

Correlation between Renal Histopathology and Differential Renal Function in Unilateral Congenital Ureteropelvic Junction Obstruction in Children

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ABSTRACT:

Congenital ureteropelvic junction (UPJ) obstruction is the commonest cause of paediatric hydronephrosis. This study was done to define the relationship of renal histopathological changes with differential renal function (DRF) and outcome of pyeloplasty in a group of patients undergoing primary pyeloplasty for UPJ obstruction. A total of 16 consecutive patients with unilateral UPJ obstruction underwent renal biopsy at the time of pyeloplasty. Patient's age ranges from 30 days to 11 years with a mean (\pm SD) of 4.94 ± 4.27 years. Renal histopathological changes were graded into three groups according to the severity. In this study 43.75% patients were in Grade-I, 43.75% in Grade-II and 12.5% patients were in Grade-III. Histopathological findings were abnormal in 56.25% patients and normal in 43.75% patients. Most of the kidneys showed post-operative improvement of DRF except one, on follow-up renal scan after 6 months. In patients of grade-I complete functional recovery was observed post-operatively after six months. In the other two grades functional recovery was more in terms of percent change but complete functional recovery in such patients was not seen. Dysplastic kidneys also showed improvement in post-operative renal function, that indicates the efficiency of pyeloplasty in an obstructed kidney. Patients of unilateral UPJ obstruction with a pre-operative DRF less than 35% have a high probability of severe histopathological changes and a low probability of full functional recovery. This study shows that histopathologically normal kidneys have a higher DRF than dysplastic (abnormal) kidneys and complete recovery of renal function is expected in these patients after pyeloplasty. In conclusion, differential renal function on diuretic renography correlated positively with histopathological grading. Pyeloplasty improves general wellbeing and growth of the children.

Keywords: Congenital ureteropelvic junction obstruction, pyeloplasty, differential renal function

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INTRODUCTION:

Congenital ureteropelvic junction (UPJ) obstruction is by far the most common cause of paediatric hydronephrosis with an incidence of about 1 in 1200 live births.¹ Narrowing or persistent obstruction at this junction reduces the flow of urine from kidney and produces retrograde changes in proximal tract which actually threatens the function of kidney. In most cases a congenital intrinsic lesion is responsible for ureteropelvic junction obstruction. Upward transmission of ureteral pressure in an obstructed kidney affects tubular pressure, tubular function, renal blood flow (RBF) and glomerular filtration (GFR).²

Parenchymal damage by ureteropelvic junction obstruction has been well documented by histological changes which are more severe in cases when differential function is less than 35%.^{3,4} Significant urinary obstruction invariably results in tubular dilatation, glomerulosclerosis (glomerulus reduces), inflammation or glomerular hyalinization, cortical cysts and interstitial inflammation with mononuclear cell infiltrate, peritubular fibrosis and tubular atrophy.⁵

Although not absolute, a good correlation may exist between the severity of these histopathologic changes and the function remaining in the affected kidneys.⁶ After reaching the diagnosis of ureteropelvic junction obstruction, it is the differential renal function of the individual kidney which is the most useful information obtained during renography.⁷ Normal function of renal unit is assumed if it exhibits

more than 40% of the total uptake on DTPA renography. Moderately reduced function is defined as 10-40% of the total uptake. Severely reduced function is defined as less than 10% of the total uptake.⁸ An important question that needs to be answered in large number of children is the potential recoverability of the renal function.

In an asymptomatic infant or child, the decision to recommend pyeloplasty is usually based on interpretation of renal scan.⁶ Split renal function by DTPA is an important investigation which helps in planning the management and follow up of hydronephrotic patient.

The aim of this study is to evaluate the relationship between differential radionuclide renography with renal histological changes secondary to UPJ obstruction in infant and children. This current study is an attempt to correlate between the diuretic DTPA renography and the renal cortical histological changes in unilateral congenital UPJO considering opposite kidney functioning is normal.

METHODS AND MATERIALS:

This is a prospective observational study carried out in the Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January 2004 to April 2006. A total of 16 (Sixteen) cases were enrolled purposively between the ages 0-15 years of both sexes with only unilateral hydronephrosis due to congenital

UPJ obstruction. Patient with bilateral hydronephrosis or patient with unilateral hydronephrosis due to other causes or non-complying patients were excluded from the study.

All the selected patients preoperatively undergone radioisotope renogram, using ^{99m}Tc, DTPA, in the Institute of Nuclear Medicine in BSMMU. Renal biopsy was taken from renal cortical tissue of affected kidney during A-H pyeloplasty and histological examinations were done in Histopathology Department of BSMMU. Tissues were fixed, processed and stained with Mayer's Hematoxylin and Eosin staining as per standard procedure.

Functional status of the kidney was assessed by split renal function and other related investigation was done to evaluate and assess the renal functional and morphological status.

Renal function: In our study renal function is expressed as differential renal function (DRF)–the relative function of each kidney is expressed as a percentage of the sum of the right and left kidneys. Usual normal values of DRF are between 45%-55% of uptake of DTPA in renography.

Grading of renal biopsies: This study also attempts to establish a grading system for the evaluation of outcome of pyeloplasty in UPJO. Histopathological findings were correlated between basal and 2 months differential renal function after pyeloplasty. There was not any established grading system of histopathology in standard text books. So we tried to set up a new grading

scale on renal biopsy by focusing on changes in glomerulus and tubules. We divided it into 3 grades according to the findings in histopathology.

Histological findings are graded as follows:

Grade I: Mild obstructive uropathy, 3 subcategories-

Gr. IA : Normal glomerulus with number and morphology per power field (PF).

Gr. IB : Normal number of glomerulus with or without sclerosis or tubular atrophy

Gr. IC : Normal number of glomerulus with sclerosis and tubular atrophy.

Grade II: Moderate to severe degree of obstructive uropathy- above changes with significant loss of glomerulus per field. 3 Subcategories-

By number of glomerulus per power field. (Range 5-8 glomerulus/PF)

Gr. II A : 7-8 glomerulus/ PF

Gr. II B : 5-6 Glomerulus/ PF

Gr. II C : <5 glomerulus/ PF

Grade III: Less than 4 glomerulus/ PF.

Here 70% or more than 70% loss of glomerulus. Average number of glomerulus per field is 10 (8-12/PF) in normal kidney.⁴

Preoperative Assessment: The patients were selected after detailed clinical history physical examination and laboratory imaging investigations. All information obtained was recorded in a predesigned data entry form. Blood count, urea, serum creatinine, electrolytes, urine R/E, chest x-ray, ultrasonography of urinary system, intravenous urogram (IVU) and DTPA renogram with split renal function were seen for the study in each patient.

Operative Management: All patients included in this study had undergone non-stented pyeloplasty through the standard anterolateral, below the 12th rib, skin crease incision. Kidney was approached extra-peritoneally by cutting and splitting different layers of abdomen. The kidney was mobilized and all steps of Anderson-Hynes pyeloplasty were completed. A perinephric drain was kept near the anastomosis.

Follow up evaluation: Each patient was followed up once after one month or more frequently if any complication arises. During follow up each patient was looked for. 1. Urine RME and C/S if UTI was suspected. 2. Blood urea and serum creatinine, if these were high preoperatively. 3. Ultrasonography (after one month). 4. DTPA renogram with split function to see the post operative differential renal function (after 2 months).

Statistical Analysis: The data were collected in a predesigned questionnaire and analyzed by Statistical Package for Social Science (SPSS-18) for Windows software to arrive at a definite conclusion according to the objectives of the study.

RESULTS:

Mean age of the patients was 4.94±4.27 years with a range of 30 days to 11 years. Among the 16 patients, seventy five percent were male and only 25% were female. In 56.3% cases had left sided hydronephrosis and 44.7% cases had right sided hydronephrosis due to UPJO. Most common presenting feature was abdominal mass (81.3%) and recurrent urinary tract infection was the second most common (56.3%) feature. Histopathological grading of hydronephrosis in UPJO is summarized in Table-I.

Table-I: Distribution of the patients by histopathological grade,

Histological grade	Frequency	Percent (%)
Grade - I	7	43.75
Grade - II	7	43.75
Grade - III	2	12.5
Total	16	100.0

A generalized trend of higher renal function is evident in post-operative differential renal function in comparison to pre-operative renal function in 15 patients (Table-II). However only one patient showed decrease in post-operative differential renal function.

Table-II: Comparison between pre and post-operative renal function

Patient no.	Pre-operative DRF	Post-operative DRF	Change (%)
1.	30%	27%	-3
2.	41%	42%	1
3.	44%	47%	3
4.	40%	44%	4
5.	35%	41%	6
6.	5%	20%	15
7.	17%	25%	8
8.	10%	18%	8
9.	5%	17%	12
10.	10%	20%	10
11.	24%	35%	11
12.	5%	20%	15
13.	20%	32%	12
14.	34%	49%	15
15.	3%	15%	12
16.	3%	10%	7

DRF: Differential renal function

Multivariate analysis of changes in renal function in different histological grade of hydronephrosis was also evident. Change in renal function is determined by subtracting the pre-operative renal function from post-operative renal function and the attribute is named as 'change' (Table-III). Mean differential renal functional change was more than 10% in Grade II histopathological patients. The attribute change is entered in the multivariate model as dependent variable. As predictors of histological grade, age and sex were entered simultaneously to find out the relation of changes in renal function with histopathological status of the hydronephrosis controlling for the effect of

age and sex as possible confounder.

Table-III: Change in renal function in relation to histopathological grade

Histopathological grade	N=16	Mean \pm SD
Grade - I	7	5.29 \pm 5.09
Grade - II	7	11.86 \pm 2.55
Grade - III	2	9.50 \pm 3.54
Total	16	8.69 \pm 4.90

Mean DRF is more than 10% found in Grade II patients

Multivariate analysis (Linear regression) reveals an overall statistically significant association between histopathological grade and changes in renal function. After adjusting for age and sex, histopathological grade was found to be a significant determinant of post-operative renal function changes in the model (Table-IV). None of the age or sex was found to exert a significant effect on changes in renal function.

Table-IV: Multivariate model for change in renal function

Sl. No.	Model	't' value	P value
1.	Histological grade	2.239	0.045
2.	Sex of patient	-0.986	0.344
3.	Age of patient	-0.374	0.715

Dependent Variable: Change

Predictors (Constant): Histopathological grade, age and sex of individual

The change in renal function was further looked into through paired comparison of pre and post-operative renal function in all three grades. Due to the small sample size a parametric paired comparison of renal functions could not be done. Hence Wilcoxon test, non-parametric counter part of paired 't' test, was applied to investigate the difference in DRF. Mean post-operative DRF (35%) in Grade I is found to be

significantly higher than the mean pre-operative DRF (30.3%) (P<0.05). In Grade II also mean post-operative DRF (27.3%) is found to be significantly higher than the mean pre-operative DRF (15.4%) (P<0.05) (Table-V).

In Grade III although pre-operative and post-operative means seem apparently different, statistical test failed to reveal any significant difference. Suboptimal number of subjects in Grade III might result the non-association. (Table-V)

Table-V: Comparison of pre and post-operative DRF among the three histological grades

Histological grade	N	Pre-operative Mean DRF	Post-operative Mean DRF	Wilcoxon # Paired test
Grade - I	7	30.30 %	35%	P 0.049 #
Grade - II	7	15.4 %	27.3%	P 0.016 #
Grade - III	2	3%	12.5%	P 0.180
Total	16	48.7%	64.8%	

Wilcoxon test considered to be significant at P <0 .05

DRF- Differential renal function

DISCUSSION: The histopathological changes of the UPJ and renal pelvis in patients with UPJO have been well categorized. However, the histopathological changes in kidneys at the time of pyeloplasty have not been well categorized in unilateral UPJO.

To evaluate the relationship between DRF, as an outcome of pyeloplasty, renal cortical biopsy for histopathology were done in a

series of children undergoing primary pyeloplasty. Histopathological findings were categorized into three groups according to the severity of the findings for evaluation of the results. This grading of histopathological changes may be a useful tool that can provide an objective method of evaluating the severity of damage due to obstruction or due to dysplasia of kidney.

In this study nearly half of the patients had normal and over a half had abnormal histopathological findings. Although 7 patients had normal histopathology designated as Grade-I change, 1 had pre-operative differential renal function below 35%. All of these patients except one had full recovery within six months after drainage was established. This reflects that with such normal or Grade- I changes complete recovery may be a rule.

As all such patients, had deterioration of DRF not <35%, it can be proposed that deterioration of renal function to such extent may indirectly indicate no or minimal histopathological changes in the affected kidneys and therefore also indicate a cut off DRF that may predict full recovery.

This study also showed that patients with abnormal histopathology undergo post-operative improvement of DRF as seen in post-operative renogram. Patients with Grade- II histopathological changes showed improvement in DRF over 10% at six months follow-up. But none of these patients showed full recovery of renal function. This indicates that the decreased renal function in such patients with UPJO is not only due to retrograde changes, as a result of the obstruction and that structural damages are also responsible. On the other hand patients with Grade- III changes in histopathology had very poor pre-operative renal function (<10%). Though the reconstructions are technically successful, the chances of full functional recovery in these patients are not possible due to the

severe histopathological changes in renal parenchyma.

This study also showed an overall positive relationship between the Grade-I and Grade- II histopathological changes with the state of pre and post-operative DRF when considered separately and also with improvement of renal function as a whole. Such correlation is not seen with Grade-III histopathological changes. Erbagci et al conducted a study on 35 patients with unilateral UPJO in children.⁹ They graded the histopathological findings according to severity of changes into I to V groups, such as: Grade-I: normal; Grade-II : mild obstructive uropathy as indicated by mild glomerular changes limited to dilated Bowman's capsule, minimal patchy interstitial fibrosis and chronic inflammation to renal cortex; Grade-III: moderate obstructive uropathy, showing changes described under Grade-II with glomerular changes, including global sclerosis, segmental sclerosis or dysplastic glomeruli affecting up to 25% of the glomeruli, cortical thinning, moderate patchy interstitial fibrosis and inflammation; Grade-IV: Severe obstructive uropathy as shown by changes seen in Grade-III with marked segmental or regional sclerosis and dysplastic glomeruli and absence of glomerular cyst with more than 25% of affected glomeruli; Grade-V: included changes as in grade-IV with multiple micro cyst beneath the renal capsule. They compared them with basal as well as with post-operative DRF at six months and at one year. In our study group Grade-IV and Grade-V described by Erbagci

et al. were included in grade-III changes. Unlike this study they did not taken into consideration the number of glomeruli in a low power field. They had also found significant change in renal function after six months as well as showed positive correlation between the severity of histopathological changes and DRF activity in all grades of changes pre and post-operatively. They also found a change of at least Grade-III in histopathology in patients with less than 40% DRF activity pre-operatively.⁹

In another study by Stock et al. renal histopathology was correlated with pre- and post-operative DRF in 17 consecutive patients and they however found no correlation between DRF and histopathological changes.¹⁰ They did not ascribe the histopathological changes to any grading and simply divided the changes into normal and abnormal category. They also did not observe any post-operative improvement of renal function. On the contrary, our study have showed improvement of renal function in all grades except one patient and there by indicate the efficiency of pyeloplasty as a standard procedure for drainage operation.

Elder studied 55 patients of UPJO and graded the histopathological changes same as described by Erbagci et al. above.^{6,9} They correlated the histopathology with pre-operative renal function. In their study differential function on diuretic renography correlated with histopathological grades. Histopathologically normal kidneys had a higher DRF. They also found patients with

DRF 40% or greater had a Grade-I or Grade-II change in histopathology.

Results of our study therefore suggest that renal biopsy for histopathological examination at the time of pyeloplasty may be a useful tool in predicting outcome of pyeloplasty. It has identified pre-operative DRF as a statistically significant predictor of improvement of renal function in patient with unilateral UPJO. With all grades of histopathological changes, pre-operative renal function as assessed by DRF, also indirectly indicates severity of histopathological changes.

Patients with unilateral UPJO and with a pre-operative DRF less than 35% have a high probability of severe histopathological changes and low probability of post-operative full functional recovery. Histopathologically normal kidneys have a higher DRF than dysplastic (abnormal) kidneys and complete recovery of renal function is expected in the former.

CONCLUSION: In our study differential renal function on diuretic renography was correlated positively with histopathological grading. Histologically normal kidneys had a higher differential renal function than dysplastic (abnormal) kidneys. There is a good recoverability of renal function even in less than 10% differential renal function and rapid wash out of radioisotope in DTPA renogram after intervention. Pyeloplasty improves general wellbeing and growth of the children. There is small percent (21%) disparity in post-operative differential renal function and histological grade in UPJO may

be due to erroneous differential renal function by DTPA or unexplained.

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