

ORIGINAL RESEARCH

Study of Association of Vesico Ureteric Reflux in Patients with Anorectal Malformations

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ABSTRACT

Background: To evaluate association of Vesico Ureteric Reflux in patients with anorectal malformations.

Materials and Methods: Retrospective and Prospective study. All neonates who were admitted with Anorectal malformation during the study period. The study period was for two years from January 2019 to December 2020.

Results: Vesicoureteral reflux (VUR) is the most common associated urinary tract anomalies with imperforate anus with an incidence of 25% - 60%. VUR is more common in males. More common in babies born at Term gestation. The most common type of ARA (Krickbeck) that is associated with VUR is Rectovesical fistula. Unilateral VUR is more common. Grade 2 VUR is more common in unilateral, Grade 3 VUR is more common in Bilateral cases. Most of the cases were conservatively managed-19 cases, surgical intervention was done in 11 patients. Bilateral Ureteric reimplantation was done in 3 cases. Unilateral Ureteric reimplantation in 8 cases, Right side -4 cases, Left side -4 cases. Conservative management in 63%. Resolution (partial+complete) was seen in 21 Renal units.

Conclusion: VUR is common in patients with ARM. Children with an abnormal R-USS are at increased risk of UTI. Performing routine MCUG does not reduce the risk of UTI in children with ARM.

Keywords: Vesico Ureteric Reflux, ARM, Unilateral Ureteric reimplantation, renal anomalies.

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INTRODUCTION

Anorectal malformations present with an incidence of 2.0 to 2.5 per 10,000 live births¹. The low anorectal malformation lesions may be managed by single stage surgical correction, but the complicated or high lesions need to be managed with multi staged operations. These surgical reconstructive procedures are associated with morbidity and mortality. The associated VACTERL (vertebral, anorectal, cardiac, tracheoesophageal, renal, and limb) anomalies if present, further add to the existing morbidity and mortality, associated with surgical reconstruction.

Of these VACTERL anomalies, Anorectal malformations (ARMs) have a high incidence of associated genitourinary (GU) anomalies, ranging from 26% to 50%.^[1,2] This significant association has led to routine diagnostic imaging to determine the presence of renal anomalies and vesicoureteral reflux (VUR). VUR has been reported in 20%–47% of children

with ARMs.^[3] VUR may cause renal damage if not diagnosed early in age, leading to chronic renal failure. Early diagnosis of VUR in neonatal period is essential in preventing future complications.

In this study done at Niloufer hospital, Hyderabad between January 2019 and December 2020, all the neonates who presented to us with Anorectal Malformation were evaluated. Age at presentation, gestational age, weight at presentation were documented. All the babies admitted with this anomaly were stabilized by intravenous fluid and intravenous antibiotics in the surgical intensive care unit. After stabilization child was evaluated with Xray chest, Xray abdomen, Xray LS spine, CTPL Xray and Classified according to Krickbeck. Primary surgery was tailored according to the type of ARM.

Post operatively baby was evaluated for VACTERL anomalies with USG Spine, USG KUB, 2D Echo. All the babies with Renal anomalies were segregated and included in this study. After chemoprophylaxis, MCUG was done only in those babies who had renal anomaly on USG KUB. Those cases with VUR that were picked up by MCUG were included in this study and followed upon to check resolution rate after the definitive procedure for ARM.

Aims and Objectives

Aim of the Study

To evaluate association of Vesico Ureteric Reflux in patients with anorectal malformations.

Objectives of the Study

- 1) To evaluate Incidence of VUR in ARM.
- 2) To evaluate the Grades of VUR in relation to the type of anorectal malformations.
- 3) To evaluate Persistence of reflux after correction of Anorectal anomaly.

MATERIALS & METHODS

Materials:

1. **Study design:** Retrospective and Prospective study
2. **Sample size:** All neonates who were admitted with Anorectal malformation during the study period.
3. **Period of Study:** The study period was for two years from January 2019 to December 2020.
4. **Sampling Technique:** Convenient.
5. **Study Tool:** (case sheet proforma attached)
6. **Inclusion criteria:** All neonates born with Anorectal malformation and radiological evidence of renal anomaly were included in the study.
7. **Exclusion criteria:** Children with other associated VACTERL anomalies
8. **Statistical analysis:** Epi info 7.0TM (developed by Centers for Disease Control and Prevention (CDC))

Methods:

All patients underwent a detailed clinical examination, evaluation and management which were done in the neonatal period. The associated urogenital anomalies were noted.

The anorectal malformations were classified according to Wingspread classification into low, intermediate, and high anomalies

The radiology workup for every case includes X-ray babygram, invertogram, lateral plain X-ray of lumbosacral spine, echocardiography, ultrasonogram of abdomen (Essota color Doppler A.S. machine with 3.5MHz convex probe and 7.5 MHz high resolution linear probe) and VCUG(voiding cystourethrogram), VCUG was done in 87 patients except for 3 patients with cloacal anomaly who underwent genitogram and panendoscopy. Bladder capacity was

calculated by the formula weight in Kg x7 = bladder volume in ml Under aseptic precautions a 6Fr infant feeding tube is passed per urethra. Required volume of 76% of urograffin one in three dilutions in required quantity was instilled in to the bladder and a radiograph was taken during micturation.

Grading of VUR (vesico ureteric reflux)

This was done according to international classification. Grade I- Reflux into nondilated ureter.

Grade II- Reflux into renal pelvis and calyces without dilatation.

Grade III- Reflux with mild-to-moderate dilatation and minimal blunting of fornices. Grade IV- Reflux with moderate ureteral tortuosity and dilation of pelvis and calyces. Grade V- Reflux with gross dilatation of ureter, pelvis, and calyces, loss of papillary impressions, and ureteral tortuosity.

The patients with normal ultrasonogram but with reflux on VCUG were noted. All children with VUR and genitourinary malformations were treated by standard protocol. The structural and functional genitourinary anomalies were in particular analyzed in an elaborate manner. The genital anomalies were diagnosed by physical examination, followed by imaging studies when needed. These patients were followed in outpatient department. The observations and results of the patients were tabulated and analyzed.

RESULTS

In this study there were total 120 anorectal malformations which were analysed by ultrasound KUB for renal anomalies. There were 50 cases where ARM was associated with renal anomalies.

Table 1: Incidence of Renal Anomalies in Arm

Total ARM cases	ARM with renal anomalies	Percentage(%)
120	50	41.6%

Out of 50 renal anomalies bilateral were 16(32%), unilateral anomalies were 34(68%).

Table 2: Incidence of Side Involvement

Number		Percentage(%)
Bilateral	16	32
unilateral	34	68

Among these 50 renal anomalies, isolated were 40(80%), multiple anomalies were 10(20%).

Table 3: Incidence of Isolated / Multiple Renal Anomalies

Number		Percentage(%)
Isolated	40	80%
Multiple	10	20%

Out of 50 renal anomalies, most common renal anomaly associated with anorectal malformation was hydroureteronephrosis, 35 units (57.4%), followed by Hydronephrosis 12 units (19.7%). Other anomalies were Renal agenesis 5 units (8.2%), Ectopic kidney 2 units (3.3%), Hypoplastic kidney 1 unit (1.6%), Ectopic ureter 1 unit (1.6%), Horse shoe kidney 1 unit (1.6%), Duplex kidney 1 unit (1.6%), crossed renal ectopia 1 unit (1.6%). MCUG was done in all 50 cases with renal anomalies.

Table 4: Types of Renal Anomalies

Renal Anomaly	Frequency	Percentage (%)
CrossedRenalEctopia	1	1.64%
Duplex	1	1.64%
EctopicKidney	2	3.28%
Hydronephrosis	12	19.67%
Horseshoekidney	1	1.64%
Hydroureteronephrosis	35	57.38%
MultiCysticKidneyKidneyDisease	2	3.28%
Renalagenesis	5	8.20%
Hypoplastickidney	1	1.64%
Ectopicureter	1	1.64%
Total	61(units)	100%

VUR was found in 30 cases (incidence of 25%). There was Unilateral involvement in most of the cases (76.7%) and bilateral involvement in 7 cases (23.3%).

Table 5: Incidence of VUR -Unilateral/Bilateral

	Number	Percentage
Unilateral	23	76.7%
Bilateral	7	23.3%
Total	30	100%

Table 6: Incidence of Right and Left VUR in MCUG 1

Grade	MCUG1R	MCUG1L	Total
1	2	2	4
2	7	6	13
3	6	7	13
4	2	3	5
5	2	0	2
		Total units	37

A total of 37 renal units were found to have Vesico-ureteric reflux at the first MCUG. Grade 1 reflux was seen in 2 units on right, 2 units on left; grade 2 was seen in 7 renal units on right and 6 renal units on left. Grade 3 was seen in 6 units on right and 7 units on left; Grade 4 was seen in 2 units on right and 3 units on left; whereas Grade 5 VUR was seen on right side in 2 units, and none on left.

Table 7: Incidence of Right and Left VUR in MCUG 2

Grade	MCUGR2	MCUG2L	Total
1	3	3	6
2	5	5	10
3	7	8	15
4	3	3	6
5	1	0	1
		Total units	38

MCUG 2 was done at a interval of 6 months after the MCUG1 to assess the status of reflux and further plan of management. Grade 1 VUR increased to 3 units on each side, making a total of 6 units. Grade 2 VUR renal units decreased in number from 13 to 10 units, number of Grade 3 units increased from 13 to 15 units. Grade 4 and grade 5 also increased by one unit each. MCUG 2 showed reflux in a total of 38 Renal units.

Table 8: Incidence of Right and Left VUR in MCUG 3

Grade	MCUGR3	MCUG3L	Total
1	6	6	12
2	5	6	11
3	6	3	9
4	1	2	3
5	1	1	2
		Total units	34

MCUG 3 was done 3 months after definitive procedure for ARM is done. A total of 34 units showed VUR on MCUG 3. Grade 1 VUR cases were doubled(12 units) which meant there were downgrading of higher grades, Grade 2 were 11 units, Grade 3 with 9 renal units, 3 units showed Grade 4 reflux and 2 units showed grade 5 reflux.

Table 9: Comparative Between right and Left VUR Units in MCUG 1,2,3

Right(Units)				Left (Units)		
Grade	MCUG1	MCUG2	MCUG3	MCUG1	MCUG2	MCUG3
1	2	3	4	2	3	6
2	7	5	5	6	5	6
3	6	7	5	7	8	3
4	2	3	1	3	3	2
5	2	1	1	0	0	1
Total	19	19	16	18	19	18

Table 10: Comparative Between Unilateral and Bilateral VUR in MCUG 1,2,3.(Number depicts Units)

	MCUG1					MCUG2					MCUG3				
	B/L		T		B/L		T		B/L		T				
	RT	LT	RT	LT	RT	LT	RT	LT	RT	LT	RT	LT			
1	2	1	0	1	4	2	2	0	1	5	2	4	2	2	10
2	5	4	2	2	13	4	3	2	2	11	2	3	3	3	11
3	3	4	3	3	13	3	5	4	3	15	3	2	2	1	8
4	0	2	2	1	5	1	1	2	2	6	0	0	1	2	3
5	2	0	0	0	2	1	0	0	0	1	1	1	0	0	2
					37					38					34

On comparing the results of MCUG 1 and MCUG 3; there is a definitive increase in Renal units showing GRADE 1 and 2 Reflux, as compared to MCUG 1; which indicates that the VUR is showing downgrading of reflux which means chemoprophylaxis and regular follow up is the treatment required in Most of the ARM cases with VUR.

Only when there is no downgrading of higher grade VUR, Recurrent UTI's, new scars or upgrade of reflux will need Surgical intervention as ureteric reimplantation.

The ARM cases were classified as per Krickenbeck and were compared to the Grades of VUR. Out of 37 cases, most of the cases were Recto vesical fistula-15 case-40.5%, followed by Recto bulbar fistula-7 cases and Congenital pouch colon 5 cases. The least were Rectal atresia and Cloaca- 1 case.

Table 11: Incidence of VUR in Different Types of ARM (Krickenbeck)

Grade	PF	RBF	RPF	RVF	RVaF	WF	RA	CPC	CL	Total
Grade 1	-	1	1	1	-	-	1	-	-	4
Grade 2	2	2	1	4	-	2	-	2	-	13
Grade 3	1	3	-	5	-	-	-	3	1	13
Grade 4	-	1	1	3	-	-	-	-	-	5
Grade 5	-	-	-	2	-	-	-	-	-	2
	3	7	3	15	2		1	5	1	37

[PF- Perineal Fistula, RBF-Recto bulbar fistula, RPF- Recto prostatic fistula, RVF- Rectovesical fistula, RVaF- Rectovaginal fistula, WF-Without fistula, RA- Rectal atresia, CPC-Congenital Pouch Colon, CL-Common Cloaca.]

Table 12: Age Distribution in VUR

Number	Percentage(%)	
<7days	27	90%
7-28days	3	10%

The 30 cases of ARM with VUR were classified based on their age of presentation as <7 days and >7 days old. There were 27 case presented before 7 days (90%) and the remaining three cases had presented to us after 7 days of age.

Table 13: Gender Distribution in VUR

Number	Percentage(%)	
Male	25	83.3%
Female	5	16.7%

25 cases were males with a incidence percentage of 83.3%,5 were females (16.7%);with a Male: Female ratio of 5:1

24 cases out of the 30 subjects included in the study,were born at Term gestation,Only 6 were born as Preterm babies.

Table 14: Gestational age Distribution in VUR

Number	Percentage(%)	
Term	24	80%
Preterm	6	20%

Table 15: Weight Distribution in VUR

Number	Percentage(%)	
NormalWeight	15	50%
LowBirthWeight	15	50%

Babies with normal weight and low birth weight were equal, i.e 15 cases each. Of these 30 subjects of study, Rectovesical fistula was seen in 12 cases, Rectobulbar fistula in 6 cases,

Recto Prostatic Fistula, Congenital Pouch Colon, Perineal Fistula- 3 cases each, Cloaca, Rectal atresia and ARM without fistula ONE case each.

Table 16: Frequency of Type of ARM in VUR

Type of ARM	Frequency	Percent
Cloaca	1	3.33%
Congenitalpouchcolon	3	10.00%
Perinealfistula	3	10.00%
Rectalatresia	1	3.33%
Rectobulbarfistula	6	20.00%
Rectoprostaticfistula	3	10.00%
Rectovesicalfistula	12	40.00%
Armwithoutfistula	1	3.33%
Total	30	100.00%

Of the 37 units with VUR, 4 units completely resolved (10.1%),17 units were partially resolved and 13 cases persisted with same grade of reflux, and 5 units increase in the reflux.

Table 17: Rate of Resolution

	Number	Percentage
Resolved completely	4	10.1%
Partially resolved	17	43.6%
Persisted	13	33.3%
Increased	5	13%

Number Of Units Resolved: 21 (Partial+ Complete Resolution)

When the results of ARM vs Status of VUR was plotted in a table and graphed, the following results were shown:

One case of cloaca persisted.

Two cases of CPC persisted and three cases showed partial resolution. One case of PF persisted, two cases showed partial resolution.

one case of RBF persisted, one resolved completely but 5 cases partially resolved. one case of RPF resolved completed, two cases had upgrade of reflux.

One case of RVF,was completely resolved, 7 cases partially resolved,6 cases persisted ,3 cases showed an upgrade in reflux.

Table 18: Type of ARM Vs Resolution

ARM	Resol, Partia, Persisted, Lly, Ted			Increased	Total
Cloaca	0	0	1	0	
Congenital Pouch Colon	0	3	2	0	
Perineal Fistula		2	1	0	
Rectal Atresia	1			0	
Recto Bulbar Fistula	1	5	1	0	
Recto Prostatic Fistula	1	0	0	2	
Recto VesicalFistula	1	7	6	3	
Arm Without Fistula	0	0	2	0	
Total	4	17	13	5	

Among these 30 cases, 25 cases were males with all the RVF cases(12) found in male children, followed By Recto Bulbar And Recto Prostatic fistula. The remaining 5 cases in females were seen in Cloaca, CPC, PF, RA, without fistula.

Table 19: Gender Based Incidence of VUR in ARM

ARM	Females	Males
Cloaca	1	
Congenital Pouch Colon	1	2
Perineal Fistula	1	2
Rectal Atresia	1	
Recto Bulbar Fistula		6
Recto Prostatic Fistula		3
Recto Vesical Fistula		12
Arm Without Fistula	1	
Total	5	25

All the 30 cases were kept on chemoprophylaxis. During the follow-up with radiological investigations following definitive procedure for ARM, it was found that 11 cases(36.4%) needed surgical intervention in the form of ureteric reimplantation, and remaining 19 cases(63.3%) were conservatively managed.

Table 20: Management

	Number	Percentage
Conservative	19	63.3 %
Surgical	11	36.4 %

Of the 17 partially resolved cases, 3 had to get operated due to presence of new scars in kidney on DMSA, and Recurrent UTI despite chemoprophylaxis.

Among the 13 cases which had persisted reflux, most of the reflux which were of grade 1 and 2 were conservatively managed, but 7 cases were operated, 4 underwent ureteric reimplantation on left side and 3 cases on right side.

There were 5 cases which increased in reflux, one new case of grade 1 unilateral reflux popped up during MCUG 3 which was managed conservatively. 4 cases were operated for ureteric reimplantation.

Table 21: Conservative Vs Surgical Management

	Total	Conservative	Surgical	
			Right	Left
Resolved completely	4	4		
Partially resolved	17	14	2	1
Persisted	13	6	3	4
Increased	5	1	2	2

Among the 14 units which were operated, 8 cases were unilateral, out of which only one case underwent unilateral Lead Better Politano Ureteric reimplantation and the remaining 7 units had Cohens cross trigonal ureteric reimplantation.

3 cases were bilateral involvement cases who needed Bilateral ureteric Cohen's trigonal reimplantation. Among this was a case of unilateral duplex moiety who had a common sheath

reimplantation, and also a case of bladder diverticulum where the diverticulum was excised and reimplantation was done.

Table 22: Type of Surgery

Cohens	Unilateral 7
	Bilateral 3
LBP	Unilateral 1

DISCUSSION

There are several reports in the literature concerning urologic difficulties associated with imperforate anus. In several large series the incidence of renal anomalies in arm was 26% - 52%. The documented incidence of renal anomalies by Partridge and Gough was 39% whereas Tank et al gave it 47%. Moore and Lawrence, 7 in studying all anomalies associated with 120 cases of imperforate anus, found 41 with urinary-tract anomalies (34%).

All the subjects in the study had USG KUB done at the time of discharge and the renal anomalies were documented. The incidence of renal anomalies in this study is 41.6% which is similar to Jaramillo D.^[4]

In this study comprising of 50 subjects, total of 61 renal units were found having renal anomalies. The most common is Hydroureteronephrosis 57.38% which was similar to et al reported incidence of Ectopic kidney and MCDK as 7% each, Duplication was 10.4%. Mo R, Kim JH et al,^[5] study reported Hydroureteronephrosis as the most common renal anomaly with 30.83%, least common was duplication with 3.26% incidence.

In this study out of 50 cases, 40 cases (80%) had single renal anomaly, 10 cases (20%) had more than one type of renal anomaly. In a study conducted by Hohlschneider AM et al,^[6] isolated anomaly was 41%, whereas 59% had multiple renal anomalies.

In this study VUR was found in 30 cases incidence of 25%, and the table below shows the incidence of VUR documented in literature, most common in males with 83.3% similar to a study conducted by Metts JC et al,^[7] which reported an 82.3%, et al showed 55% and Sabrina Et al reported 41.4% in males.

The incidence of VUR in literature in patients with anorectal malformation in various studies ranged from 19 - 47.2%. In this study the incidence of VUR was 25% which was almost similar to the study conducted by Sabrina et al with an incidence of 30.83%. Peña A et al,^[8] gave a 47 % incidence of VUR in his study. There was Unilateral involvement in 23 cases (76.7%) and bilateral involvement in 7 cases (23.3%). Fernbach SK et al,^[9] showed a VUR incidence of 46% with 66.7% unilateral occurrence and 33.3% bilateral occurrence. The table below shows the incidence of VUR, Unilateral and Bilateral occurrence as per various studies.

In this study, Grade 2 and Grade 3 VUR were most common with 35.1%, which is similar to Mittal A et al,^[10] with 16.67%. et al study showed Grade 3 VUR as most common with 32.3%.

There are very few studies in literature which have compared the association of ARM (Krickenbeck classification) with Vesicoureteric reflux. The Adoption of the Krickenbeck criteria allows a more standardised comparison between groups of patients with ARM in various centres and allows a more precise and streamlined evaluation of prognostic factors. In this study VUR was most commonly found in ARM with RectoVesical Fistula- 40% and least common with Rectal atresia/Common Cloaca and Without Fistula; but in a study by Mittal A et al,^[11] VUR was mostly seen in Common Cloaca -27%. Genitourinary malformations are most frequent in those with rectovesical fistula.

The kidneys which are most vulnerable to scarring are of young children with severe reflux. Since urinary tract bacterial contamination is unavoidable when there is a Recto urinary fistula, it is essential to recognise the presence of associated VUR as early as possible in babies.^[10,11]

Out of the 30 children included in this study with VUR, all the children were on chemoprophylaxis, 19 CASES (63.3%) were treated conservatively and are followed upon, but 11 cases (36.4%) were operated for Ureteric reimplantation due to one of the following reasons-i) increase in the grade of reflux during subsequent MCUG, ii) development of new scars on DMSA, iii) no downgrading of reflux iv) if the child presented with Recurrent Urinary tract Infection despite chemoprophylaxis. Similar values were documented by Mittal et al,^[11] with 66.6% conservative management of VUR cases, and 33.4% surgical intervention was needed.

CONCLUSION

To conclude, Every child born with ARM, should be investigated for VACTERL anomalies, placing special and utmost focus on Renal anomalies and in particular VUR because of its high rate of incidence compared to any other anomaly. In this study we purposely did not do MCUG on every child with ARM, because

- MCUG is an Interventional procedure.
- It has high chances of inducing sepsis.
- May cause Acute Kidney Injury.
- Hazardous in children with Single Kidney.

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