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Lower urinary tract dysfunction in cases of anorectal malformations

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ABSTRACT

Introduction: Association of genitourinary anomalies in patients with ano-rectal malformations (ARM) is well known and its incidence is reported to be 30 -50%. Many of these anomalies either have less number of functioning renal units or have conditions with risk of continuous damage to renal units, increasing the risk of developing End stage renal disease (ESRD) in adolescence or adulthood. Although frequently described as associated malformations but few of these entities like Vesico ureteric reflux (VUR) could be the result of lower urinary tract dysfunctions.
Aim: To study incidence and spectrum of Lower urinary tract dysfunction in toilet trained patients of ARM.
Objectives: To find whether LUTD is the cause of worsening of VUR/HUN/ renal functions in patients with ARM.
Material and Methods:
Study duration: 2 years (October 2018 to 30^{th} September 2020)
Study site: Department of Paediatric surgery, Chacha Nehru Bal Chikitsalaya, Geeta Colony Delhi
Study design: Prospective observational study.
Study Sample: Forty-two patients of ARM, meeting all inclusion criteria were enrolled in the study.
Inclusion criteria: All the following criteria were checked for enrolment of patient in the study. 1. Patients of all categories of anorectal malformations who were toilet trained; 2. Age more than 4 years; 3. Completed set of investigations planned for diagnosis of LUTD. 4. Consented to participate in the study and for follow up as and when required.
Exclusion criteria: Central cause of neurological deficits.
Observations and Results: A total of 125 patients who underwent PSARP during our study period. However only 42 patients met the inclusion criteria and got their work up completed for urological problems.
Conclusion: 1. LUTD and renal failure can be seen even in absence of spinal malformations in patients with ARM; 2. Severity of LUTD in absence of neurological involvement changes with time; 3. Thorough history and clinical evaluation may provide important clues in suspecting presence of occult LUTD.

1. Introduction

Association of genitourinary anomalies in patients with ano-rectal malformations (ARM) is well known and its incidence is reported to be 30 -50%.[1] Many of these anomalies either have less number of functioning renal units or have conditions with risk of continuous damage to renal units, increasing the risk of developing End stage renal disease (ESRD) in adolescence or adulthood. Although frequently described as associated malformations but few of these entities like Vesico ureteric reflux (VUR) could be the result of lower urinary tract dysfunctions.

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2. Review of Literature

The association between anorectal malformations (ARMs) and genitourinary anomalies is well established. Most studies have reported a 25 to 50% incidence of genitourinary anomalies in patients with ARMs.[1,2] The most commonly associated genitourinary malformations are.

1. Vesicoureteric reflux (30-40%) (VUR)
2. Renalagenesis (10-20%)
3. Neurogenicbladder (6 5%)
4. Hypoplasia -dysplasia (5-6%)
5. Pelvi ureteric junction Obstruction (1-2%) (PUJO)
6. Multicystic kidney disease (1-2%)

Although frequently described as associated malformations but few of these entities like VUR could be the result of lower urinary tract dysfunctions. Anomalies of the genitourinary tract can have a dramatic impact on the length and quality of these children's lives.[2] These children can have both structural and functional abnormalities of the upper and lower urinary tract as well as significant genital anomalies.[3,4] The importance of investigating and treating the urinary tract dysfunctions in patients born with anorectal malformations (ARM), has until recently been underemphasized.[3]

2.1. LUTD male vs females

The incidence of genitourinary problems depending on the sex of the patient is confusing. In their early series, Metts et al. showed clearly that boys had more problems than girls (50% versus 30%), and this difference continued to be significant even when the severity of the abnormality was considered.[5] Ratan, however, showed the opposite, with girls more frequently affected.[6] McLorie and Warne identified no significant difference between the sexes for renal abnormalities Fistulas between the rectum and bladder or bladder neck occur in around 10% of all ARM and represent the most complex malformations in males.[7] The etiology of lower urinary tract dysfunction in ARM and cloacal anomalies is poorly understood.[8] However, bladder dysfunction causes significant urological morbidity in these patients resulting in renal damage from recurrent urinary tract infections and urinary incontinence, both of which can cause profound morbidity and disability.[5,9]

2.2. LUTD and level of fistula

Strine et al in their series of 67 patients concluded that patients with rectobladder neck fistulas were rarely able to achieve continence with spontaneous voiding alone.[10] Giuliani et al followed 321 patients of ARM and found that cloacal malformation in females and recto bladder neck fistulae in males are at highest risk of developing renal insufficiency.[1]

Kyrklund K concluded that prevalence of LUTS and age at completion of toilet training was comparable to controls in patients with low anorectal malformations. Adult females, who were managed conservatively for anterior anus, had incidence of LUTD comparable to normal females.[11]

Historical studies have used different classification systems. The incidence of urinary anomalies increases according to the severity of the anorectal lesion.[4,12] The incidence of an associated genitourinary anomaly also increases when a lumbosacral defect is present.[1]

Genital maldevelopment is less frequent, but still a significant problem. Interestingly, those patients with a urinary anomaly are more likely to have a genital tract problem (26%) compared with those without a urinary defect (14%). However, a genital anomaly is much better at predicting a urinary problem, as 55% of these patients have both.[5]

Occult lower urinary tract dysfunction in association with anorectal malformations

Overall, approximately 40% of patients have a urinary tract anomaly and 10% have a genital anomaly.[13,14]

Renal failure remains one of the most significant cause of morbidity in patients with anorectal malformation.[1] Neurogenic bladder in patients with ARMs is multifactorial. Potential contributing factors include a congenital anatomic or neurologic anomaly, iatrogenic neurologic injury from surgical correction, and late neurologic sequelae of a tethered cord. In the study conducted by Brian Vander Brink et al[15] cause of renal failure, whether a chronic kidney disease or a function of intrinsic renal dysplasia or an acquired renal injury from dysfunction of lower urinary tract could not be confirmed. However, it is well known that severe dysfunction of lower urinary tract poses significant risk to upper tracts when untreated. Bishoff et al when retrospectively reviewed patients of ARM who developed ESRD they felt that even when missed opportunities were identified, the impact of interventions to prevent or delay the onset of ESRD could not be proven.[16]

2.3. Reflux in lower urinary tract dysfunction

The reported incidence of vesicoureteric reflux varies greatly from 2 to nearly 50%.[5] The variation depends appears to depend entirely upon the number of patients who undergo a diagnostic micturating cystogram to detect reflux. All grades of reflux have been described: in 1996, Boemers et al. reported that 27% of their cohort had reflux; of the 24 patients (37 kidneys) with reflux, 6 were grade I, 4 were grade II, 5 were grade III, 9 were grade IV, and 3 were grade V.[4] This suggests that higher-grade reflux is seen than in patients with primary vesicoureteric reflux; however, large series have not been well reported and an association between reflux with and that without a neuropathic bladder has not been documented.

Recurrent urinary tract infection may be overlooked or attributed to coexisting vesicoureteric reflux or renal anomalies, which are prevalent in a high proportion of these children.[4] Recurrent UTI can be manifestation of LUTD. Detecting bladder dysfunction at an early age is essential in avoiding deterioration in renal function.[4,17,18]

2.4. Occult lower urinary tract dysfunction with ARM

Their identification and appropriate management are critical, as they represent a significant source of morbidity and mortality in these patients.[19] Irrespective of type of ARM, presence or absence of vertebral anomalies, presence or absence of clinical or radiological abnormalities of the lower urinary tract, occult lower urinary tract dysfunction had been described in few studies.[20,21] Poor bowel function was often seen together with LUTD. In children with Bladder Bowel Dysfunction (BBD), the connection was attributable to a mutual impairment of the nerve supply to both systems. Children with non-neurogenic and non-urological causes of the LUTD also had lower bowel scores than those with normal bladder function; although not significant, it suggests that poor bowel function was responsible for an increase in LUT symptoms.[22]

2.5. LUTDs status pre verses post PSARP

Lower urinary tract dysfunction secondary to inadvertent surgical injury of the pelvic nerves and nerve plexus can develop in children with ARM but In terms of risk factors for incontinence, Samuk et al. observed a worse prognosis in patients who required a re-operative PSARP (23%) and with a sacral ratio of 0.40 (23% for sacral ratio0.41verses 68% for sacral ratio-0.70) in their series.[23] In a retrospective study of 32 patients with ARMs at a single institution.[23] Boemers et al. evaluated the effect of PSARP on lower urinary tract function with pre-operative and postoperative UDS. They reported a deterioration of function in three (9%) male patients with a recto-urethral fistula, two of which required a combined abdominal and posterior sagittal approach. They suggested that the minority of male patients with ARMs who require a more extensive retrovesical dissection are at risk of a deterioration of function.[24] Warne S et al proposed that posterior sagittal anorectoplasty (PSARP) by virtue of being strictly in midline is believed to have no deleterious effects on lower urinary tract. Abdomino-perineal approach for ano-rectoplasty (APSARP) may cause some neurogenic dysfunction as the rectal pouch is mobilized close to the urinary tract.[12] Other studies have not observed a deterioration of lower urinary tract function following PSARP.[25,26]

Neurovesical dysfunction can be congenital in patients affected by ARM and is not a sequela of surgery.[27]

2.6. LUTDs and spinal malformation

In their series of 90 patients of ARM, Boemer et al found high incidence (24%) of voiding dysfunctions, mostly attributable to sacral agenesis. They also mention that neurological deficit in these patient is subtle and difficult to diagnose as it affects V only the pelvic floor muscle and continence organs. Due to acceptability of some degree of incontinence in society the patient usually comes as late presentation and they have concluded that urologic and sacral agenesis should receive urodynamic investigation.[24]

Occult spinal dysraphism with tethered cord, syrinx, diastomatemyelia have been recognised as cause of lower urinary tract dysfunctions in patients with ARM however cases without such associations too have been found to have dysfunctions of lower urinary tract.[28]

Borg et al in their study for assessing the routine need of urodynamic study in patients with anorectal malformation concluded that all children with innate NBD had a spinal cord malformation either as spinal cord regression or tethering with or without a lipoma. In their study Innate NBD was not found in any child with normal spinal cord.[29]

Stathopoulos on the contrary found that Lower urinary tract dysfunction is common in patients with anorectal malformations. Normal spine or spinal cord does not exclude Lower urinary tract dysfunction. Myelodysplasia or vertebral anomaly does not determine occurrence or absence of lower urinary tract dysfunction. They recommended preoperative urodynamic assessment of the bladder and magnetic resonance imaging of the spine in children with anorectal malformations.[30]

Taskinen et al mentioned that the state of the spinal cord is not the only factor explaining lower urinary tract function. Thus, the possibility of lower urinary tract dysfunction should be considered in each patient with anorectal abnormalities. If the patient has symptoms or findings suggesting abnormal lower urinary tract function urodynamic evaluation should be performed.[31]

2.7. Urethral problems

Posterior urethral valves, megaurethra, and urethral duplication have been reported in association with ARM. The most commonly reported urethral problems are iatrogenic and include urethral strictures, large diverticula, or remnants of the rectal pouch from incomplete dissection of the rectal fistula at the time of pull-through.[5] These complications are now seen less frequently with the development of PSARP, which allows good visualization of the urethral fistula. Stones may form if a urethral diverticulum is left, precipitating recurrent infections, and it can be technically difficult to catheterize the urethra in those patients who require CIC for neurogenic bladder.[7]

3. Aim

To study incidence and spectrum of Lower urinary tract dysfunction in toilet trained patients of ARM.

4. Objectives

To find whether LUTD is the cause of worsening of VUR/HUN/ renal functions in patients with ARM.

5. Material and Methods

5.1. Study duration

2 Years (October 2018 to 30th September 2020.

5.2. Study site

Department of Paediatric Surgery, Chacha Nehru Bal Chikitsalaya, Geeta Colony Delhi

5.3. Study design

Prospective observational study.

5.4. Study sample

Forty-two patients of ARM, meeting all inclusion criteria were enrolled in the study.

5.5. Inclusion criteria

All the following criteria were checked for enrolment of patient in the study.

1. Patients of all categories of anorectal malformations who were toilet trained.
2. Age more than 4 years.
3. Completed set of investigations planned for diagnosis of LUTD.
4. Consented to participate in the study and for follow up as and when required.

5.6. Exclusion criteria

Central cause of neurological deficits.

6. Observations and Results

A total of 125 patients who under went PSARP during our study period. However only 42 patients met the inclusion criteria and got their work up completed for urological problems.

6.1. Age

Mean age at enrolment of these cases was 5.3 years in our study (Range 4 years to 12 years, Standard Deviation +/-2.0)

6.2. Sex distribution

Male: Female ratio was 1.2:1 in our study.

Table 1: Sex distribution

Sex	No. of patients	Percent
Male	23	54
Female	10	45.2
Total	42	100

Most frequently encountered cases in the series were of vestibular fistula, and the second most common was recto bulbar fistula.

Table 2: Type of ARM

	Number	Percentage
Vestibular fistula	14	33%
Cloaca	3	7.1%
Rectal atresia	1	2.4%
Recto prostatic fistula	11	26%
Recto bulbar fistula	12	28%
Rectovaginal fistula	1	2%
Total	42	100.0%

6.3. Urological symptoms

Were present in 50% of the patients. Common symptoms seen in our series were dysuria, dribbling of urine, frequency, urgency, incontinence and straining. Most common symptom was dribbling of urine which was seen in 8/ 21 symptomatic patients. Of the 42 patients we have defined 31 patients to be LUTD.

Table 3: Number of patients with urinary symptoms

	Number. of patients	Percent
No	21	50.0
Yes	21	50.0
Total	42	100.0

Table 4: Distribution of urinary symptoms

Urinary symptom	Number of cases with symptom (N=42)	% of included cases
Frequency	7	16.7%
Dysuria	5	11.9%
Dribbling	8	19.0%
Incontinence	3	7.1%
Straining	7	16.7%

Apart from a screening USG KUB, in our study we have included one follow up study (At least at interval of one year) to see any progression or regression in abnormal KUB parameters. We found upper tract affection in 31 % (13/42)

Table 5: USG with renal anomaly (hydronephrosis, renal anatomy raised cortical echogenicity)

	Number of patients	Percent
No anomaly	29	69.0
With anomaly	13	31.0
Total	42	100.0

Table 6: USG with bladder changes

	Number of patients	Percent
No	34	81.0
Yes	8	19.0
Total	42	100.0

Table 7: USG with ureteric changes

	Number of patients	Percent
No	40	95.2
Yes	2	4.8
Total	42	100.0

Table 8: Comparision between USG 1 and USG 2

Parameter	USG 1	USG 2	Percentage of improvement
Bladder wall thickening	8 patients	5 patients	7.1
Renal changes	13	10	7.2
Ureteric changes	2	1	2.4
PVRV	2	0	100

cases while 19 % patients had bladder wall thickening. Abnormal PVRV was found in 2 patients

MCU anomalies-The most commonly seen urological anomalies in MCU in patients with ARM were bladder changes, seen in 14/42 (33.1%) patients and was 45% prevalent in patients with LUTD. Vesico-ureteral reflux and urethral anatomical abnormalities were found in 26.2, 9.5 % respectively.

Table 9: MCU normal/abnormal

	Total number of patients	Percentage
Abnormal	25	59.5
Normal	17	40.5
Total	42	100.0

MRI Spine was done to rule out neurogenic bladder causing lutd or whether there were other causes for it and in those, we found that around 21.4% of them had neurogenic bladder with spinal anomaly as diastomyelia, cord tethering and spinal dysraphism and etc. Of the 31 LUTDs 9 had spinal cord anomaly.

In our study we took 42 patients and in them 31 patients came under LUTD which were defined according to their

Table 10: MCU with bladder changes (Trabeculations, diverticulae, sacculations)

	Tot al number	Percentage
Number of patients with no bladder changes.	28	66.9
Patients with bladder changes	14	33.1
Total	42	100.0

Table 11: MCU WIH VUR

	Total number of patients	Percentage
No	31	73.8
Yes	11	26.2
Total	42	100.0

Table 12: MCU with urethral anomaly (dilated posteriorurethra, urethral kinking and flat verumontanum)

	Total number of patients	Percentage
No	38	90.5
Yes	4	9.5
Total	42	100.0

Table 13: MRI L.Sspine

	Total number of patients	Percentage
Not done	6	14.2%
Normal	27	64.2%
Abnormal	9	21.4.8%
Total	42	100.0%

symptoms, USG, MCU and MRI spine. Out of 31 nine were neurogenic bladder.

Table 14: Normal serum creatinine levels for age

Age	mg/dl	micromol/L
0-1 week	0.6- 1.1	53-97
1 week- 1 month	0.3- 0.7	27-62
1-6 month	0.2-0.4	18-35
7-12 month	0.2-0.4	18-35
1-18 years	0.2-0.7	18-62

Lutd Correlation with Serum Creatinine

7. Discussion

The study here was planned to find whether apart from anatomical genito urinary anomalies and spinal malformations, there are other factors too existing with ARM, which can affect functioning of lower urinary tract. Borg et al when excluded neurological and urological causes of LUTD, the remaining children with LUTD had lower bowel scores than those with normal bladder function, but the difference was not significant.[22]

Table 15: Observation between number of patients and raised serum creatinine and usg /mcu/mri who had anomalous findings.

Number of patient with raised creatinine	Number of Symptomatic patients	Number of patients with abnormal USG findings. Present/absent	Number of patients with abnormal MCU findings. Present/absent	Number of patients with abnormal MRI findings. Present/absent
7	4	5	6	1

Table 16: Corelation creatinine value in LUTD patients

	Total Number of patients	Mean	Standard deviation
LUTD present	31	0.46	0.36
LUTD absent	11	0.36	0.05

LUTD is defined as any functional anomaly of the bladder and/or urethra that has negative influence on voiding function. In our study we found a remarkably high incidence of patients having lower urinary tract dysfunction. This high incidence is partially contributed by the fact that most of our symptomatic patients and patients with positive radiological findings completed their work up during the study period while those who were asymptomatic and were having normal USG KUB have got their hospital visits postponed due to corona pandemic. Goosens et al in their retrospective review of 331 patients found 52% incidence of urological anomalies. Most common were hydronephrosis, VUR, LUTD and urinary incontinence with a total incidence of 24,18,14,12% respectively. 8% of patients with LUTD had no spinal abnormalities.[14] In a longitudinal study done by Borg et al they found fluctuating difference between the incidence with age, more LUTD was seen in earlier age group.[22]

7.1. Krickenbeck's classificaton of ARM and LUTD

Fabro et al haven't found any correlation of severity of these non neurological voiding disturbances with the level of anatomical defect in their study in 22 patients.[32] Goosens et al have found decreased incidence of urological anomalies with diminishing complexity of the ARM. Treatment invasiveness increased with the increase of complexity of ARM in their study.[14] Many other studies too have reported higher incidence of VUR, LUTD, Spinal anomalies in patients with higher anorectal malformations. Our study too have higher incidence of LUTDS in patients with higher complex anomalies

7.2. Urological symptoms and LUTD

Jindal et al found high incidence of LUTD in ARM even in the absence of clinical and radiological evidence of lower urinary tract abnormalities, in addition they have also noted changes in neurovesical function post PSARP even though the changes were statisticaly insignificant.[33]

Symptom in patients with ARM are usually attributed to clinical and subclinical UTI which is thought to be a sequlae of coexisting fistulous communications, bowel dysfunction and coexisting urinary tract anomalies like VUR. Overlooked lower urinary tract dysfunction in such cases might adversely affect bladder functioning.

Of the enrolled patients three (7%) are categorised to have probable LUTD based only on clinical symptoms. In these patients urinary symptoms were significant and persisted even in absence of urinary tract infection.

7.3. USG in predicting LUTD

Increased bladder wall thickness is found in association with LUTD. It may be the first sign to be observed in many cases of LUTD. Blatt et al found it as a sensitive diagnostic tool for early diagnosis of LUTD.[34]

We had observed a significant level of tolerance in society for urinary symptoms. USG in such cases could be an important help in early diagnosis of LUTD.

Although we could not calculate ratio of full and empty bladder wall thickness, three of our patients were considered to have LUTD as they were having thickened bladder. All three patients had urinary symptoms as well changes in their MCU.

7.4. MCU and LUTD

Nine patients from this study had VUR without any spinal cord anomaly as well as mechanical cause of obstruction to bladder outlet. These patients had multiple episodes of UTI. Patients with associated VUR are known to have increased likelihood of having urinary tract infection. Recurrent UTI may then cause urethritis /cystitis subsequently causing various urinary symptoms. It is exceedingly difficult to differentiate these cases from primary VUR. We had labelled these cases as having LUTD as these were much more symptomatic than those having VUR without ARM. These patients are kept under close follow up and are awaiting UDS. As none of these patients underwent MCU in their initial work up we could not compare their MCU for any worsening or improvement in VUR. Surprisingly, USG screening of their kidney ureter and bladder could not pick up HUN in 5 patients.

One patient with vestibular fistula had short urethra and incompetent bladder neck without any spinal cord

anomaly. Two more patients with vestibular fistula have thick walled, elongated bladder with significant post void residual volume. One of these is requiring CIC while other has shown clinical improvement on anticholinergics.

7.5. Acquired urethral abnormalities and LUTD

Acquired urethral abnormalities were seen in 4 of our patients. 2 of these patients had urethral kinking following pull through done by dai or some local physian. One patient developed urethral stricture as a consequence of UTI. One patient had posterior urethral valve. Zaccara et al have found higher incidence of UTI and epididymorchitis in patients with ARM with recto urethral fistula a total of 89 patients were contacted. Ten cases of epididymo orchitis were found, and all occurred in patients with recto-urethral fistula after reconstruction. The patients' age at first episode ranged between 4 and 11 years. RU fistula patients experiencing epididymo orchitis.[35]

7.6. Spinal cord Anomalies and LUTD

Fabbro et al found 22 patients with voiding disturbances and without any spinal cord anomalies. Two had incontinence while 20 had no incontinence for urine.

Borg et al found 56% incidence of overall LUTD in their series of 41 patients. In nine (22%) patients, the dysfunction was of neurogenic origin, caused by spinal cord malformations and in eight and as a result of the PSARVUP. Nonneurogenic LUTD was estimated to be present in 14/41 (34%) at least in one of the follow-up investigations. Most of the children had a dysfunction classified as detrusor hyper reflexia, and only a few had Over Active Bladder syndrome. Typical of this group was that the LUTD was not constant during follow-up, in contrast to the children with NBD. More children had dysfunction early, at the 5-year investigation, as compared with the 15-year follow-up. No difference in frequency or grade of the nonneurogenic LUTD was seen in the different fistula groups.[22]

7.7. Renal failure

Although end stage renal disease and Chronic renal failure are known in patients with anorectal malformations but less number of studies have reviewed it prospectively. Mclorie et al have reported an incidence of 2 to 6 percent of death of these patients due to renal insufficiency and mentioned that there are high incidence of renal failure in cases of high ARM as compared to low ARM.[7]

Out of 42 patients in our series 8 had raised creatinine value for their age. Spinal malformation was found in 3/7 patients and 4 had VUR with recurrent UTI. These patients did not have any history of failed surgeries or any iatrogenic injury to lower urinary tract. Bladder changes in these patients are similar to neurogenic bladder but MRI spine was normal in 4/7 patients. We categorised all these patients as cases of probable LUTD and planned them for UDS. In a study done by Giuliani et al in 329 patients of ARM 6 developed renal failure and hence they concluded that Complex GU anomalies associated with ARM require a long-term approach by specialized pediatric and adult clinicians to optimize the care of this selected population of patients.[1]

8. Source of Funding

None.

9. Conflicts of interest

There are no conflicts of interest.

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