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# Fetal Megacystis: Experience of a Single Tertiary Center in Switzerland over 20 Years

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**Key Words**
Megacystis · Lower urinary tract obstruction · Fetal therapy · Vesicoamniotic shunting · Urinary biochemistry · Prune belly syndrome

**Abstract**
***Objectives:*** Megacystis (MC) is rare and often associated with other structural and chromosomal anomalies. In euploid cases with early oligohydramnios, prognosis is poor mainly due to pulmonary hypoplasia and renal damage. We report our experience of the past 20 years. ***Methods:*** A retrospective review of cases with prenatally diagnosed MC was performed. Complete prenatal as well as postnatal medical records from 1989 to 2009 were reviewed focusing on diagnostic precision, fetal interventions [vesicocentesis (VC), vesicoamniotic shunt (VAS)], short- and long-term outcome, and potential prognostic factors. ***Results:*** 68 cases were included. Follow-up was available in 54 cases (9 girls and 45 boys including 3 cases with aneuploidy). We found 39 isolated MC at sonography (5 girls and 34 boys). 24 fetuses with isolated MC underwent VC and VAS at 19.6 ± 6.3 and 20 ± 4.9 weeks of gestation, respectively. Survival rate was higher in male than in female fetuses (51 vs. 33%). Renal problems occurred in 4/14 prenatally treated fetuses and in 1/10 when cases with prune belly syndrome (PBS) were excluded from the analysis. ***Conclusions:*** Our study shows that a careful selection of cases with MC excluding fetuses with PBS and early treatment has still the potential to improve outcome.



## Introduction

Overall urogenital anomalies are the most frequent pathologies encountered prenatally with an incidence of 3–4%. On the contrary, megacystis (MC) is rare and often associated with other structural and chromosomal anomalies. The leading cause of MC is a lower urinary tract obstruction (LUTO) due either to urethral atresia, stenosis or posterior urethral valves (PUV) (fig. 1–3). Other possible etiologies such as megacystis-microcolon-intestinal hypoperistalsis syndrome (MMHS), prune belly syndrome (PBS) without PUV or primary MC are challenging to diagnose prenatally. PUV has an incidence of 1/25,000–1/8,000 deliveries and is one of the possible causes of LUTO and responsible for 4% of perinatal deaths [1]. In case of second-trimester oligohydramnios the perinatal mortality rate without therapy approaches 90–95% [2–4]. This is due to the increased pressure within the urogenital tract, which induces renal injury. On the other hand, the incapability to void bladder generates ol-

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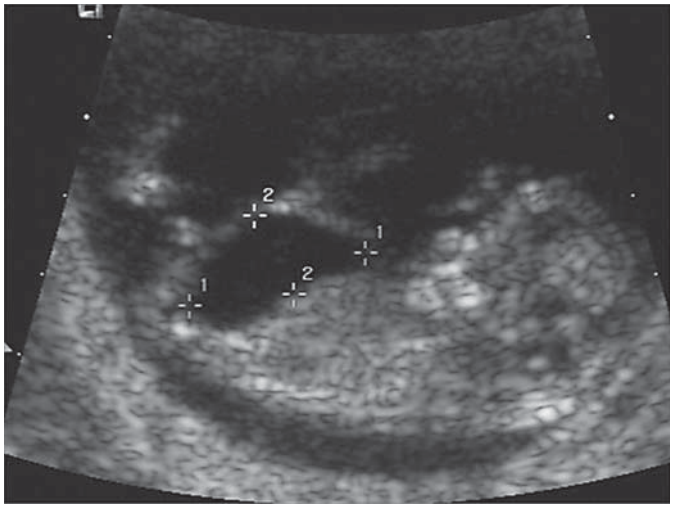

**Fig. 1.** MC at 12 weeks of gestation.

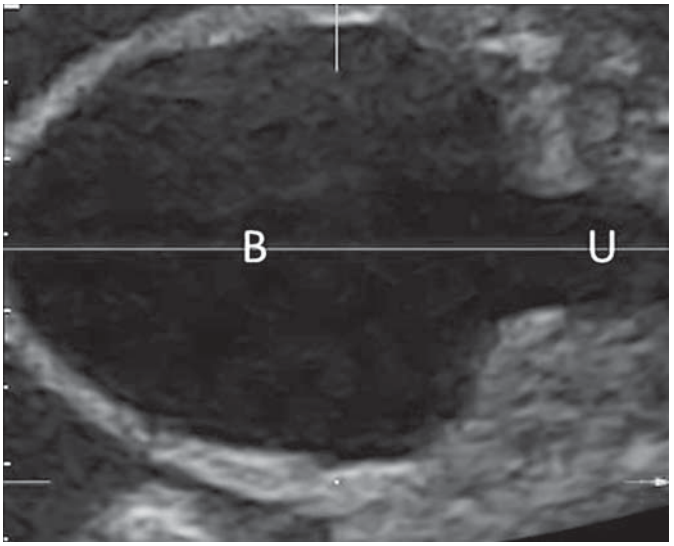


**Fig. 2.** MC (B) with dilated urethra (U) because of LUTO at 24 weeks of gestation.

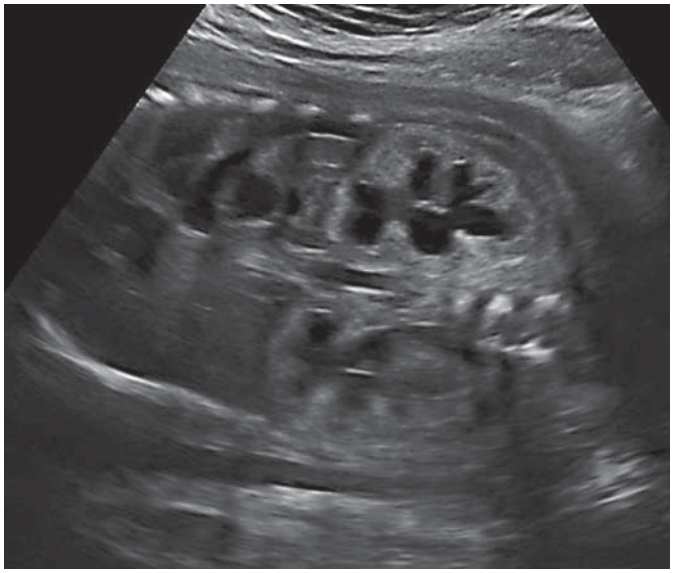

**Fig. 3.** Echogenic hydronephrotic kidneys in a fetus with MC and urine ascites after VC at 24 weeks of gestation.

igohydramnios leading to pulmonary hypoplasia. Moreover, gestational age at diagnosis and the severity and type of obstruction influence also the outcome, as well as the type of prenatal intervention – although the latter is under considerable debate [5–7]. If neonates survive, renal failure, voiding disorders, failure to thrive and infertility are common causes of morbidity [8]. Some studies [5, 7, 9] suggest that a bladder decompression before 20 weeks of gestation may reduce mortality and morbidity. Indeed, we have to restore amniotic fluid before the end of the canalicular stage of the lungs (24 weeks) in order to prevent pulmonary dysplasia, which is one of the leading causes for mortality in otherwise normal fetuses [5, 6, 10]. The second reason is the possible reversibility of renal damage by restoring normal pressure within the urinary tract. Of note, the number of glomeruli is higher if the release of pressure happens earlier [5, 7, 9]. However, invasive prenatal interventions such as vesicocentesis (VC) and vesicoamniotic shunt (VAS) are temporary solutions, while newer techniques such as fetal cystoscopy could have the potential to definitively remove the obstacle in cases with PUV [11–13]. Moreover, the true etiology of MC cannot always be accurately defined prenatally. Therefore, careful postnatal examination (autopsy included) is important to increase our understanding about this particular pathology and helping us in better counselling our patients. Fetal cystoscopy could indeed improve both diagnosis and treatment [12–14], but is unfortunately not always available even in tertiary care centers. Moreover, this method has a longer learning curve and is associated with more complications (death, ascites) than VC or VAS [12]. We report on our experience over the last 20 years about our clinical approach and management in case with MC.

## Material and Methods

Computerized obstetrical and uropediatric databases were searched for fetuses and neonates with MC and LUTO diagnosed between 1989 and 2009. Cases with complete prenatal as well as postnatal information were included. Diagnostic criteria for MC are different depending on gestational age. In the first trimester, MC is diagnosed if the longitudinal bladder diameter is >7 mm while in the second and third trimester this diagnosis was based on a distended bladder (>P95) [15] with hydronephrosis and/or oligohydramnios (deepest vertical pocket <2 cm). In our institution a persistent bladder diameter of ≥5 cm is considered pathologic too. Hydronephrosis is defined as dilated pyelon ≥5 mm [2] (≥3 mm in first trimester [16]) in the second and third trimester and in our institute staged according to additionally enlarged calyces and/or reduced or hyperechogenic renal parenchyma. Our institutional classification is similar to the one used by the Society of Fetal Urology [17] and has not changed during the study period. Parents were offered karyotyping. Because the MC by female fetuses is frequently associated with urethral atresia, MMHS and other severe malformations, we excluded female fetuses from prenatal therapy. If a euploid male fetus was found, further invasive investigation was discussed to differentiate which fetus may beneficiate or not from prenatal therapy such as VAS. VAS was offered if after serial VC normal urinary biochemistry was found [excluding the results from the first VC; $Na^+$ (mmol/l) <95th percentile for gestational age, $Ca^{2+}$ <2 mmol/l] [18] and no spontaneous voiding occurred. Rarely, VAS was chosen because of parents' request after extensive counselling. All these prerequisites for prenatal intervention have not changed during the observed period. For VAS we used the Rodek double pigtail catheter (Rocket, London, UK) placed under sonographic guidance and local anesthesia. To improve image quality and in particular to improve the placement of the catheter, an amnion infusion with normal saline at body temperature through a 20-gauge needle is given in cases with oligo- or anhydramnios.

The aim of the present study was to present and critically discuss our experience and as well as the short- and long-term outcome of cases which received fetal therapy (VC or VAS). Statistical analyses were performed with GraphPad Prism version 5.0 for Windows (GraphPad Software, San Diego, Calif., USA). Proportions were analyzed using the $\chi^2$ test or ANOVA. Statistical significance was considered when $p < 0.05$. The study was approved by the local Ethical Committee (Kantonale Ethikkommission Bern).

## Results

During the study period, 68 fetuses with MC were included. 14 cases were excluded because they were lost to follow-up. The characteristics of the study population are depicted in tables 1 and 2. Mean gestational age at diagnosis was 20 weeks (range $10^{4/7}$–$39^{4/7}$); 9 fetuses were female and 45 male. The prevalence of chromosomal abnormalities was 3/54 (5.6%). 19 cases had oligo- or anhydramnios and 26 cases showed hydronephrosis, while 7 had signs of renal dysplasia or hypoplasia. 39 cases had isolated MC, 5 female fetuses and 34 male fetuses. A VAS was performed in 13/34 (38.2%) normal male fetuses. Mean gestational age at first VC and VAS was 19.6 ± 6.3 and 20 ± 4.9 weeks, respectively. VC was performed between 1 and 4 times per case. Mean sodium concentration after first VC (27 cases) was 106.8 ± 23.9 mmol/l and mean calcium concentration was 1.9 ± 0.6 mmol/l. Fetal shunting was in place for a mean duration of 14.7 weeks (range 1.1–24.2). The main complications of VAS were dislocation which occurred in 69% of cases followed by urine ascites (3 cases), iatrogenic laparoschisis (2 cases), 1 case of chorioamniotic separation with amniotic fluid leakage (spontaneous resolution), and 1 failure of insertion due to technical problems.

Among the 9 female fetuses, 4 presented associated anomalies of which 1 underwent an autopsy and demonstrated urethral atresia in the context of complex urogenital malformation. One had a spontaneous resolution but showed a hydrocephalus. Of the 5 female fetuses with isolated MC, 2 survived and had a spontaneous in utero resolution. One was found to have a cloacal malformation with stenosis of urethra. Of the 2 last females, we do not know the final accurate diagnosis.

Among the 45 male fetuses, 11 (24%) presented prenatally associated anomalies, of whom only 2 survived. The first neonate was found to have cerebral abnormalities (corpus callosum hypoplasia) and the second one had a coarctation of the aorta. For the remaining 9, 3 had aneuploidy. Two fetuses had an autopsy; one showed a PBS with urethral stenosis in the context of cloacal malformation, and 1 fetus was suspected of having an omphalocele-cloacal exstrophy-imperforate anus-spinal defect (OEIS). We have no accurate postnatal diagnosis for the remaining 4 fetuses.

34 male fetuses were considered to have isolated MC. 10 received no treatment and 24 underwent VC/VAS. Of the 34 cases, 21 survived and 13 died or the parents opted for termination of pregnancy (TOP). The survival rate was 7/10 (70%) in case of no treatment and 14/24 (58%) after treatment (VC and VAS) and 7/13 (54%) after VAS. If we exclude TOP (6 cases) or spontaneous resolution (3 cases), then this survival rate changed as follows: 4/7 (57%), 14/18 (78%) and 7/10 (70%), respectively. 16 fetuses were operated for PUV; 1 presented a hydronephrosis without PUV and 1 a PBS in the context of amniotic band syndrome. Among the 13 non-surviving fetuses, we had performed only three autopsies, which showed one urethral atresia with cloacal malformation, one urethral stenosis and one PBS without PUV. No accurate final diagnosis was available in 10 cases.

**Table 1.** Cases without prenatal intervention

| Case No. | GA at first diagnosis | Karyotype | Associated anomalies | Procedure | Postnatal confirmation |
|---|---|---|---|---|---|
| 1 | $12^{1/7}$ | XY | None | Spontaneous resolution | Normal |
| 2 | $12^{4/7}$ | XY | None | Spontaneous resolution | Normal |
| 3 | $13^{0/7}$ | XY | None | Spontaneous resolution | Normal |
| 4 | $13^{0/7}$ | XY | None | Missed abortion | No information |
| 5 | $26^{1/7}$ | XY | None | Death at birth | No information |
| 6 | $28^{0/7}$ | XY | None | Birth at term, operation for PUV | PUV. Hydronephrosis, megaureter, vesicoureteral reflux, transitory renal failure |
| 7 | $30^{0/7}$ | XY | None | Birth at $36^{6/7}$ GW, operation for PUV | PUV. Associated anomaly: hypoplastic ear. Secondary diurnal enuresis |
| 8 | $33^{0/7}$ | XY | None | Birth at $33^{6/7}$ GW, operation for PUV | PUV. Associated anomaly: gastroesophageal reflux with operation at 6 days of life. Vitiligo |
| 9 | $34^{5/7}$ | XY | None | Birth at term, operation for PUV | PUV. Urinary infection, at 5 years: laser resection of suburethral stenosis |
| 10 | $35^{2/7}$ | XY | None | Death at birth | No information |
| 11 | $12^{1/7}$ | XY | Associated anomalies: increased nuchal translucency, microcephaly and pericardial effusion at sonography. Hypoplasia of the corpus callosum | Spontaneous resolution | No information |
| 12 | $12^{2/7}$ | XY | Hydrops and cyst of umbilical cord | Missed abortion | No information |
| 13 | $14^{3/7}$ | XY | Associated anomalies: sacral regression syndrome with sacral dysgenesis and thoracal hypoplasia | TOP | No information, possible VATER association |
| 14 | $14^{4/7}$ | XY | SUA | TOP | PBS at autopsy with cloacal malformation associated with urethral stenosis, renal dysplasia, imperforate anus and single umbilical artery |
| 15 | $39^{4/7}$ | XY | Asymmetric cardiac cavities | Birth at term, ablation of a sediment in the pyelon | Hydronephrosis, urinary infection. Associated anomalies: aorta coarctation |
| 16 | $10^{4/7}$ | XX | None | TOP | No information |
| 17 | $15^{6/7}$ | XX | None | Spontaneous resolution | Normal |
| 18 | $26^{0/7}$ | XX | None | Death | No information |
| 19 | $31^{4/7}$ | XX | None | Death at birth | Cloacal malformation including anal atresia, hydronephrosis with polycystic kidney, associated with heptadactyly and club-foot |
| 20 | $33^{6/7}$ | XX | None | Spontaneous resolution | Normal |
| 21 | $13^{4/7}$ | XX | MC in continuity with allantois | Death | No information |
| 22 | $15^{1/7}$ | XX | Lumbar scoliosis, suspicion of urinary and skeletal abnormalities | TOP | Aplasia of the external urethral ostium, the vagina, the uterus, the anal canal and the right lung. Hypoplasia of the left lung and the both kidneys. Low-set ears, short neck and thorax, lumbar scoliosis, club-hand and short fingers, face and neck edema |
| 23 | $20^{0/7}$ | XX | Abnormality without precision | TOP | No information |
| 24 | $31^{3/7}$ | XX | Hydrocephalus, IUGR | Spontaneous resolution | Associated anomalies: hydrocephalus, IUGR, consanguinity |
| 25 | $11^{0/7}$ | 47, XY+18 | Subcutaneous edema, cyst of umbilical cord | TOP | No information |
| 26 | $12^{6/7}$ | 47, XXY | SUA | TOP | No information |
| 27 | $18^{4/7}$ | 47, XY+21 | Plexus choroid cyst | TOP | No information |

GA = Gestational age; GW gestationnel weeks; IUGR = intra uterine growth restriction; PBS = prune belly syndrome; PUV = posterior urethral valves; SUA = single umbilical artery; TOP = termination of prengancy.

**Table 2.** Cases with VC and/or VAS

| Case No. | GA at first diagnosis, weeks | Karyo-type | Associated anomalies | Time between first diagnosis and VC, days | GA at VC | Time between first diagnosis and VAS, weeks | GA at VAS | Procedure | Final diagnosis and outcome | Complication of VAS |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 13 1/7 | XY | None | 8 | 14 2/7 | 3 6/7 | 17 | Operation for PUV | PUV, PBS, cryptorchidism, mild renal dysfunction, urinary infection, voiding disorder, hearing disorder | |
| 2 | 13 4/7 | XY | None | 4 | 14 1/7 | 1 4/7 | 15 1/7 | TOP | Cloacal anomaly with urachal cyst, no identified bladder, renal hypoplasia without cyst and urethral atresia | Dislocation |
| 3 | 13 5/7 | XY | None | 5 | 14 3/7 | 2 1/7 | 15 6/7 | TOP | Urethral stenosis with renal dysplasia and megaureter | Dislocation |
| 4 | 15 0/7 | XY | None | 1 | 15 1/7 | 5/7 | 15 5/7 | Operation for PUV | PUV | |
| 5 | 15 6/7 | XY | None | 0 | 15 6/7 | 6/7 | 16 5/7 | Renal transplantation | PUV, PBS, cryptorchidism, ESRD, inguinal hernia, failure to thrive | Dislocation and gastroschisis |
| 6 | 16 0/7 | XY | None | 4 | 16 4/7 | 6 6/7 | 22 6/7 | Death | Unknown | Dislocation |
| 7 | 16 1/7 | XY | None | 1 | 16 2/7 | 2 | 18 1/7 | Operation for PUV | PUV, PBS, cryptorchidism, mild renal dysfunction, voiding disorder, hypertension, mild hypertensive retinopathy, learning disorder | Dislocation |
| 8 | 17 2/7 | XY | None | 1 | 17 3/7 | 6/7 | 18 1/7 | Renal transplantation | PUV, ESRD, failure to thrive | |
| 9 | 18 2/7 | XY | None | 3 | 18 5/7 | 1 6/7 | 20 1/7 | TOP | No information | Dislocation |
| 10 | 18 3/7 | XY | None | 0 | 18 3/7 | 1 6/7 | 20 2/7 | Operation for PUV | PUV | Abdominal wall defect |
| 11 | 20 5/7 | XY | None | 0 | 20 5/7 | 1 4/7 | 22 2/7 | Death | No information | Dislocation |
| 12 | 21 4/7 | XY | None | 6 | 22 3/7 | 11 | 32 4/7 | Operation for PUV | PUV | Dislocation |
| 13 | 23 3/7 | XY | None | 3 | 23 6/7 | 1 4/7 | 25 | Death | No information | Dislocation, drained ascites |
| 14 | 13 0/7 | XY | None | 0 | 13 | – | | No operation | Hydronephrosis, normal bladder | |
| 15 | 15 5/7 | XY | None | 0 | 15 5/7 | – | | TOP | Renal dysplasia, megaureter, MC. No identified PUV. PBS? | |
| 16 | 16 0/7 | XY | None | 7 | 17 | – | | Intervention other than for PUV | Amniotic band syndrome, PBS, cryptorchidism, club foot and hypoplasia of right lower limb | |
| 17 | 16 6/7 | XY | None | 0 | 16 6/7 | – | | Operation for PUV | PUV | |
| 18 | 17 1/7 | XY | None | 0 | 17 1/7 | – | | Operation for PUV | PUV | |
| 19 | 18 0/7 | XY | None | 2 | 18 2/7 | – | | TOP | No information | |
| 20 | 19 3/7 | XY | None | 0 | 19 3/7 | – | | TOP | No information | |
| 21 | 25 0/7 | XY | None | 29 | 29 1/7 | – | | Operation for PUV | PUV, urinary infection, transitory renal insufficiency | |
| 22 | 31 1/7 | XY | None | 21 | 34 1/7 | – | | Intervention for PUV and other intervention | PUV, double kidney, mild stress urinary incontinence | |
| 23 | 33 1/7 | XY | None | 0 | 33 1/7 | – | | Operation for PUV | PUV | |
| 24 | 34 2/7 | XY | None | 1 | 34 3/7 | – | | Death | No information | |
| 25 | 13 2/7 | XY | SUA, abnormality of the posterior fossa, the cerebellum and the heart | 5 | 14 | – | | TOP | No information | |
| 26 | 17 1/7 | XY | Omphalocele | 6 | 18 | – | | TOP | Possible OEIS complex or body stalk anomaly. Hypoplasia of ureters | |
| 27 | 17 5/7 | XY | Hydrops, omphalocele, atrioventricular septal defect | 0 | 17 5/7 | 2/7 | 18 | Death at birth (33 weeks) | Possible VATER association. MRI (in utero 33 weeks): megacisterna magna, hypoplasia of aorta, pulmonary hypoplasia, hydrops fetalis with skin edema, pleural effusion and ascites, renal micro- and macrocysts, megaureter, thick wall of bladder, omphalocele, SUA. External postmortem only: prominent occiput, deformed nose, omphalocele | Dislocation |

ESRD = End stage renal disease; GA = gestational age; MC = megacystis; MRI = magnetic resonance imaging; OEIS = omphalocele-cloacal exstrophy-imperforate anus-spinal defect; PBS = prune belly syndrome; PUV = posterior urethral valves; SUA = single umbilical artery; TOP = termination of prengancy; VC = vesicocentesis; VAS = vesico-amniotic shunt.

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Short-term outcome is difficult to interpret and we are aware that statistical analysis is hazardous, firstly due to the small number of cases by group and secondly because of the non-randomized character of the study. Nevertheless, global survival rate by gender was 33% for girls (3/9) and 51% for boys (23/45). We analyzed the global survival rate of male fetuses after having stratified our results by gestational age (more or less than 20 weeks at diagnosis) and we found no statistical difference. Interestingly, all survivors of the group without treatment were diagnosed after 20 weeks and all survivors diagnosed before 20 weeks underwent treatment. We also analyzed the value of calcium and sodium in the group of male fetuses with isolated MC. In the group of cases who died, the mean urinary calcium concentration at first and second VC was higher (first VC 2.2 ± 0.2 mmol/l, second VC 1.9 ± 0.1 mmol/l) than that of fetuses who survived (first VC 1.7 ± 0.2 mmol/l, second VC 1.6 ± 0.2 mmol/l). However, this difference did not reach statistical significance. Similarly the mean sodium concentration at first and second VC was respectively 117.3 ± 4.2 and 101.9 ± 8.1 mmol/l in the group of non-survivors compared to 104.1 ± 6.7 and 94.40 ± 5.0 mmol/l in the group of survivors.

A median follow-up of 7.8 (range 1–16) years was available in 17 cases. 4 children (23.5%) showed renal malfunction. 2 cases (11.8%) developed end-stage renal disease necessitating transplantation and both also had failure to thrive. The other 2 boys suffered from mild renal insufficiency, 1 with hypertension. Interestingly, 3 out of 4 children with PBS presented renal problems. Other long-term findings were cryptorchidism (4 cases all associated with PBS), recurrent urinary tract infection (3 cases), inguinal hernia (2 cases), urinary incontinence (1 case), diurnal enuresis (1 case), voiding difficulty (2 cases), hearing disorder (1 case), and learning difficulty (1 case).

## Discussion

Our results underline the inherent difficulty to prenatally make a diagnosis and to predict the outcome of fetuses with MC. Furthermore, an important limitation of our study is the fact that only 7/28 (25%) of the cases who died or underwent TOP had an autopsy.

The prevalence of chromosomal and structural abnormalities in our cohort is similar to that published so far [19–25]. We have to underline that urethral pathology is different according to gestational age. Indeed, while in the first trimester, LUTO is mainly due to stenosis or atresia [20, 23, 26]; in the second or third trimester it (or LUTO?) is mainly due to PUV [8, 19, 25, 27, 28]. Another important etiology of LUTO is PBS, characterized by MC always associated with other malformations (urogenital tract and abdominal muscle hypoplasia). Three of our 4 cases who survived with PBS have developed mild to severe renal insufficiency. This observation is consistent with that of Biard et al. [29]. Conversely, Freedman et al. [4] found in their series a better outcome of neonates with PBS. Of note, none of our 6 cases were prenatally diagnosed as being affected by PBS. It has been reported that no keyhole sign and thin bladder wall associated with oligohydramnios may be a clue finding in PBS [30]. However, these sonographic signs are not specific enough as PBS cases associated with PUV have been already described [31]. Pathologic studies have demonstrated that these infants are also affected by abnormal prostate, seminal ducts, and vesicles. Unfortunately, these findings are not detectable prenatally [31]. Recently, it has been reported that PBS may be associated with a deletion of the hepatocyte nuclear factor-1β gene underlying the genetic cause of PBS [32–34]. We believe that fetuses with PBS represent a unique group and should probably not be considered for prenatal treatment, as there seems to be a general problem affecting different organ systems. In the future, specific genetic testing may help to clarify this diagnosis. A promising method to increase diagnostic accuracy seems to be fetal cystoscopy [12, 14, 35, 36]. It cannot only be used for diagnostic purposes but also as a treatment option especially when it is associated with laser [37]. In a systemic review by Morris et al. [35] this relatively new approach also reduces the risk of voiding disturbances in later life.

Prenatal treatment is still controversially discussed in the literature. Unfortunately, the only randomized study to date investigating the role of VAS in fetuses with LUTO has been stopped due to recruitment problems [19, 38]. Concerning urinary electrolytes, in our experience, the urinary calcium concentration seems of value in discriminating between cases with a better prognosis and those with a poorer one. Again, because of our small number of cases we do not reach sufficient power to have significant value. This point is also controversially discussed in the literature [6, 9, 19, 39–42].

Concerning long-term outcome, renal morbidity after prenatal interventions is an important subject for counselling. After intrauterine interventions, the incidence of chronic renal problems has been described as high as 62.5% [39, 43, 44]. Of those, up to 37.5% developed end-stage renal disease requiring transplantation [39, 43]. We

found only 23.5% with renal problems. This better outcome could be explained by the fact that gestational age at diagnosis and in particular at fetal treatment was lower in our study compared to the literature. Moreover, after excluding our PBS cases, the risk of renal problems after prenatal interventions dropped to only 10%.

In conclusion, our results show that a careful selection of cases with MC including urinalysis and early treatment but eventually with exclusion of cases with PBS may be a valuable option for parents. In the future we believe that genetic techniques, cystoscopy or perhaps MRI will be included in the decisional process.

## References


1 Schmidt S, Hofmann R, Tekesin I, Sierra F, Becker T: Operative fetoscopical management of intrauterine obstructive uropathia by urethral stent. J Perinat Med 2003;31:313–316.
2 Callen PW: Ultrasonography in Obstetrics and Gynecology, ed 3. Philadelphia, Saunders, 1994, pp 389–419.
3 Ruano R: Fetal surgery for severe lower urinary tract obstruction. Prenat Diagn 2011;31:667–674.
4 Freedman AL, Johnson MP, Gonzalez R: Fetal therapy for obstructive uropathy: past, present, future? Pediatr Nephrol 2000;14:167–176.
5 Harrison MR, Filly RA: The fetus with obstructive uropathy: pathophysiology, natural history, selection, and treatment; in Wonsiewicz MJ (ed): The Unborn Patient: Prenatal Diagnosis and Treatment, ed 2. Philadelphia, Saunders, 1991, pp 328–402.
6 Evans MI, Sacks AJ, Johnson MP, Robichaux AG 3rd, May M, Moghissi KS: Sequential invasive assessment of fetal renal function and the intrauterine treatment of fetal obstructive uropathies. Obstet Gynecol 1991;77:545–550.
7 Shimada K, Hosokawa S, Tohda A, Matsumoto F, Johnin K: Histology of the fetal prune belly syndrome with reference to the efficacy of prenatal decompression. Int J Urol 2000;7:161–166.
8 Freedman AL, Johnson MP, Smith CA, Gonzalez R, Evans MI: Long-term outcome in children after antenatal intervention for obstructive uropathies. Lancet 1999;354:374–377.
9 Daïkha-Dahmane F, Dommergues M, Muller F, Narcy F, Lacoste M, Beziau A, Dumez Y, Gubler MC: Development of human fetal kidney in obstructive uropathy: correlations with ultrasonography and urine biochemistry. Kidney Int 1997;52:21–32.
10 Morris RK, Malin GL, Khan KS, Kilby MD: Systematic review of the effectiveness of antenatal intervention for the treatment of congenital lower urinary tract obstruction. BJOG 2010;117:382–390.
11 Quintero RA, Shukla AR, Homsy YL, Bukkapatnam R: Successful in utero endoscopic ablation of posterior urethral valves: a new dimension in fetal urology. Urology 2000;55:774.
12 Welsh A, Agarwal S, Kumar S, Smith RP, Fisk NM: Fetal cystoscopy in the management of fetal obstructive uropathy: experience in a single European centre. Prenat Diagn 2003;23:1033–1041.
13 Ruano R, Duarte S, Bunduki V, Giron AM, Srougi M, Zugaib M: Fetal cystoscopy for severe lower urinary tract obstruction – initial experience of a single center. Prenat Diagn 2010;30:30–39.
14 Ruano R, Yoshisaki CT, Salustiano EM, Giron AM, Srougi M, Zugaib M: Early fetal cystoscopy for first-trimester severe megacystis. Ultrasound Obstet Gynecol 2011;37:696–701.
15 Maizels M, Alpert SA, Houston JT, Sabbagha RE, Parilla BV, MacGregor SN: Fetal bladder sagittal length: a simple monitor to assess normal and enlarged fetal bladder size, and forecast clinical outcome. J Urol 2004;172:1995–1999.
16 Whitlow BJ, Lazanakis ML, Kadir RA, Chatzipapas I, Economides DL: The significance of choroid plexus cysts, echogenic heart foci and renal pyelectasis in the first trimester. Ultrasound Obstet Gynecol 1998;12:385–390.
17 Society of Fetal Urology Grading of Infant Hydronephrosis. URL http://www.uab.edu/images/peduro/SFU/sfu_grading_on_web/sfu_grading_on_web.htm (accessed January 19, 2013).
18 Nicolaides KH, Cheng HH, Snijders RJ, Moniz CF: Fetal urine biochemistry in the assessment of obstructive uropathy. Am J Obstet Gynecol 1992;166:932–937.
19 Malin G, Tonks AM, Morris RK, Gardosi J, Kilby MD: Congenital lower urinary tract obstruction: a population-based epidemiological study. BJOG 2012;119:1455–1464.
20 Favre R, Kohler M, Gasser B, Muller F, Nisand I: Early fetal megacystis between 11 and 15 weeks of gestation. Ultrasound Obstet Gynecol 1999;14:402–406.
21 Liao AW, Sebire NJ, Geerts L, Cicero S, Nicolaides KH: Megacystis at 10–14 weeks of gestation: chromosomal defects and outcome according to bladder length. Ultrasound Obstet Gynecol 2003;21:338–341.
22 Jouannic JM, Hyett JA, Pandya PP, Gulbis B, Rodeck CH, Jauniaux E: Perinatal outcome in fetuses with megacystis in the first half of pregnancy. Prenat Diagn 2003;23:340–344.
23 Boissier K, Varlet MN, Chauleur C, Cochin S, Clemenson A, Varlet F, Bellicard E, Chantegret C, Patural H, Seffert P, Chêne G: Early fetal megacystis at first trimester: a six-year retrospective study. Gynecol Obstet Fertil 2009;37:115–124.
24 Peyrière MP, Roth P, Combourieu D, Vavasseur C, Bouvier R, Guibaud L, Gaucherand P: Aetiology and prognosis of prenatally diagnosed megacystis regarding gestational age at discovery. A six-year retrospective study (in French). Gynecol Obstet Fertil 2010;38:663–667.
25 Al-Hazmi H, Dreux S, Delezoide AL, Dommergues M, Lortat-Jacob S, Oury JF, El-Ghoneimi A, Muller F: Outcome of prenatally detected bilateral higher urinary tract obstruction or megacystis: sex-related study on a series of 709 cases. Prenat Diagn 2012;32:649–654.
26 Robyr R, Benachi A, Daikha-Dahmane F, Martinovich J, Dumez Y, Ville Y: Correlation between ultrasound and anatomical findings in fetuses with lower urinary tract obstruction in the first half of pregnancy. Ultrasound Obstet Gynecol 2005;25:478–482.
27 Lissauer D, Morris RK, Kilby MD: Fetal lower urinary tract obstruction. Semin Fetal Neonatal Med 2007;12:464–470.
28 Bornes M, Spaggiari E, Schmitz T, Dreux S, Czerkiewicz I, Delezoide AL, El-Ghoneimi A, Oury JF, Muller F: Outcome and etiologies of fetal megacystis according to the gestational age at diagnosis. Prenat Diagn 2013, 13:1–5.
29 Biard JM, Johnson MP, Carr MC, Wilson RD, Hedrick HL, Pavlock C, Adzick NS: Long-term outcomes in children treated by prenatal vesicoamniotic shunting for lower urinary tract obstruction. Obstet Gynecol 2005;106:503–508.
30 Osborne NG, Bonilla-Musoles F, Machado LE, Raga F, Bonilla F Jr, Ruiz F, Pérez Guardia CM, Ahluwalia B: Fetal megacystis: differential diagnosis. J Ultrasound Med 2011;30:833–841.
31 Stephens FD, Gupta D: Pathogenesis of the prune belly syndrome. J Urol 1994;152:2328–2331.
32 Decramer S, Parant O, Beaufils S, Clauin S, Guillou C, Kessler S, Aziza J, Bandin F, Schanstra JP, Bellanné-Chantelot C: Anomalies of the TCF2 gene are the main cause of fetal bilateral hyperechogenic kidneys. J Am Soc Nephrol 2007;18:923–933.

33 Murray PJ, Thomas K, Mulgrew CJ, Ellard S, Edghill EL, Bingham C: Whole gene deletion of the hepatocyte nuclear factor-1β gene in a patient with the prune belly syndrome. Nephrol Dial Transplant 2008;23:2412–2415.
34 Haeri S, Devers PL, Kaiser-Rogers KA, Moylan VJ Jr, Torchia BS, Horton AL, Wolfe HM, Aylsworth AS: Deletion of hepatocyte nuclear factor-1β in an infant with prune belly syndrome. Am J Perinatol 2010;27:559–563.
35 Morris RK, Ruano R, Kilby MD: Effectiveness of fetal cystoscopy as a diagnostic and therapeutic intervention for lower urinary tract obstruction: a systematic review. Ultrasound Obstet Gynecol 2011;37:629–637.
36 Morris RK, Kilby MD: Long-term renal and neurodevelopmental outcome in infants with LUTO, with and without fetal intervention. Early Hum Dev 2011;87:607–610.
37 Quintero RA, Johnson MP, Romero R, Smith C, Arias F, Guevara-Zuloaga F, Cotton DB, Evans MI: In-utero percutaneous cystoscopy in the management of fetal lower obstructive uropathy. Lancet 1995;346:537–540.
38 Morris RK, Malin GL, Quinlan-Jones E, Middleton LJ, Hemming K, Burke D, Daniels JP, Khan KS, Deeks J, Kilby MD: Percutaneous vesicoamniotic shunting versus conservative management for fetal lower urinary tract obstruction (PLUTO): a randomised trial. Lancet 2013;382:1496–1506.
39 Freedman AL, Bukowski TP, Smith CA, Evans MI, Johnson MP, Gonzalez R: Fetal therapy for obstructive uropathy: specific outcomes diagnosis. J Urol 1996;156:720–724.
40 Wilkins IA, Chitkara U, Lynch L, Goldberg JD, Mehalek KE, Berkowitz RL: The nonpredictive value of fetal urinary electrolytes: preliminary report of outcomes and correlations with pathologic diagnosis. Am J Obstet Gynecol 1987;157:694–698.
41 Johnson MP, Bukowski TP, Reitleman C, Isada NB, Pryde PG, Evans MI: In utero surgical treatment of fetal obstructive uropathy: a new comprehensive approach to identify appropriate candidates for vesicoamniotic shunt therapy. Am J Obstet Gynecol 1994;170:1770–1779.
42 Morris RK, Quinlan-Jones E, Kilby MD, Khan KS: Systematic review of accuracy of fetal urine analysis to predict poor postnatal renal function in cases of congenital urinary tract obstruction. Prenat Diagn 2007;27:900–911.
43 Holmes N, Harrison MR, Baskin LS: Fetal surgery for posterior urethral valves: long-term postnatal outcomes. Pediatrics 2001;108:E7.
44 Eckoldt F, Heling KS, Woderich R, Wolke S: Posterior urethral valves: prenatal diagnostic signs and outcome. Urol Int 2004;73:296–301.