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Research Article

Postnatal Outcomes in Cases of Prenatally Detected Dilated Fetal Bladder

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Abstract

Objectives: To explore the long-term outcomes in foetuses presenting with an enlarged bladder antenatally.

Methods - Design: A retrospective cohort study was conducted over a 15-year period between 2003 and 2018.

Setting and participants: Foetuses suspected to have enlarged bladders antenatally were included.

Outcome measurements and statistical analysis: Analyses were done based on the trimester the enlarged bladder was detected, live births, terminations, surgical interventions, creatinine levels and bladder measurements post-delivery, and subsequent health outcomes.

Results: From the 50 foetuses identified prenatally, detections were as follows: first trimester (9 cases), second trimester (30 cases), and third trimester (11 cases). There were 14 terminations (28%), 5 stillbirths (10%), and 31 live births (62%). Among the terminated and stillbirth/neonatal death cases, the most frequent diagnosis in males was PUV (57%). Two female foetuses were terminated due to lumbosacral spina bifida and sacrococcygeal teratoma obstructing the ureters, respectively. In surviving males, PUV was predominant (48.3% of 29 males). In five cases megacystis had resolved by birth, including one following in-utero surgery. Among the two female cases, one issue was resolved by birth, and the second had bilateral ureteroceles. Post-birth, surgical intervention was needed in 61% of males and 50% of females. The commonest surgery was ablation of posterior urethral valves. The median age for surgery was 1.5 months with a median follow-up of 4 years and the longest follow-up of fourteen years. Six children had no postnatal renal or urological follow-up. The mean peak creatinine level was 132, dropping to 47 in the latest measurement. Half of the patients with pathology evident at birth exhibited abnormal bladder function. There was one neonatal death. Three patients necessitated a kidney transplant due to chronic kidney disease.

Conclusion: Foetuses diagnosed with an enlarged bladder in the second trimester most frequently had the posterior urethral valve as the underlying cause. For patients continuing the pregnancy, most had live births. About 1 in 10 posterior urethral valve survivors developed chronic kidney conditions, leading to a renal transplant.

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Introduction

Ultrasound can identify the fetal bladder from week 10 of gestation when fetal urine production begins [1]. In the first trimester, megacystis (enlarged bladder) is defined as a longitudinal bladder length greater than 7 mm and is present in 0.06% of pregnancies [2]. An enlarged fetal bladder may be a transient variability of normal bladder filling and emptying. However, other associated findings, along with changes that persist over time, may indicate an abnormality of the urogenital tract. The most typical causes of the dilated bladder are Posterior Urethral Valves (PUVs) in male foetuses (approximately 1 in 8000 male births) and urethral atresia in female fetuses [3]. The antenatal finding of an enlarged bladder can be associated with the development of a thick-walled bladder, vesicoureteric reflux, and hydroureteronephrosis that can eventually lead to renal parenchymal maldevelopment and reduced renal function up to End-Stage Renal Disease (ESRD) with the need for renal support in the form of dialysis or renal transplant [4]. Lack of urine excretion during fetal life can also lead to early pregnancy renal anhydramnios (EPRA), resulting in pulmonary hypoplasia, a substantial cause of death in newborns [5].

Objective

In this study, we aimed to review the pre- and post-natal outcomes of children presenting with an enlarged/distended fetal bladder on antenatal ultrasound.

Methods

Data collection

This study was conducted at St. Thomas Hospital in London. The study included women whose foetuses were thought to have enlarged bladders and who had scans in the 15 years between 2003 and 2018.

Inclusion and exclusion criteria

The inclusion criteria for the study population were as follows:

- Fetal bladder distension was defined as a sagittal length of more than 7 mm. in the first trimester or a sagittal length of Gestational Age (GA) ± 7 mm after the first trimester
- Both male and female foetuses
- Pregnant women who delivered at St Thomas' Hospital only
- Pregnancies that ended in any outcome (termination, intrauterine death, and livebirth)
- A major exclusion criterion for the study population was as follows:
- Those where the postnatal outcome was not available.

Antenatal data collection

The Fetal Medicine Unit (FMU) of St Thomas Hospital, Astraia (v1.24.9, ©*astraia software gmbh*, Munich, Germany, 2015) is used to store and manage obstetric scan records. Cases from this database were identified for inclusion in the initial project database. The following data were collected.

- Date of Appointment at the FMU
- Gestational Age
- Bladder measurements
- Liquor volume
- Presence or absence of ureteric dilatation
- Bladder ultrasound findings

Postnatal data collection

Data about delivery and the newborn were collected from Badgernet (v2.9.1.0, ©*clevermed*, Edinburgh, UK, 2016) and the Electronic Patient Records of Guys and St Thomas' (EPR) (v1.6 ©*2004 iSOFT Group plc*) system. Data collected included postnatal ultrasound scans, final diagnosis, investigations, and other interventional procedures and were expressed in percentages.

- Serum creatinine measurements
- Age at last follow-up
- Bladder function
- Age at first surgical intervention

The diagnosis stated in the patient notes and clinic letters were noted. For those cases where TOP occurred, the diagnosis stated on the postmortem report was noted; when this was not available, the presumed diagnosis from prenatal ultrasound findings was used.

Results

We identified 65 cases of megacystis; of these, 15 were excluded because of a lack of outcome data.

Out of the 50 foetuses identified prenatally, 9 (18%), 30 (60%), and 11 (22%) were detected in the first, second and third trimesters, respectively. Forty-seven (94%) were male foetuses, and 3 (6%) were female.

Underlying aetiopathology and outcome

Of all 50 cases, spontaneous resolution was noted antenatally (4) or postnatally (2) in six patients (12%). All foetuses with spontaneous resolution in utero survived and had no urological/renal consequences postnatally.

The most common cause of megacystis was PUV (n: 20), accounting for 40% of cases. This is approximately 45%, excluding the cases of spontaneous resolution. In 27.2% (n: 6) of PUV cases, termination was opted for, and live birth occurred in 72.2% (n: 14).

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Among the survivors, there was also one case of anorectal malformation and one of patent urachus. Complete survival, termination, and death rates are summarised in Table 1.

The percentage contribution of each aetiology to the total number of cases is summarised in Figure 1.

Termination of pregnancy and aetiology in those cases

Fourteen cases (28%) ended in Termination of Pregnancy (TOP) following diagnosis in the first, second, and third trimesters in 6 (out of 9), 7 (out of 30), and 1 (out of 11) cases, respectively. Among the cases that ended in termination of pregnancy, the most typical diagnosis among males was PUV (n: 6), accounting for 43% of all terminations. Two of the 14 terminations were female foetuses, one of which was detected with a lumbosacral spina bifida and the other a sacrococcygeal teratoma. In one case, a termination was carried out in the third trimester. In this circumstance, the woman had her booking appointment late. Multiple congenital abnormalities, including brain and urinary defects, were noted on her first scan (at 27+2 weeks of gestation).

All patients with chromosomal abnormalities, spinal cord defects, and other congenital abnormalities suffered miscarriage/stillbirth or opted for termination of pregnancy.

In a case presenting in the first trimester as multiple pregnancies, one of the twins showed signs of congenital malformation and was karyotypically positive for trisomy 18. Selective fetocide of this twin was performed. The other twin had normal anatomy and survived. In one case, the postmortem revealed a rare combination of findings, including megalourethra, renal agenesis on the right side, and left MCDK. The diagnosis of patients who underwent termination is given in Figure 2.

Table 1: Complete survival, termination, and death rates in relation to liquor volume.

Liquor volume	No of cases	Termination	Continued pregnancies	Pregnancy loss (out of continuing pregnancies)	Livebirth	Neonatal death
Normal	34 (68.0%)	6 (42.9%)	28 (77.8%)	2 (40.0%)	27 (87.1%)	0 (0.0%)
Oligohydramnios	8 (16.0%)	4 (28.6%)	4 (11.1%)	1 (20.0%)	2 (6.5%)	0 (0.0%)
Anhydramnios	6 (12.0%)	4 (28.6%)	2 (5.6%)	0 (0.0%)	2 (6.5%)	1 (100.0%)
Polyhydramnios	2 (4.0%)	0 (0.0%)	2 (5.6%)	2 (40.0%)	0 (0.0%)	0 (0.0%)

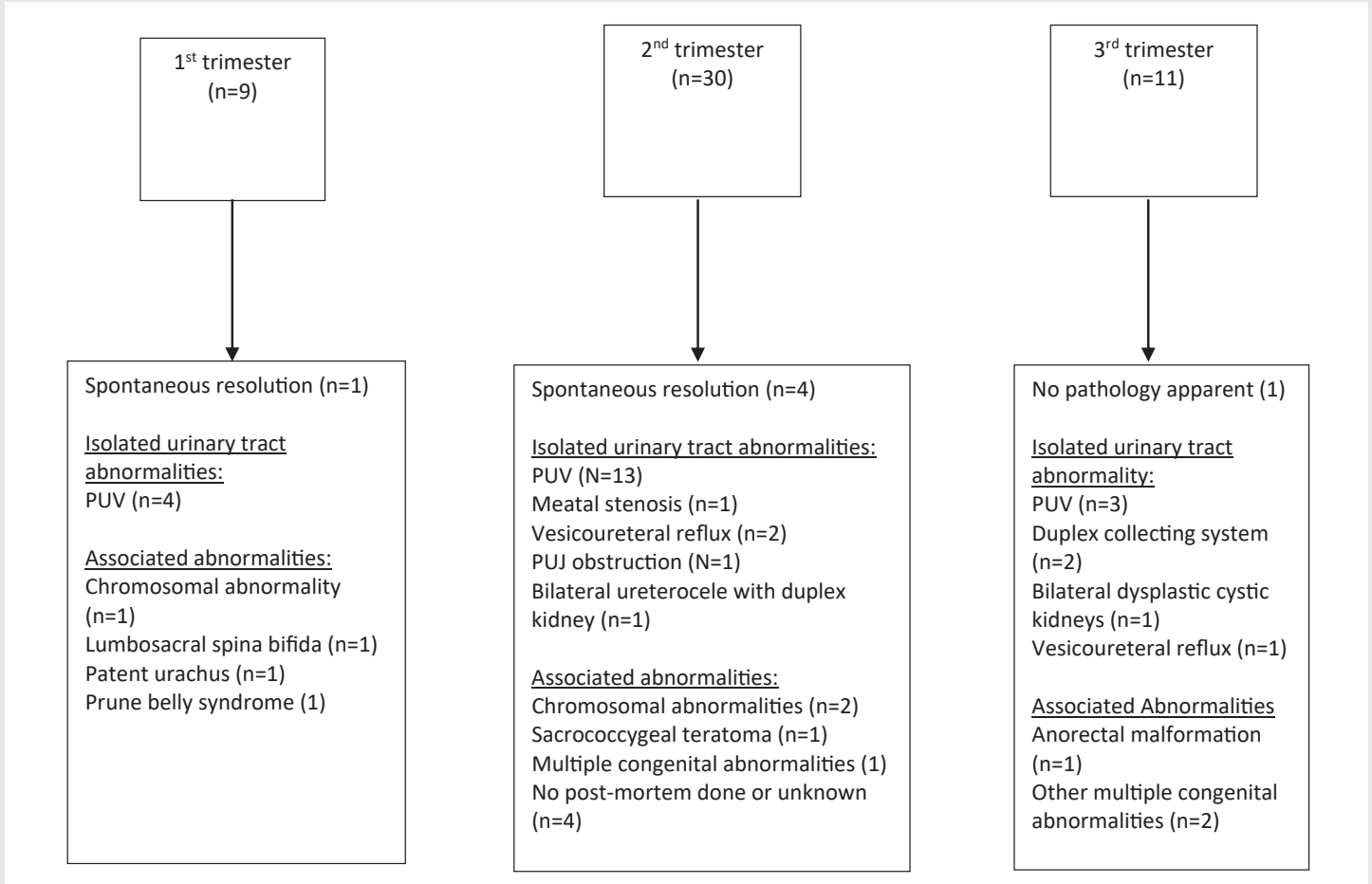

Figure 1: Flow chart to show the underlying aetiology of enlarged bladder.

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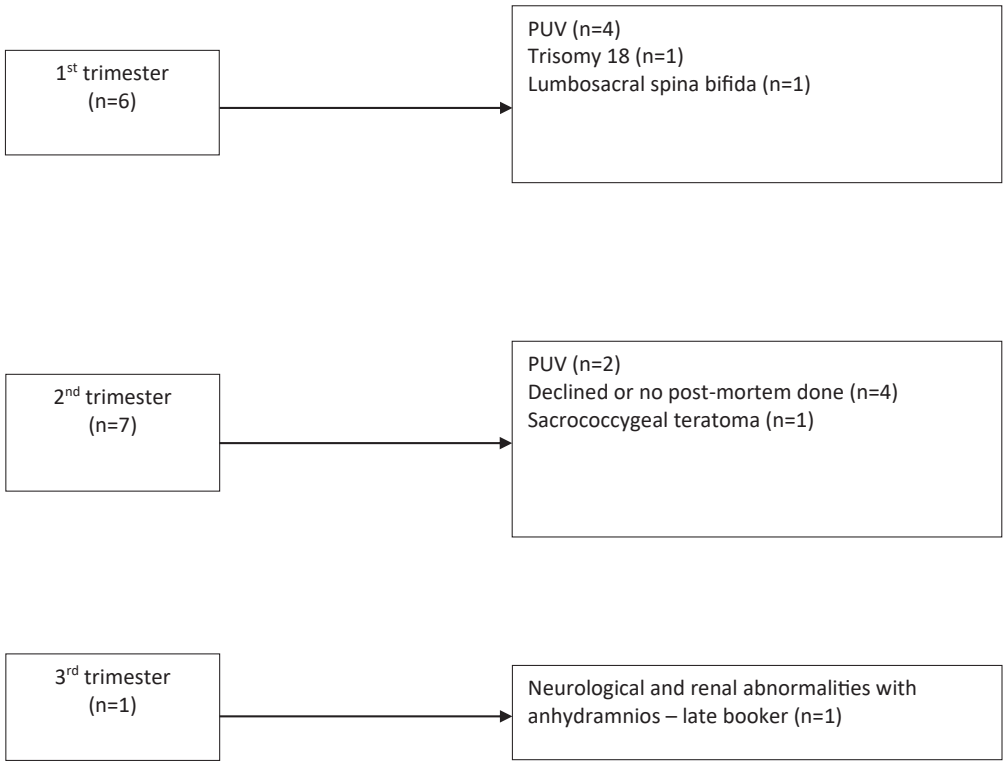

Figure 2: Flowchart showing the postmortem findings or presumed diagnoses of the terminated foetuses.

Stillbirth/miscarriage and aetiology in these cases

In five of the 36 cases (14%) where pregnancy continued, stillbirth/miscarriage occurred. One case of trisomy 13 ended in miscarriage, and another case of trisomy 18 resulted in antepartum stillbirth. In the other three cases of stillbirth, multiple abnormalities were observed, and there was a high risk for chromosomal aberrations in the screening results.

Neonatal outcome and diagnosis

In total, an additional 4 patients were lost to follow-up as they underwent treatment at other hospitals. A total of 27 infants with postnatal follow-up were included. The most common diagnosis was, again, PUV (51.8%, n = 14), followed by vesicoureteric reflux (11%, n = 3); other cases of ureterocoeles and anorectal and abdominal wall abnormalities. One case of neonatal death resulted from bilateral dysplastic cystic kidneys.

Amniotic fluid volume and survival rate

Liquor volume was normal, with oligohydramnios, anhydramnios, and polyhydramnios in 34 (68%), 8 (16%), 6 (12%), and 2 (4%) patients, respectively. The outcome of pregnancies in relation to liquor volume is shown in Table 1.

In utero intervention and outcome

Five patients (10%) had Vesicoamniotic (VA) shunts placed. Of those, there was one case of intrauterine demise. The second patient resulted in live birth followed by neonatal death due to pulmonary hypoplasia. One patient survived with a patent urachus diagnosed postnatally, and the remaining two survived and underwent postnatal treatment for PUV.

Postnatal ultrasound findings

Excluding those where resolution had occurred antenatally, 27 infants had postnatal follow-up, 2 of whom had no pathology demonstrated postnatally (7%). Two of the 27 infants were female (7%), and the remaining 25 were male (93%). Renal/genitourinary ultrasound was performed after birth (from 24 hours to one week of life).

Postnatal bladder findings and function

Generally, the bladder findings on the first ultrasound scan confirmed the presence of an enlarged/dilated bladder with or without a thickened wall, with some reports describing bladder trabeculation. A dilated bladder was seen in 22.2% of cases, a dilated and thickened bladder was seen in 11%, and a thickened wall with normal bladder size was seen in 44% of cases (this may be because, after catheterisation, the bladder returned to normal size) and a normal bladder was seen in 22% of cases. In one of the latter, no pathology was found postnatally.

A thick-walled bladder or trabeculated bladder appearance was observed in 73.3% of the boys with a diagnosis of PUV. An underfilled bladder with normal wall thickness was observed in 2 of the 3 cases with a diagnosis of VUR.

The incidence of abnormal bladder function (among those with pathology apparent at birth) was 50%. To assess this, we looked through clinic letters identifying chief complaints

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at the latest follow-up, such as incontinence, the need for catheterisation, or any other intervention/symptom.

Among the 27 survivors, the most typical diagnosis among males (25 males included) was PUV in 14 (56%), spontaneous resolution in 3 (12%), VUR in 3 (7.2%), bilateral dysplastic kidneys in 1 (4%), anorectal malformation with bladder fistula in 1 (4%), ureterocoele with right duplex kidney in 1 (4%), urethral meatal stenosis in 1 (4%) and patent urachus with abdominal wall deficiency in 1 (4%).

Among females, (2) one case was resolved by birth, and the second had bilateral ureteroceles, which needed intervention.

Postnatal renal function - creatinine levels

Creatinine values were used to measure renal function in the infants; Table 2 shows the age and level of the first and highest creatinine samples. Acute renal failure was observed in four patients, two of whom required a kidney transplant. This was also the case for the infant who developed CKD later.

Table 2: Age and level of the initial and highest creatinine values to measure renal function in infants.

	Initial creatinine level (umol/L)	Age (days)	Highest creatinine level (umol/L)	Age (days)	Associated complications
1	80	3	80	34	
2	25	41	25	41	
3	79	0	302	7	ARF (acute renal failure) and eventual CKD (chronic kidney disease)
4	85	30	125	31	CKD
5	60	0	96	1	
6	67	0	94	1	
7	79	2	79	2	
8	54	0	109	0	Pulmonary hypoplasia and neonatal death
9	66	0	66	0	
10	65	0	144	3	Moderate renal insufficiency
11	63	30	157	33	
12	60	0	132	26	
13	35	6	35	6	
14	62	0	62	0	
15	104	0	107	2	
16	71	0	414	7	ARF
17	73	0	85	2	
18	67	0	121	2	
19	82	0	392	7	ARF
20	60	0	127	2	
21	37	9	37	18	
22	93	0	265	4	ARF
23	66	0	66	0	
24	85	0	94	1	
25	75	0	100	1	
26	102	4	102	6	
27	59	0	98	1	

Note: Table showing the date/age at which the first and highest creatinine was taken along with any notes on the patient's renal function from the EPR. Infants are anonymised using numbers 1 to 27.

Postnatal management

In three out of 27 survivors (11.1%), there was severe Lower Urinary Tract Obstruction (LUTO) and bilateral renal damage resulting in Acute Renal Failure (ARF) and, eventually, End-Stage Renal Disease (ESRD), necessitating a kidney transplant. All patients with PUV underwent valve ablation and resection of the valves, with two of these patients also requiring a kidney transplant due to declining renal function.

Surgical intervention was needed in 61% of males (excluding cases that resolved in utero). The most common surgical intervention was ablation of posterior urethral valves.

Discussion

This study has shown that distended bladder detected on prenatal scans has variable aetiopathology and outcomes. The presence of associated urinary tract and other system abnormalities, liquor volume, sex of the foetus, and the gestation at which the findings are detected impact the outcome of the pregnancy and beyond. Hence, counselling should be individualised.

Termination of pregnancy is opted for when the abnormalities are detected in the first trimester and are associated with oligo/anhydramnios. This is due to the risk of pulmonary hypoplasia secondary to lack of fluid at 16-22 weeks and the related poor prognosis for long-term renal function. We can speculate that an early presenting condition is likely to represent the end of the spectrum for poor renal function and lung development.

In our study, the most common diagnosis associated with antenatal detection of a distended bladder was PUV (40% of all cases and 45% of persistent cases). This was slightly lower than the proportion (57%) reported by Taghavi, et al. [6,7] This difference could have been because we reported isolated PUV, separate from associated abnormalities.

As suggested by antenatal USS findings, the actual incidence of chromosomal or genetic association is likely to be higher than the 6% reported. Nevertheless, due to declining postmortem examination and genetic analysis of the fetal sample by parents, this could not be confirmed in all suspected cases. We also found that megacystis appeared to be part of much more complex anatomical malformations in some cases rather than a sign of an isolated LUTO. Prune belly accounted for 2% in our series (4% in the systematic review) [7]; however, again, this value may be higher due to the cases of 'multiple abnormalities' where a postmortem was declined [8].

In the retrospective study by Bernardes, et al. [9], the importance of a susceptibility test for PUV is discussed. It was concluded that prenatal diagnosis of PUV, based on Longitudinal Bladder Diameter (LBD), bladder wall thickness, and the presence of the 'keyhole' sign, was compassionate (94%) but

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had a low specificity (43%). In our series, three VUR cases were noted as the confirmed postnatal diagnosis. In all three cases, the bladder was seen to be enlarged antenatally, and in one, it was confirmed postnatally. Three cases of a duplex collecting system were identified with the associated ureterocoele leading to obstruction and distended bladder antenatally.

In the systematic review by Taghavi, et al. [7] in approximately 36.5% of cases, there is no definitive diagnosis. It could be postulated that other urinary tract abnormalities, such as those observed in this study, often present as distended bladder on prenatal scans or simply transient distension without any clear pathology. Cases of VUR, MCDK as well as some of neurogenic nature were observed in our study population.

In the systematic review by Taghavi, et al. [7] it was concluded that, overall, approximately 50% of foetuses with megacystis are terminated, and it was mentioned that this varies in different parts of the world. In our study, the rate of termination was 28% (including foetuses in whom megacystis resolved spontaneously in utero).

A retrospective study by Sarhan, et al. [10] concluded that early presentation was viewed as a poor prognostic indicator and alluded to more severe obstruction; in our study, we looked specifically at PUV as an outcome. The results from our study are in keeping with this conclusion [10]. The finding of those presenting in later pregnancy resulting in minor degrees of obstruction, with a higher survival rate, was noted in our study, where 85.7% of patients presenting in the 3rd trimester had a live birth [11].

We also noted the role that measuring Amniotic Fluid Volume (AFV) played in assessing prognosis. In cases where oligohydramnios or anhydramnios was reported on the first presentation, TOP was often advised (50% and 66.7%, respectively); in fact, none of the foetuses with anhydramnios in whom the pregnancy was continued survived. The AFV used in conjunction with other factors, especially GA age at presentation, are helpful indicators of prognosis. Various studies have shown that oligohydramnios predicts poor outcomes in more than 80% of cases filed [1,2,12].

Opting to report on renal function in the neonatal period primarily and beyond, particularly progression to CKD and ultimately kidney transplant, in our study, we identified three individuals who developed CKD and eventually required a kidney transplant (10.7%). This number is lower than that reported in many other studies looking at the outcome of prenatally detected PUV. This could be explained by including all causes of the distended bladder in our research. In four cases where severe LUTO occurred, bilateral renal damage led to acute renal failure. In two cases of ARF, renal function recovered. The ultrasound findings for infants with PUV showed that, most commonly, where hydronephrosis occurred, it was bilateral (69.2%), as would be expected with LUTO. Echogenic changes were observed in 3 individuals with PUV, and two patients with these changes progressed to CKD. These results demonstrate that despite hydronephrosis and even unilateral renal damage, renal function can recover when appropriate care is given. A study by Bilgutay, et al. [13] examined risk factors for progression to renal failure in infants with PUV. They found that antenatal diagnosis, abnormal renal cortex, and loss of corticomedullary differentiation on first renal USS were associated with CKD and end-stage renal disease [13]. Indeed, in our study, two of the three PUV patients presenting with echogenic changes progressed to CKD.

To report long-term outcomes, a longer follow-up period would provide a better idea of the renal function of infants. The study by Trellu, et al. [14] followed up on all patients over seven years. However, they stated that renal function at one year was perhaps the best predictor for renal outcome [14]. In our study, we identified three individuals (10.7%) whose renal function declined to the extent of necessitating a kidney transplant. The study by Sarhan, et al. [10] reported that Chronic Kidney Disease (CKD) developed in 19% of antenatally diagnosed PUV cases [14]. CKD and ultimately kidney transplants occurred in 15.4% of PUV cases.

It was also difficult to ascertain the effect of fetal intervention, i.e., shunting, on survival rates in this study. Only a small number of infants (5) in our study were shunted, with several having multiple shunts placed. Only one of five foetuses died prenatally, and another died in the neonatal period. The three remaining foetuses became live births. They survived into infancy, with one showing a pathology other than PUV postnatally and the final two undergoing postnatal management for PUV.

Our study's strengths are that all cases of distended bladder detected on antenatal scans from the first to the third trimester were included. We have obtained complete information regarding the postnatal outcome of these cases because of data accessibility due to linked fetal-neonatal databases. Our study's limitations are that the numbers are small, but the outcome information was complete for the cases included in the study. However, for some cases we were only able to state a prenatal diagnosis based on ultrasound findings, we know that interpretation based purely on antenatal imaging may of course be incorrect and in many cases, findings of LUTO may be part of genetic disorders of smooth muscle dysfunction or bladder denervation. In several cases, post-mortem and indeed genetic testing were declined.

This study could be extended into a more extensive multicentred project, where the long-term outcomes may be prospectively collected by linking maternal-fetal-neonatal-pediatric outcomes through the creation of linked databases. Furthermore, we also acknowledge that the exclusion of cases who did not deliver at St. Thomas' (those lost to follow-up), is a significant limitation meaning that many of the less severe pathologies are not represented in the postnatal outcomes. The findings of this study help us to further understand the prognosis and likely course of disease progression, which ultimately enables parents to make informed decisions about continuing their pregnancy or prepares them for issues infants may experience postnatally.

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Conclusion

The main findings of this study suggest that presentation in early pregnancy is more likely to result in TOP (60%), particularly when associated with oligo/anhydramnios. Survival was most likely in those presenting in late pregnancy (85.7% livebirth presenting in the 3rd trimester) with normal AFV. PUVs are the most common cause of megacystis, accounting for approximately 40% of cases. However, we also noted that megacystis was a feature of a multisystemic abnormality in at least 6 patients (11.8%). In approximately 50% of infants, a thick-walled bladder was observed on postnatal USS, potentially impacting bladder function. CKD occurred in three patients (10.7%), necessitating a renal transplant.

Acknowledgment

We would like to thank the team at Guy's and St Thomas' NHS Trust who cared for these patients.

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Bulleted statements

What's already known about this topic?

- Ultrasound can identify an enlarged fetal bladder from the 10th week of gestation,
- This condition is relatively rare.
- Enlarged bladders are most commonly caused by posterior urethral valves in males and urethral atresia in females.
- The condition may lead to severe complications like renal parenchymal maldevelopment and early pregnancy renal anhydramnios, which can cause pulmonary hypoplasia in newborns.

- What does this study add?

- This 15-year retrospective cohort study provides long-term outcomes for foetuses with antenatally detected enlarged bladders.
- It reveals that foetuses diagnosed in the second trimester predominantly had posterior urethral valves as the cause.
- Among survivors, about 1 in 10 developed chronic kidney conditions requiring renal transplant.
- The study also provides nuanced statistics on terminations, stillbirths, and live births, as well as postnatal surgical interventions and renal or urological follow-up.

Data availability

The raw datasets generated during the current study are not publicly available because it is possible that individual privacy could be compromised. It is possible to apply for permission to obtain access to the raw anonymised data through the corresponding author.

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