Paediatric pelvi-ureteric junction obstruction

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Introduction

Pelvi-ureteric junction obstruction (PUJO) is defined as an obstruction to the free flow of urine from the renal pelvis to the proximal ureter[1]. It is the most common cause of obstructive uropathy in the paediatric age group[1,2]. Majority with this condition will have a spontaneous resolution, but 20% will need some form of intervention due to progression of the obstruction or associated complications[3]. Intervention has evolved from traditional open surgery to minimally invasive procedures[3]. In this literature review we aim to present the aetio-pathogenesis, management and new developments with regard to this common paediatric condition.

Epidemiology, presentation, and aetio-pathogenesis

The incidence of neonatal hydronephrosis ranges from 1 in 1000 to 1 in 2000 pregnancies. Majority of them are transient (48%) or physiologic (15%) phenomena. PUJO is the commonest pathological cause and it accounts for 11% of all cases with neonatal hydronephrosis[4]. A 2:1 male preponderance has been noted for this condition and the left kidney is affected in 67% while 10-40% can have both kidneys being affected[2].

Incidentally detected dilated renal pelvis and proximal ureter on ultrasound scan (USS) is the commonest mode of presentation of PUJO at the present time. Advances in neonatal ultrasonography has increased the numbers of such cases detected[2,5]. Painless palpable abdominal mass, renal calculi, recurrent urinary infections, haematuria, abdominal pain and hypertension are the other possible presentations[1]. Intermittent abdominal pain coinciding with increased fluid intake and resolving

spontaneously with diuresis, eponymously known as Dietl crisis, was the most common presentation of this condition prior to advances in neonatal ultrasonography[6]. Infection in isolated PUJO is thought to be rare unless associated with concomitant reflux. High grade vesico-ureteric reflux can be associated with PUJO in up to 14%[4,7].

Theories on aetiology of PUJO can be broadly classified as intrinsic and extrinsic[2,4]. The pelvi-ureteric junction (PUJ) is initially formed as a solid structure which is re-canalized at around 10-12 weeks in utero. The intrinsic theory postulates that the obstruction is a result of defective recanalization of this region. This leads to a segment with abnormal peristalsis due to neuromuscular discontinuity. Another possibility is the presence of residual valve like structures which causes obstruction to free flow. Intrinsic obstruction is considered a functional obstruction and it is 'probe patent', i.e. a probe passed retrogradely will navigate the obstruction and reach the renal pelvis[8]. Lower pole vessels crossing in front of the PUJ causing narrowing or kinks, congenital abnormalities of the kidney such as horseshoe kidney or pelvic kidney and scarring of the PUJ region due to instrumentation or infection are some extrinsic causes that may lead to this condition[4]. Sometimes, intrinsic and extrinsic abnormalities may coexist[4]. In the study done by Braga *et al.* who compared antenatally detected cases of PUJO vs postnatally detected cases, intrinsic obstruction was the commonest cause for obstruction in the first group while extrinsic causes in the form of ureteric kinks predominated in the latter[9].

The obstruction to free flow of urine at the PUJ leads to pressure build up in the renal pelvis and as a response the renal pelvis and the proximal ureter dilate. With time this pressure reduces as a result of afferent arteriolar vasoconstriction, drop in renal blood flow and the glomerular filtration rate (GFR). Histologically there is tubular dilatation, glomerular sclerosis, inflammation and fibrosis not only in the affected kidney but in the opposite kidney as well. At a molecular level Angiotensin II plays a major role in renal vasoconstriction and producing the histological changes that are noted with PUJO[2,4].

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Workup

Ultrasound scan (USS) is the initial imaging modality used for evaluation of the urinary tract and it has obvious advantages such as availability and lack of radiation exposure but operator dependability and lack of functional information are the main disadvantages[10]. Most cases with antenatal hydronephrosis are diagnosed by ultrasound at 16-20 weeks of gestation. Twenty-eight weeks is considered the optimum time for performing ultrasound to detect fetal urological anomalies[11]. Measuring the anteroposterior diameter at the renal pelvis remains the most common diagnostic criterion used for diagnosing hydronephrosis and in the 3rd trimester it should be less than 7 mm. Society of Fetal Urology (SFU) grading of hydronephrosis (Table 1) is an alternative ultrasound based criterion for diagnosing and grading the severity of hydronephrosis[4,6]. Diagnosis of hydronephrosis *in utero* needs further sonographic evaluation to determine the laterality and the severity of the hydronephrosis, echogenicity of the kidneys, presence of hydroureter, status of the contralateral kidney and the bladder, gender of the fetus and the amniotic fluid volume[11].

Table 1: *Society of Fetal Urology grading of hydronephrosis*

Grade 1	No hydronephrosis
Grade 2	Only the renal pelvis visualized
Grade 3	Few but not all renal calyces visualized in addition to the renal pelvis
Grade 4	All calyces visualized
Grade 5	Similar appearance of the calyces as grade 3, but compared to the normal kidney, the involved kidney has parenchymal thinning

In the neonate whose hydronephrosis was diagnosed antenatally, USS should be repeated 48 hours after birth unless there are indications for an immediate postnatal scan such as bilateral hydronephrosis, hydronephrosis in a solitary kidney or oligohydramnios[11]. Otherwise, a gap of 48 hours is recommended to avoid a false negative scan as the newborn becomes relatively dehydrated during this initial period[2]. If the postnatal USS is negative for hydronephrosis, which will be the case in 21-28%, a repeat scan after 4-6 weeks is recommended[4,10].

Use of duplex ultrasound to differentiate obstructive and non-obstructive hydronephrosis, use of ultrasound elastography to determine the degree of hydronephrosis and use of 3D ultrasound to assess the kidney volume are some of the novel developments in ultrasound used in the evaluation of the hydronephrotic kidney[12]. A micturition cystouretherogram (MCUG) is indicated if alternative or coexisting pathology is suspected such as a posterior urethral valve or vesico-ureteric reflux[4,10].

Ultrasonically suspected PUJO needs further evaluation by Technetium 99m-diethylenetriamine pentaacetic acid (DTPA) or Technetium 99m-mercaptoacetyltriglyine (MAG3) diuretic renography to assess the function of the affected kidney and to confirm the obstruction to free flow of urine[10]. MAG3 is preferred over DTPA as it provides better information[13]. It is recommended to time the diuretic renogram 1-2 months after birth as the kidneys of the newborn tend to respond poorly to administered diuretics before this time[10]. Diuretic renography is not a perfect investigation and the study should be done under standard conditions with adequate hydration and urethral catheterization to minimize errors[2,11].

The typical obstructive pattern on a diuretic renogram shows normal uptake of the radioisotope but delayed or no excretion even after administration of frusemide[2,6]. When split renal function is calculated, a value of 40% or less in the affected kidney is considered significant[2,11]. Occasionally, a paradoxical increase in the split function of the hydronephrotic kidney is seen which is defined as a split function more than 55% in the presence of a normal bladder and a normal opposite kidney. Increase in the nephron mass or increase in renal blood flow as a response to the obstruction have been put forward as possible mechanisms leading to this observation[2].

Response to the administered diuretic and the split renal function are the traditional parameters evaluated by a diuretic renogram in an obstructed kidney but a novel parameter termed the Tissue Transit Time (TTT) that can be evaluated by the same study is claimed to have a better correlation with renal function. The TTT increases with the dropping GFR and with progression of histological changes associated with PUJO[14]. Magnetic resonance urography is an alternative to diuretic renography and it provides excellent anatomical and functional details. Lack of availability, need for sedation and the cost limit the use of this as a routine investigation but it may become the investigation of choice in the future[4,6]. Dynamic pressure flow studies (Whitaker test) with direct cannulation of the renal pelvis were used in the past for cases with equivocal results on radioisotope scans but it is not recommended at present in children due to its invasive nature and the need for anaesthesia[4,6].

Endoluminal ultrasound which uses a fine ultrasound probe within the ureter is used to delineate the anatomy around the pelvi-ureteric region and to determine the optimum site for placing the endopyelotomy incision[6].

Novel biomarkers
Urinary biomarkers that indicate renal injury such as β2-microglobulin, N-acetyl-β-D-glucosaminidase and certain growth factors (e.g. epidermal growth factor, platelet derived growth factor) that are excreted with urine have been used in the assessment of the kidney with PUJO, but these assays are not readily available and they are not in widespread use at present[2,4].

Management
Guidelines recommend management decisions to be based on serial investigations done under the same conditions at a single institution rather than on a single investigation[11]. The aims of intervention are to prevent deterioration of renal function and to alleviate symptoms[4]. All newborns with antenatally detected hydronephrosis should be started on antibiotic prophylaxis until vesico-ureteric reflux is excluded. Trimethoprim in a night dose of 1-2mg/kg or cephalexin in a night dose of 5mg/kg are recommended antibiotics[4].

As only a minority of these conditions will need intervention, watchful waiting as a management option seems reasonable and robust evidence supporting this policy was provided by the landmark study by Koff and colleagues. They conservatively followed up a group of neonates with unilateral hydronephrosis irrespective of the degree of renal pelvis dilatation or the split renal function. Only 7 out of 104 children ultimately required surgical intervention for deterioration of renal function which was defined as more than 10% drop in split renal function. Following intervention, the functions of the affected kidneys were restored back to their pre-deterioration values[15]. The conclusions of the authors were that PUJO in children was a relatively benign condition and watchful waiting was an appropriate strategy in the majority. They further stressed the fact that no investigation was able to predict accurately which kidneys will deteriorate and which will not; hence frequent re-evaluation with USS and renography was recommended to identify increase in hydronephrosis and deterioration of split function, respectively.

As a result of evidence supporting conservative management of this condition, currently the policy is neither aggressive observation nor prompt intervention[16]. Intervention is indicated for patients with symptoms, a split renal function of less than 40%, deterioration of split renal function by more than 10% on follow-up, increasing AP diameter, or

SFU grade 3 and 4 hydronephrosis[11]. Standard form of intervention is open Anderson-Hynes dismembered pyeloplasty[11], where the tissue at PUJ is resected and the ureter spatulated and re-anastomosed to the renal pelvis in a watertight manner. It has a success rate of over 95% in relieving the obstruction and symptoms. The anastomosis is usually bridged with a double J stent. In cases with extrinsic obstruction due to vessels crossing in front of the PUJ, this procedure transposes the PUJ away from the culprit vessels[6].

Clear guidelines for management of bilateral PUJO do not exist. In a study done by Kim et al, which included a group of children with SFU grade 3 and 4 hydronephrosis affecting bilateral kidneys, initial intervention was done for the kidney with the higher grade of hydronephrosis unless the grade was similar bilaterally, where they considered the kidney with the lowest split function to prioritize intervention. Following unilateral surgery, spontaneous improvement of the contralateral kidney was noted in some, so the authors recommended delayed pyeloplasty for the opposite kidney when both were affected by PUJO[17].

With the growing enthusiasm for minimally invasive surgery, pyeloplasty in children has progressed from traditional open surgery to laparoscopic and robot assisted procedures. In a meta-analysis done by Huang *et al*, where they compared open vs laparoscopic pyeloplasty in the paediatric age group, laparoscopy had similar outcomes with a shorter hospital stay and less complications but with more prolonged operative times. The conclusion of the author was that laparoscopic pyeloplasty for paediatric PUJO was feasible and safe especially when performed in high volume centres by experienced surgeons[18]. Enthusiasts claim that robot assisted pyeloplasty in children is even superior to laparoscopy as it allows better tissue handling and a precise anastomosis with a more efficient learning curve[19]. The main disadvantage of robot assisted procedures is the increased cost[11].

The question of whether to stent or not routinely following pyeloplasty is another area of controversy and a clear consensus does not exist[21,22]. Proposed advantages of using a stent are that it helps to maintain the alignment of the anastomosis and minimizes extravasation of urine caused by the transient obstruction to flow due to surgical oedema. However, stenting has its own complications such as increased infection rates, stent migration, strictures and prolonged hospital stay. Furthermore, a second general anaesthetic is required for removal of the stent[20,21].

Endo-urological management options for PUJO include balloon dilatation and endopyelotomy via a retrograde or an antegrade approach[2]. Endopyelotomy involves making a full thickness incision from within the ureter at the stenosed segment up to the peri-ureteric and peri-pelvic fat. The incision is bridged with a double J stent[6]. A long term success rate of 80% has been reported following this procedure, which is less compared to surgery[4]. However, a failed endopyelotomy does not preclude subsequent salvage surgery and it can be used as a 2nd line option after failed surgery as well[2,4]. It has been recommended as the procedure of choice when there are coexisting renal calculi that need to be treated and when the patient is unfit for a prolonged surgical procedure[6].

Follow-up

Following pyeloplasty (open or minimally invasive) an USS is obtained at 6 weeks post-operative or at 6 weeks after stent removal to confirm that the hydronephrosis is resolving. A diuretic renogram is done after 1 year, and if drainage is normal, the child can be discontinued from follow-up. There is a 5% risk of failure after surgery which will need re-intervention in the form of repeat surgery or endopyelotomy[4]. Data on follow-up protocols after endo-urological intervention are scarce but long term imaging up to 2-3 years post procedure has been suggested to detect re-stenosis[4].

If conservative management is pursued, a more frequent follow-up schedule is indicated. According to the Great Osmond Street protocol, after the initial USS and radioisotope studies, a MCUG (if it was not done before) and a repeat USS is done at 3 months of age. In those who fulfil the criteria for continuous conservative management, USS and renogram are repeated in 6 months, 1 year and annually thereafter up to 5 years of age. Repeated annual renograms are not done in those with improvement of hydronephrosis. USS and renograms were done at 7, 10 and 15 years of age for the purpose of long-term follow-up[22].

Conclusion

In paediatric PUJO, who needs intervention and when to intervene are questions that need clear-cut answers. Developments in urinary biomarkers that indicate renal injury and imaging modalities such as MR urography may provide better understanding on whom to intervene early and who needs long term follow-up. With accumulating experience on minimally invasive pyeloplasty, it may become the gold standard in the near future.

References

1. Sikandar AM, Sirajuddin S. Pelvi-ureteric junction obstruction in children. *Journal of Surgery Pakistan* 2008; **13**(4):163-6.

2. Lee H, Han SW. Uretero-pelvic junction obstruction: What we know and what we don't know. *Korean Journal of Urology* 2009; **50**(5): 423-31, https://doi.org/10.4111/kju.2009.50.5.423

3. Herndon CD, Kitchens DM. The management of uretero-pelvic junction obstruction presenting with prenatal hydronephrosis. *Scientific World Journal* 2009; **9**:400-3. https://doi.org/10.1100/tsw.2009.51 PMid: 19484161 PMCid: PMC5823226

4. Hashim H, Woodhouse CRJ. Uretero-pelvic junction obstruction. *European Urology Supplements* 2012; 11(2): 25–32. https://doi.org/10.1016/j.eursup.2012.01.004

5. Sharma G, Sharma A. Postnatal management of antenatally detected hydronephrosis. *World Journal of Clinical Urology* 2014; **3**(3): 283-94. https://doi.org/10.5410/wjcu.v3.i3.283

6. Chugh A, Agarwal PN, Singh R, Mishra A, Jain V, Meena M. Management of PUJ obstruction. *International Journal of Sciences and Applied Research* 2015; **2**(2); 22-31.

7. Pastore V, Aceto G, Niglio F, Basile A, Cocomazzi R, Faticato MG, et al. Clinical characteristics and management of children with uretero-pelvic junction obstruction and severe vesicoureteral reflux: preliminary results. *Annals of Pediatric Surgery* 2013; **9**:114–6. https://doi.org/10.1097/01.XPS.0000430523.83127.93

8. Alberti C. Congenital uretero-pelvic junction obstruction: physiopathology, decoupling of tout court pelvic dilatation-obstruction semantic connection, biomarkers to predict renal damage evolution. *European Review for Medical and Pharmacological Sciences* 2012; **16**(2):213-9. PMid: 22428472

9. Braga LH, Liard A, Bachy B, Mitrofanoff P. Uretero-pelvic junction obstruction in children: two variants of the same congenital anomaly? *International Brazilian Journal of Urology* 2003; **29**(6):528-34.
https://doi.org/10.1590/S16775538200300
0600010
PMid: 15748309

10. Yamaçake KG, Nguyen HT. Current management of antenatal hydronephrosis. *Pediatric Nephrology* 2013; **28**(2):237-43.
https://doi.org/10.1007/s00467-012-2240-7
PMid: 22836304

11. Tekgül S, Dogan HS, Hoebeke P, Kocvara R, Nijman JM, Radmayr C, et al. EAU guidelines on paediatric urology. European Association of Urology 2016.

12. Choi YH, Cheon JE, Kim WS, Kim IO. Ultrasonography of hydronephrosis in the newborn: a practical review. *Ultrasonography* 2016; **35**(3):198-211.
https://doi.org/10.14366/usg.15073
PMid: 27156562 PMCid: PMC4939717

13. Demirel BB, Balci TA, Tasdemir B, Koc ZP. Comparison of DTPA and MAG3 renal scintigraphies in terms of differential renal function based on DMSA renal scintigraphy. *Pakistan Journal of Medical Sciences* 2012; **28**(5):795-99.

14. Schlotmann A, Clorius JH, Rohrschneider WK, Clorius SN, Amelung F, Becker K. Diuretic renography in hydronephrosis: delayed tissue tracer transit accompanies both functional decline and tissue reorganization. *Journal of Nuclear Medicine* 2008; **49**(7):1196-203.
https://doi.org/10.2967/jnumed.107.04989
0
PMid: 18552148

15. Koff SA, Campbell KD. The non-operative management of unilateral neonatal hydronephrosis: natural history of poorly functioning kidneys. *Journal of Urology* 1994; **152**(2 Pt 2):593-5.
https://doi.org/10.1016/S00225347(17)32
658-7

16. Cheng HL. Surgical indications for unilateral neonatal hydronephrosis in considering uretero-pelvic junction obstruction. *Urological Science* 2004; **25**(2): 73-71.

17. Kim J, Hong S, Park CH, Park H, Kim KS. Management of severe bilateral uretero-pelvic junction obstruction in neonates with prenatally diagnosed bilateral hydronephrosis. *Korean Journal of Urology* 2010; **51**(9): 653–6.
https://doi.org/10.4111/kju.2010.51.9.653
PMid: 20856652 PMCid: PMC2941816

18. Huang Y, Wu Y, Shan W, Zeng L, Huang L. An updated meta-analysis of laparoscopic versus open pyeloplasty for uretero-pelvic junction obstruction in children. *International Journal of Clinical and Experimental Medicine* 2015; **8**(4):4922-31.
PMid: 26131065 PMCid: PMC4483847

19. Peters CA. Pediatric robot-assisted pyeloplasty. *Journal of Endourology* 2011; **25**(2):179-85.
https://doi.org/10.1089/end.2010.0597
PMid: 21241192

20. Laddha AK, Khare E, Lahoti BK, Mathur RK. A comparative study of outcome of pyeloplasty in stented and non-stented children with PUJ Obstruction. *Journal of Surgery and Anesthesia* 2018; **2**: 114.

21. Kočvara R, Sedlacek J, Drlık M, Dıte Z, Belacek J, Fiala V. Unstented laparoscopic pyeloplasty in young children (1-5 years old): A comparison with a repair using double-J stent or trans-anastomotic externalized stent. *Journal of Pediatric Urology* 2014; **10**: 1153-9.
https://doi.org/10.1016/j.jpurol.2014.04.01
7
PMid: 24957464

22. Dhillon HK. Prenatally diagnosed hydronephrosis: the Great Ormond Street experience. *British Journal of Urology* 1998; **81** Suppl. 2:39-44.
https://doi.org/10.1046/j.1464410X.1998.
0810s2039.x
PMid: 9602794