean serum creatinine on admission was 6.35 (1.2 to 22) mg/d. At the end of follow up the mean value had reduced to 1.6 (0.4 to 3.2) mg/dl. Student's T test comparing the means of the pre and post treatment values gave p = 0.0017 showing the difference to be highly significant.

We were able to complete follow up of 2 years for 40 out of 43 patients. Two of the 3 patients who were excluded after being initially recruited left the hospital without a definitive diagnosis being established and 1 had posterior uretheral valve but could not complete the follow up. The outcome of the treatment revealed an encouraging trend (Figure 3: Outcome of Renal Status). Twenty seven (67.5%) of our patients left the hospital with good functioning kidneys and had no residual impairment of renal function on follow up. 5 patients (12.5%) had chronic renal

Table 3: Etiologyof Obstructive Uropathy

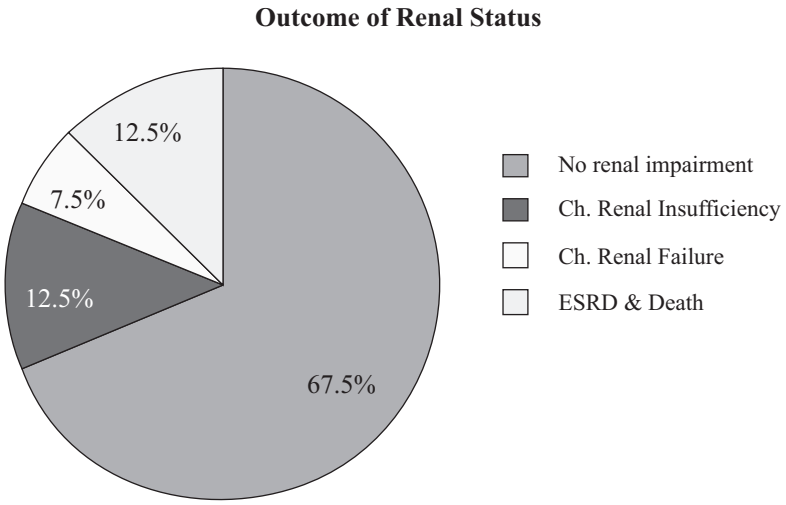
Cause	Number	Percentage
Post. Urethral Valve	18	45
Renal Stones	14	35
Bladder Neck Obstruction	3	7.5
Bladder Stone	3	7.5
Post-traumatic Stricture	2	5

Table 4: Treatment Offered

MEDICAL MANAGEMENT		
	n	
Antibiotics	15	
Antibiotics + Draingae	6	
Hemodialysis	7	
SURGICAL MANAGMENT		
	n	**Percentage**
Transuretheral Valve Ablation	18	45%
Open Nephrolithotomy	6	15%
ESWL*	5	12.5%
Percutaneous Nephrolithotomy	3	7.5%
Open Cystolithotomy	3	7.5%
Internal Uretherotomy	2	5%
Endoscopic Incision of Ureterocele	2	5%
Percutaneous Suprapubic Cystolitholapaxy	1	2.5%

* Extracorporeal Shock Wave Lithotripsy

Figure 3: Outcome of Renal Status



insufficiency. 3 patients (7.5%) had chronic renal failure while 5 patients (12.5%) patients developed ESRD and were referred for transplant.

DISCUSSION

Renal failure has tremendous implications regarding the quality as well as the duration of life. It imposes significant financial burden on the patient and the society. The commonest cause for renal failure in children is obstructive uropathy[7]. Obstructive uropathy accounted for 16.5% of all pediatric renal transplants in 1997 in United States. In the antenatal period as many as 1 in 100 fetuses show an abnormality of genitourinary tract ultrasonography[8]. Severe obstruction in the prenatal period can cause renal dysplasia; while post natal obstruction can cause dilatation of the upper urinary tract with changes ranging from minimal tubular changes to glomerular and interstitial fibrosis[9]. These changes may be partially or completely reversible at the initial stage and kidney function can be wholly restored if intervention is done early[1,9]. The significant role played by obstructive uropathy in the development of ESRD makes early and definitive treatment of this clinical entity imperative. Hence, conditions leading to obstructive uropathy need to be highlighted and studied in detail.

Obstructive Uropathy comprises 33 - 52% of the overall causes of chronic renal failure[10,11]. In our series the commonest cause was posterior urethral valve. This is in accordance with published literature[8] and commonly observed experience. 67.5% of our patients had posterior urethral valves and expectedly all were males. The second most common cause was renal stones, in 17.5% of our patients. Fortunately, both these causes are detectable by ultrasonic screening. However, they reach a symptomatic stage only when renal impairment is already advanced. And by then some irreversible damage to the kidneys has occurred. Hence, any suspicion of a condition leading to CRF needs screening for a possible cause. The focus therefore needs to be shifted to prevention rather than detection[4,12].

Preventive strategies need to be devised and effectively implemented. Prenatal ultrasound is the corner stone of early detection[5]. Emerging research for early detection include using elevated beta 2 microglobulin levels in fetal serum as a marker[13]. Amniotic alpha feto protein has also been found to correlate with prenatal obstructive uropathy[14]. Animal studies have indicated that intranatal urinary tract obstruction effects renal development by promoting fibrosis and mal-development which can be partially reversed by intranatal relief of obstruction[15] now made possible by the emerging field of fetal surgery[16]. Unfortunately, despite these advances we continue to see children with obstructive uropathy presenting with CRF or ESRD requiring renal replacement therapy[17].

Growth failure continues to be a significant obstacle affecting children with renal failure. Majority of our patients had significant growth retardation; their weight and height being below average. 87.5% had weight below 25th Centile. This finding has been reproduced in other studies as well[17,18]. Many of these patients

suffer from anorexia, sodium deficiency and acidosis[19,20]. Calcium metabolism disturbances secondary to prolonged obstructive uropathy have also been seen, especially in poorer social strata. It is postulated that these children may use energy less efficiently than healthy children, making their caloric needs higher than normal[19]. So the dietary intake in these patients should be increased and measures to correct the calcium metabolism should be taken to counteract the growth deficit.

The long term prognosis of children with early relief of obstructive uropathy has been scantily studied. More than two thirds of our patients completed the follow up with renal function tests within the normal range while a majority of the rest had significant reduction of serum creatinine. However workers have suggested that these patients may suffer a relentless progression to ESRD[9,21]. There may be a component of this disease as yet undiscovered; which could be controlled with better designed interventions. A variety of intrarenal factors have been discovered to lead to progressive interstitial fibrosis, including the newly described process of epithelial-mesenchymal transition, whereby tubular epithelial cells are transformed into activated fibroblasts. A number of endogenous antifibrotic counter-regulatory molecules have been identified, opening the possibility of enhancing the kidney's own defenses against progressive fibrosis[15].

CONCLUSION

We conclude that obstructive uropathy is an important cause of preventable renal failure in children. The need is to diagnose it early and treat it promptly if the renal function is to be saved. A good prognosis may be achieved in most patients. Aggressive nutritional strategies need to be adopted to counter the associated growth retardation. In addition the focus should be on prevention rather than treatment. And once detected no delay should be allowed in treatment. There is also need to repeat these studies on a wider scale to detect the true incidence in our population and the effectiveness of the strategies that we employ to combat it.

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None Declared

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CONTRIBUTORS

SZK, FF & KM conceived the idea, planned the study, did the data collection and analyzed the study. All the authors contributed significantly to the research that resulted in the submitted manuscript.