

Plasma rennin activity: Early indicator of renal injury in bilateral pelviureteric junction obstruction in children

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Abstract

Objective: The objective of the present study is to analyze the early indicators of renal injury in children with bilateral pelviureteric junction obstruction.

Materials and Methods: We investigated 23 children, 46 kidney units who were diagnosed with bilateral pelvi-ureteric junction obstruction (PUJO) and underwent unilateral or bilateral pyeloplasty between January 2001 and December 2011. Ipsilateral kidney biopsy was performed during pyeloplasty. Kidney biopsy results were divided into three categories. Pre-operative investigation included ultrasonography with the Society of Fetal Urology (SFU) grading, plasma rennin activity (PRA) and differential renal function (DRF).

Results: Out of 23 children there were 17 (73.9%) boys while 6 (26.1%) girls. Median age at operation was 35.4 months (range: 9-60 months). Unilateral pyeloplasty was performed in 14 (60.8%), simultaneous bilateral pyeloplasty in 2 (8.6%) and sequential bilateral pyeloplasty in 7 (30.4%).

Conclusion: In bilateral PUJO where DRF and SFU grading of hydronephrosis did not correctly reflect renal injury, PRA showed a significant relationship with renal histopathologic grade and could be an early indicator of renal injury in bilateral PUJO.

Key Words: Bilateral pelvi-ureteric junction obstruction, lumbotomy, plasma renin, pyeloplasty, renal histology

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INTRODUCTION

Pelvi-ureteric junction obstruction (PUJO) is the most common site of obstruction in the upper urinary system. The gold standard for managing PUJO in children is pyeloplasty. Severity of hydronephrosis on ultrasonography (USG) (society of fetal urology [SFU] Grading) and differential renal function (DRF) on renal scintigraphy have been identified as major factors determining pyeloplasty.^[1] The reported incidence of bilateral PUJO is 10-40%.^[2] Lots of controversy exists regarding

management protocol for bilateral PUJO when compared with unilateral PUJO where clear cut guidelines are available. Despite the fact that DRF could not be applied in bilateral PUJO because it might present as a normal DRF even when there is simultaneous bilateral renal function deterioration, the decrease of DRF and worsening hydronephrosis has been used as an indicator for the need of pyeloplasty in children with bilateral PUJO.^[3-5] In this study, we try to establish the role of plasma rennin activity (PRA) as an early biomarker for renal injury in children with bilateral PUJO and try to correlate the levels of PRA with histopathologic changes in the kidney.

MATERIALS AND METHODS

With the approval of the Institutional Ethical Committee, we performed a retrospective analysis of records of cases that underwent pyeloplasty for bilateral PUJO. Bilateral PUJO was defined as bilateral hydronephrosis with unilateral

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PUJO. Inclusion criteria children who underwent unilateral or bilateral pyeloplasty between January 2001 and December 2011 with a minimum follow-up period of 1 year. Exclusion criteria include the presence of vesicoureteric reflux, ureteric dilatation, duplex system, neurogenic bladder and infravesical obstruction. Indications for pyeloplasty included the worsening of hydronephrosis, symptomatic with urinary tract infection (UTI), pain and renal lump. Pre-operative investigations include baseline renal function test, USG (SFU Grading), renal dynamic scan (RDS) and PRA. The PRA was measured by radioimmunoassay using a commercially available kit. Increase in PRA was expressed as percent increase from the initial values. Normal laboratory PRA is 4-8 ng/ml/h at age: 1-12 months, 1-9 ng/ml/h at 1-3 years, 1-5 ng/ml/h at 3-6 years, 1.4-2.6 ng/ml/h at 6-15 years and less than 4.3 ng/ml/h at 15-18 years.

RDS was done using 99 technetium diethylenetriamine pentaacetic acid. The standard Anderson Hynes dismembered pyeloplasty was done in all cases by single experienced surgeon using lumbotomy approach.^[6] As per our standard protocol initially unilateral pyeloplasty was done in all cases followed by regular close follow-up using USG, and RDS. If the PRA level remain high even after unilateral pyeloplasty and child become symptomatic i.e. lump, UTI, surgical intervention was done on contralateral kidney as well. Renal histopathological analysis was performed in children with initial unilateral pyeloplasty or synchronous bilateral pyeloplasty. Renal biopsy was performed from the lower pole of the kidney under vision. Renal biopsy results were divided into four categories as described by Zhang *et al.*^[7] Grade of renal wedge biopsies was defined as Grade 1: No abnormality, Grade 2: Occasional glomerulosclerosis; otherwise unremarkable; minimal tubular atrophy, Grade 3: Great variation but with generally limited glomerulosclerosis; mild interstitial fibrosis and tubular atrophy, Grade 4: severe alterations including "dysplastic changes" over 20% glomerulosclerosis, extensive interstitial fibrosis and tubular atrophy, as well as extravasation of Tamm-Horsfall protein-like material.

Post-operative follow-up included USG, RDS and PRA at 3 months, 6 months and annually thereafter.

RESULTS

Out of 23 children there were 17 (73.9%) boys while 6 (26.1%) girls. Median age at operation was 35.4 months (range: 9-60 months). Unilateral pyeloplasty was performed in 14 (60.8%) simultaneous bilateral pyeloplasty in 2 (8.6%) and sequential bilateral pyeloplasty in 7 (30.4%). The median interval between operations was 6.3 months. Worsening hydronephrosis was the cause among the 7 children who

underwent bilateral pyeloplasty at a later stage. Pre-operative PRA, USG (SFU Grade) were performed at median 0.7 months before the operation. Details regarding preoperative PRA, USG (SFU Grade), RDS and Post-operative PRA, USG (SFU Grade), RDS and renal histology are shown in Tables 1 and 2 respectively.

DISCUSSION

Congenital UPJO constitutes a significant cause of morbidity in children and exists in a wide range of severity and clinical manifestations. It produces a variety of renal parenchymal changes which may, in part, reflect abnormal development. When untreated, it will impair nephron growth and function causing progressive renal deterioration.^[8] PUJO is commonly seen with a single system with the girls more affected than boys. These cases are now a day diagnosed prenatally. Incidence of bilateral PUJO varies from 10% to 40% with both synchronous and asynchronous occurrences.^[2] Management of cases with bilateral PUJO is totally different from unilateral PUJO because compensatory hypertrophy of the contralateral kidney is highly unpredictable.^[9,10] When diagnosed prenatally,

Table 1: Comparison of pre-operative and post-operative variables among groups according to histological grade after initial pyeloplasty

Variables	Histological			
	Grade 1 (n=12)	Grade 2 (n=6)	Grade 3 (n=3)	Grade 4 (n=2)
Gender (male/female)	10/2	4/2	2/1	1/1
Age (months)				
<24	4	1	1	-
>24	8	5	2	2
SFU grade				
3	7	4	2	1
4	5	2	1	1
Mean PRA (ng/l) (range)				
Pre-operative	12.7±2.7	14.3±2.7	15.9±2.1	18.1±2.6
Post-operative	3.6±1.20	4.1±2.4	4.8±2.4	5.3±2.3
DRF (%)				
Pre-operative	41.7	40.3	39.6	34.8
Post-operative	42.9	41.2	40.8	47.5

SFU: Society of fetal urology, PRA: Plasma rennin activity, DRF: Differential renal function

Table 2: Correlation of SFU, PRA, and DRF with the need for pyeloplasty contra lateral kidney

Variables	Contralateral kidney (n=23)	
	Improved (n=14)	Pyeloplasty (n=9)
SFU grade		
3	11	3
4	3	6
PRA (ng/ml)		
Pr-operative	6.4±1.6	7.3±1.6
Post-operative	-	4.4±1.2
DRF (%)		
Pre-operative	51.4	57.9
Post-operative	-	31.2

SFU: Society of fetal urology, PRA: Plasma rennin activity, DRF: Differential renal function

bilateral PUJO has been recommended to be re-evaluated promptly after birth as compared to unilateral PUJO.^[5] Recently, the focus has been to identify the biomarkers for predictors of early renal injury. Epidermal growth factor, monocyte chemotactic protein-1, β 2-microglobulin, and carbohydrate antigen 19-9 are shown to be a promising marker for chronic obstructive disorders of the kidney.^[11,12] At present, there is a lot of confusion regarding which site to be operated first, timing of surgery and the indications for surgery in cases of bilateral PUJO. Provet and Hanna has recommended early surgical correction with synchronous bilateral PUJO.^[13] In a study by Kim *et al.* performed early unilateral pyeloplasty without initial conservative management in all cases with bilateral PUJO.^[14] Our protocol is conservative management with close follow-up and operate on the side with lower differential function first. Largely the Confusion exists due to the lack of proper information about the degree of insult to the renal parenchyma and lack of definitive pointers of early renal insult in cases of bilateral PUJO. In our study, preoperative PRA level was related to renal histopathological changes as shown in the table. The risk of contralateral kidney requiring pyeloplasty has been studied by Kim *et al.* who performed 8 (61.5%) additional contralateral pyeloplasty after 13 unilateral pyeloplasty. They concluded that the severity of hydronephrosis in the contralateral kidney is related to future needs for delayed operation.^[14] The role of PRA level as an early marker of renal injury in unilateral PUJO is well-established.^[15] To the best of our knowledge, this is the first study assessing the predictive factors by analysis of renal histopathological changes and correlating it with PRA in bilateral PUJO. However, there are certain limitations to this study. Being retrospective in nature is one of them other limitations include lack of the standardization classification in renal histopathologic changes in obstructive kidney disease, small sample size.

CONCLUSION

Estimation of PRA levels is more reliable and early predictor of renal injury in cases of bilateral PUJO were DRF and SFG has limited role to play, therefore should be considered as gold

standard as far as assessment regarding the need for pyeloplasty is concerned.

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