

Evaluation of Fetoscopy Role in Fetal Surgery and Fetal Medicine

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Abstract

Introduction: This study aimed to evaluate, discuss and illustrate the role of fetoscopy diagnostically and therapeutically. **Material and Methods:** This study was conducted in private center in under the supervision of the professors of Azhar University, Egypt from Dec-2012 to Mar-2017. Women with confirmed fetal congenital malformations, and willing to do fetoscopy were recruited. Fetoscopy was attempted in all cases to treat the underlying fetal conditions. Follow up was made until delivery. **Results:** Twenty patients with 22 fetuses were included in this study with different congenital anomalies. Therapeutic drainage or coagulation was made in all cases. In cases of lower urinary tract obstruction, fetoscopy confirmed pre-suspected urethral atresia and changed the diagnosis from complete PUV to urethral atresia in some cases. The procedure succeeded in all cases. However, the on-going success rate was 17 (77.3%) of fetuses. The overall number of live birth was 11 fetuses (50%). Overall, 15 (75%) of the 20 patients experienced some complication with preterm labor the most prevalent 15 (75%). **Conclusion:** Fetoscopy can diagnose and differentiate between posterior urethral valve (PUV) and atresia, and manage well-selected cases of twin to twin transfusion syndrome (TTTS), and have a reasonable survival rate in lower urinary tract obstruction (LUTO).

Keywords

Fetoscopy, Lower Urinary Tract Obstruction, LUTO, Twin-to-Twin Transfusion Syndrome, Hydrocephalus, Hydrothorax, Sacrococcygeal Teratoma, Complications Rate

1. Introduction

During the last decades, the fetal surgery started to play a prominent role in the

diagnosis and management of different types of congenital anomalies [1]. Nowadays, the use of fetoscopy has been established all over the World. It is a growing research area that has many opportunities for the innovation of new techniques, new technologies for the management of congenital anomalies as well as for diagnosis [2] [3] [4] [5] [6]. Now, fetoscopic interventions are very effective for treating several fetal anomalies like lower urinary tract obstruction (LUTO), and sacrococcygeal teratoma (SCT) [7] [8].

Posterior urethral valves are considered to be the most common anomalies of the fetal urinary tract. They can lead to pulmonary hypoplasia, oligohydramnios, and even can be dangerous causing death. Drainage of the obstructed urinary tract and the restoration of amniotic fluid to its normal levels is a must in such cases to save their life. Vesico-amniotic shunting was initially made by open fetal surgery and now can be done percutaneously with good results which depend upon the selection of cases and the timing of the intervention [9].

Some fetuses have sacrococcygeal teratoma (SCT) and are susceptible to death in utero due to the hyperdynamic circulation resulted from the growing vasculature of the SCT resulting in hydrops from high output heart failure.

The blood flow to the SCT can be stopped efficiently using percutaneous radiofrequency ablation which has shown to be effective in saving the lives of fetuses. However, injury to the adjacent fetal soft tissues may occur [10] [11].

In monochorionic twin pregnancies, TTTS is a devastating complication, in which vascular connections in the placenta leads to the stealing of blood supply from one fetus to the other, eventually resulting in the death of both fetuses. Mortality in cases of TTTS is higher than 80%. However, fetoscopic laser ablation of the abnormal placental vessels can be a good option for those cases [12].

Egypt is a developing country with low resources and a high prevalence of congenital anomalies [13] [14]. Also, it lacks such technology and expertise. Thus, our research study is a trial to help with the introduction of this scientific development and to share our experience with the current World pioneers. Therefore, this case series study aimed to evaluate, discuss and illustrate the role of Fetoscopy in fetal medicine diagnostically and therapeutically.

2. Patients and Methods

The study was a case series study adopted the globally accepted standards of Good Clinical Practice and conformed to the national laws and regulations of the authors' institutions. The Local Ethics Committee approved the protocol. The study was carried out in a well-equipped private Obstetrics and Gynecology center in Cairo under the supervision of Azhar University, Egypt from December 2012 to March 2017. In total, 20 pregnant women more than 19 weeks of gestation with confirmed fetal congenital malformations by ultrasonography (Voluson B8, GE, USA), and willing to undertake fetoscopy, were included in this study. Exclusion criteria were: women who refused to participate; Rh-negative women, women with a medical disorder; women with any complications during the pregnancy like rupture of membrane or bleeding per vagina. The purpose of

this study was explained in Arabic to all women attending the center before their enrollment.

Fetoscopy was indicated in all cases as follows: In cases with LUTO, it was indicated to prevent renal hypoplasia, pulmonary hypoplasia, and oligohydramnios by therapeutic drainage of the bladder using shunt or fulguration of PUV. In cases with SCT, it was indicated to prevent cardiac failure due to hyperdynamic circulation by coagulation of the SCT vasculature. In cases with TTTS, it was indicated to prevent cardiac failure and/or neurological damage at the time of in utero death by coagulation of the anastomotic vessels between the twins. In cases with hydrocephalus, it was indicated to prevent neurological damage and in utero death by shunting and drainage. In cases with hydrothorax, it was indicated to prevent respiratory failure and in utero death by shunting and drainage.

All who enrolled provided written informed consent. All women underwent a detailed pre-anesthetic evaluation in the form of detailed obstetric history and examination. Then, we explained in details to the patient the idea of the intervention and its consequences. Blood samples for serum panel, coagulation profile, liver function, and kidney function. Ultrasonography was done to confirm the diagnosis and to find the fetal position, lie, comorbid conditions, and any pathology hinder the entry, besides, to localize the placental attachment, to do the intrauterine mapping and make a mark for entry. Pre-procedural assessment, simulation, was done to search for the best entry during the procedure.

All patients were sedated by midazolam 0.02 mg/kg IV. ASA-standard monitors were applied including ECG, oximetry, noninvasive blood pressure and capnography. Anesthesia was induced by fentanyl 2 mg/kg then propofol 2 mg/kg, and atracurium besylate 0.5 mg/kg to facilitate endotracheal intubation. Anesthesia was maintained by isoflurane 2% in 100% Oxygen. After patients' extubation and recovery, they were transferred to the Post-Anesthesia Care Unit (PACU) and observed for 30 minutes till full recovery, then, they were transferred to the ordinary ward. Blood pressure was kept at 80% of the baseline value for the sake of the circulation of the baby.

Before starting the study, the principal author along with two other co-authors traveled and met Prof. Kypros H. Nicolaides (Harris-Birthright Research Centre for Fetal Medicine, Department of Obstetrics and Gynecology; King's College Hospital Medical School). He explained the techniques that can be used to do the interventions successfully. Besides, he showed the authors the instruments, and where can they get them, and how can be used appropriately, and what the precautions of using these tools are. The principal author had hand-on training under the supervision of Prof. Kypros H. Nicolaides.

Semi-rigid 0° straightforward miniature endoscope (Karl Storz fetoscopes) ranging from 1 to 3.6 mm in diameter and is made of over 10,000 pixels and endoscope is connected to the focusing eyepiece. The needle-scope is connected to the 18 gauge "1.3 mm" trocar via a lateral female Lure-lock adaptor to enable the suction and irrigation procedure. Monitoring of the fetuses was done during and

after the process by US & Doppler (Fetal heart rate, umbilical artery Doppler).

2.1. Procedures and Follow Up

Ultrasound was performed to identify the fetal position as well as the placental site to mark the point of entry for the fetoscope. We introduced the trocar and cannula through a small 3-mm incision in the abdomen and uterine wall into the amniotic cavity under US-guidance, avoiding the placenta. Then, we removed the cannula and introduced the fetoscope through the trocar to visualize and examine the fetal face, limbs, abdominal wall, and umbilical cord insertion, the back... etc. Whenever possible, we investigated the placenta for vessels or any abnormalities. We noted the clarity of vision, intra-amniotic bleeding, or any procedural problems. Continuous ringer lactate amnioinfusion system was used to maintain the visibility while monitoring the volume infused. Each congenital anomaly was dealt with accordingly, and corrections of the underlying conditions were made in all cases. All cases were followed-up after one week, two weeks, and every two weeks till delivery.

2.2. Statistical Analysis

The primary outcome measure was the on-the-table success and the on-going success rates of Fetoscopy in correcting the underlying fetal conditions discussing the procedural problems faced in each condition.

The on-the-table success defined as the success on correcting the underlying condition in each case during the operation such as the success of placing a shunt and drainage to the amniotic fluid. The on-going success defined as the sustainability of the correction in the postoperative follow-up period.

All statistical tests were done using a significance level of 95%. SPSS software (Statistical Package for the Social Sciences, version 20.0, SSPS Inc., Chicago, IL, USA) was used for statistical analyses. The study was exploratory. Thus no sample size calculation was needed. Twenty cases with 22 fetuses, who came to the center during the period of the study, were included in this study.

3. Results

All women (40) who came to the center with a fetus having a congenital anomaly and eligible for Fetoscopy were asked to participate in the study. Six declined to participate. One patient was excluded because she did not meet the inclusion criteria and two have leakage or bleeding per vagina during pregnancy. Four have multiple congenital anomalies, and three have bilateral renal agenesis confirmed by Doppler US. Other four patients have severe hydrocephalus; leaving 20 participants involving 22 fetuses enrolled to in the study.

The mean age of patients was 27.3 ± 3.4 years with a range of (20 - 34). Seven patients (35%) had positive consanguinity. There was no significant association between congenital anomalies and consanguinity (p -value = 0.369). Six patients (30%) were primigravida and 14 (70%) multigravida. Fifteen of them (75%) had

no live children, 4 (20%) had one live child and one (5%) had two live children. Three patients (15%) had one normal vaginal delivery (NVD), and two (10%) had two NVD. Eight patients (40%) had one CS, and three (15%) had two CS. None of the cases have undergone ovulation induction or assisted reproductive technique. None of them have taken any specific medication known to cause congenital anomalies.

The fetus of eight patients (40%) had LUTO, five (25%) obstructive hydrocephalus, four (20%) hydrothorax, two (10%) TTTS and one SCT case (5%). The mean time for Fetoscopy was gestational week 23.8 ± 3.3 with a minimum of 19.0 and a maximum of 31.5 weeks.

Therapeutic drainage of hydrocephalus to the amniotic fluid by shunt was done in all cases of hydrocephalus, 5 (25%) and for all cases of hydrothorax, 4 (20%). Besides, fetoscopic coagulation of large vessels to SCT by bipolar forceps was made in one case (5%).

In LUTO cases, therapeutic drainage of the bladder to the amniotic fluid was done by fulguration and flushing in three cases (15%) and by shunt in 5 cases (25%). Besides, Fetoscopy had added value for changing the diagnosis in two cases with suspected complete PUV (10%) to be urethral atresia. Besides, in cases with TTTS, therapeutic laser photocoagulation of unidirectional arteriovenous vessels on the surface of the twin placenta was done in the two cases (10%). A coiled cord was observed around the leg causing congested vessels in one case (**Figure 1(a)**).

On-the-table, the fetoscopy succeeded in the correction of the anomaly in all cases. However, the on-going success rate of correction of the underlying fetal condition was (77.3%) 17 fetuses and recurrence occurred in (22.7%) of fetuses, as shown in **Table 1**. From 22 fetuses included in our study, one fetus died in utero within four days of the surgery, and four died after birth from complications of prematurity, with a mean interval of 12 weeks from the procedure. The overall number of live birth was 11 fetuses (50%). Their distribution according to the congenital anomalies is shown in **Table 1**.

Overall, 15 (75%) of the 20 patients experienced some complication. Although intra-amniotic bleeding was diagnosed in 4 (20%) of these patients, the bleeding was minimal and did not require blood transfusion or prolonged hospitalization. Rupture of membranes was diagnosed within two weeks of the procedure in 6 (30%) patients, and chorioamnionitis occurred in 2 (10%) patient. Preterm labor occurred in 15 patients (75%), as shown in **Table 2**.

4. Discussion

This study presents the first detailed information regarding endoscopic fetal surgery in Azhar University, Egypt completely by an Egyptian team. Our primary task was to evaluate its complications and its usage as a tool in a developing country with no big resources. The results of this case-series study showed that fetoscopy succeeded in the correction of the underlying conditions in all cases.

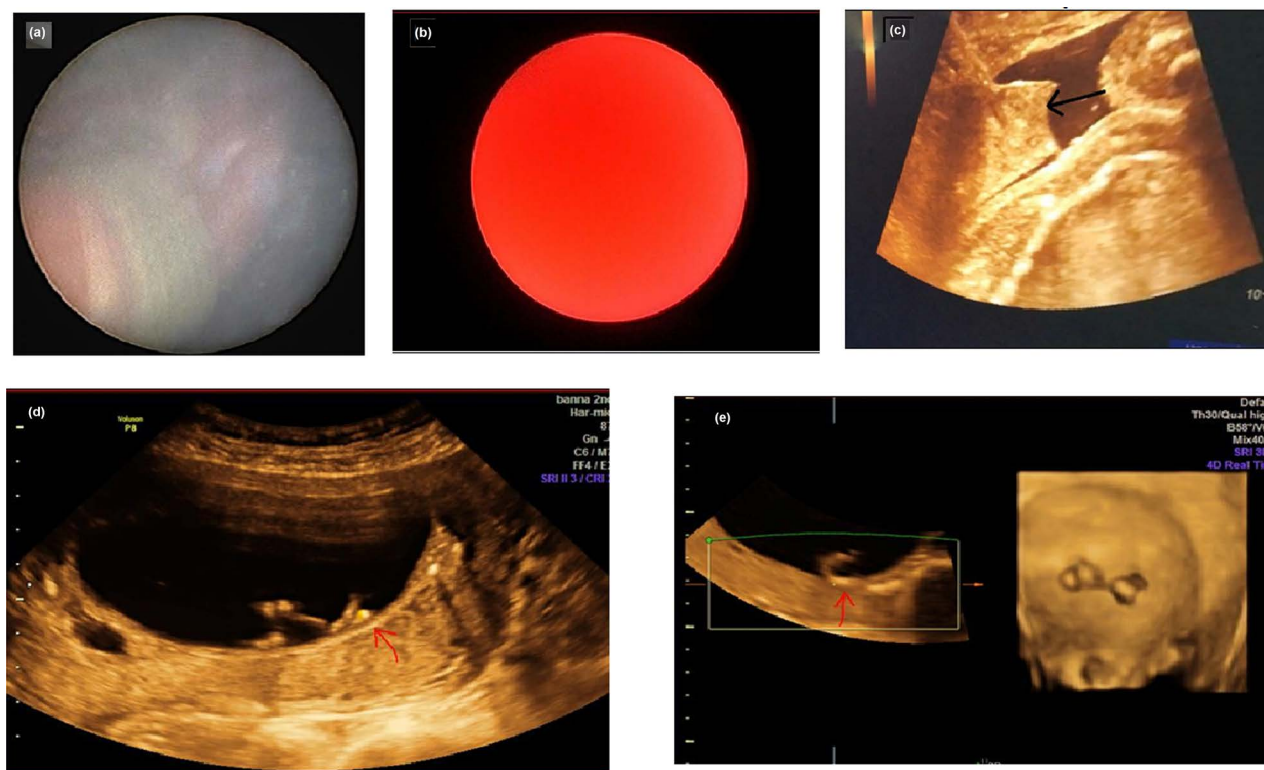


Figure 1. Fetoscopic images [(a): Umbilical cord around the fetus leg, (b) & (c): Bloody field and hematoma formation, (d) & (e): Catheter obstruction].

Table 1. The on-going success rate of Fetoscopy in each congenital anomaly.

	<i>On-going success rate</i>		<i>Recurrence</i>	<i>Live birth</i>
	n	n (%)	n (%)	n (%)
Hydrocephalus	5	4 (80%)	1 (20%)	3 (60%)
Hydrothorax	4	3 (75%)	1 (25%)	2 (50%)
LUTO ¹	8	5 (62.25%)	3 (37.75%)	3 (37.27%)
SCT ²	1	1 (100%)	0 (0%)	1 (100%)
TTTS ³	4	4 (100%)	0 (0%)	2 (50%)
Total number	22	17 (77.3%)	5 (22.7%)	11 (50%)

Fifteen patients experienced some complication. Patients must, therefore, be counseled regarding risks and benefits of endoscopic fetal surgery. The overall maternal safety was excellent in our study; however, the PROM and preterm delivery are the most frequent problems faced which is similar to that reported in the literature elsewhere [15] [16].

As fetal surgeries involve two or three patients simultaneously, some anesthesia challenges are there [17] [18] [19]. A substantial anesthesia challenge is the movement of the abdominal muscles of the mother during respiration. Thus, the

¹Lower urinary tract obstruction.

²Sacroccygeal teratoma.

³Twin to twin transfusion syndrome.

Table 2. Post-Fetoscopy complications.

	Number	Percentage
Preterm labor	15	75%
LUTO ⁴	5	25%
Hydrocephalus	5	25%
Hydrothorax	3	15%
TTTS ⁵	2	10%
Chorioamnionitis	2	10%
LUTO	1	5%
TTTS	1	5%
PROM	6	30%
LUTO	2	10%
Hydrocephalus	2	10%
Hydrothorax	1	5%
TTTS	1	5%

anesthesiologist must be aware of when to reduce the movement to help the fetoscopy surgeon to do the procedure. Occasionally, the uterus becomes highly flexible and moveable; hence we need to support it to enter through the right access. In our experience, anesthesia of the baby was not required. Moreover, obese patients with their thick abdominal wall were challenging when we penetrate with the trocar to reach the uterus. Some experts prefer to use local anesthesia because the patient is aware and can hold her breath which is very helpful during the procedure [20] [21] [22].

To those who never experienced to use fetoscopy, they may think it is like laparoscopy. You cannot navigate easily in fetoscopy. Thus, the point of access is critical and may be one point only to reach the targeted area. Sometimes, we do not have enough amniotic fluid. It is very hard to re-navigate during the fetoscopy. Thus, we have to stress on the mapping of the baby. Mapping means where the fetus is lying, its orientation to the mother and the access point to reach the target area that we are going to do the surgery. The difficult entry was in cases with no or low amniotic fluid in the second trimester. In most of the cases, the amniotic fluid was very turbid in; thus we cannot do fetal mapping easily without washing. However, the easiest entry was when polyhydramnios is present [16]. Hematomas happened when we entered close to the placenta. Once we had a bloody fluid, the vision is impossible (**Figure 1(b)** & **Figure 1(c)**). Here, the role of irrigation is vital. Ninety percent of the patients we worked have a turbid fluid. Thus, we made suction and irrigation in all of them. It has to be done carefully. The rate of suction must be equal to that of irrigation. Else,

⁴Lower urinary tract obstruction.

⁵Twin to twin transfusion syndrome.

rupture on the table can occur. That happened once during our cases. It happened that we succeeded to put a catheter to drain the bladder of the fetus, but the rupture of the membrane made it close (**Figure 1(d)** & **Figure 1(e)**), and the procedure failed, and serial bladercentesis had performed after that.

Good selection of cases is important in the management of hydrocephalus. We chose bilateral obstructive moderate cases. Fetoscopy helped to direct us under the vision and helped us to navigate until reach behind the ear without jeopardizing critical brain areas, and we could put a shunt in the proper site and adjusting it by a grasper under vision. Sometimes the head was impacted. Thus, we made external cephalic version (ECV) successfully to push it to the area with abundant amniotic fluid. In some cases, recurrence occurred. We recommend research to innovate flexible fetoscopy which is highly needed to enter endonasal in these cases.

In cases of hydrothorax, we used the fetoscope to search for the chest wall and see exactly the direction of the point that we will go through and put a shunt. The patients got immediate results. One disadvantage of doing US-guided shunting in hydrothorax is once you get a hematoma, you cannot do anything further. However, under fetoscopy, we are inside the action, and we can do a lot of washing and use graspers to make the shunt opens.

In cases of TTTS, the right way is the mapping and going from the sac of the recipient to the donor as the first has enough amount of the amniotic fluid. On reaching the separating membrane covering the donor, we traced and tackled the anastomotic vessels between the recipient to the donor. The treatment of TTTS by laser therapy has been investigated in several research studies which showed that fetoscopic laser coagulation of the chorionic plate vessels is the most effective treatment [16] [23] [24].

We have a late third-trimester case of large SCT with hyperdynamic cardiopulmonary effects. The baby was anemic as well as the mother. We found entirely turbid amniotic fluid with hairs in it; thus, we did amniotic wash and reached the cleavage between the SCT and the back of the baby. Sealing for the vessels by a fetoscopic bipolar device, was not 100% accurate. The tool is very successful in the surface vessels, not the deep ones.

In LUTO cases, drainage of the bladder to the amniotic fluid was successful by fulguration and flushing in three cases and by shunt in five cases. Recurrence was reported in three cases at 1 - 2 weeks due to blockage of the shunt passage in one case, and in the other two cases, the shunts openings were blocked by the uterine wall due to PROM and anhydramnios. Successful shunting in LUTO cases has been reported in other studies [25] [26] [27]. Also, the recurrence due to a migration of the shunt has been reported [25] [26]. In those cases of LUTO, the earlier the intervention; the better is the prognosis. Thus, selection of cases is an essential step as the bladder may become hugely enlarged and compresses the heart. Hydronephrosis develops rapidly and impacts the renal cortex. Sometimes, the high pressure in the hydronephrotic kidneys opens the obstruction

and drains the fluids from the bladder, and the process repeated. Proximal urethric obstruction may also be diagnosed as PUV and operated upon without any success [25]. However, in our series, we did not face this condition.

From our experience, the fulguration using the guide wire was very easy. In the case of atresia, we go back under the vision from the bladder wall, and we can see its closure under the fetoscopy and then the closure of anterior abdominal wall (Figure 2), and stick the shunts quickly with adjustment by graspers sometimes. Just after closure the bladder, we did the amniocentesis for anhydramnios babies in the right place which is very difficult to do under US guidance.

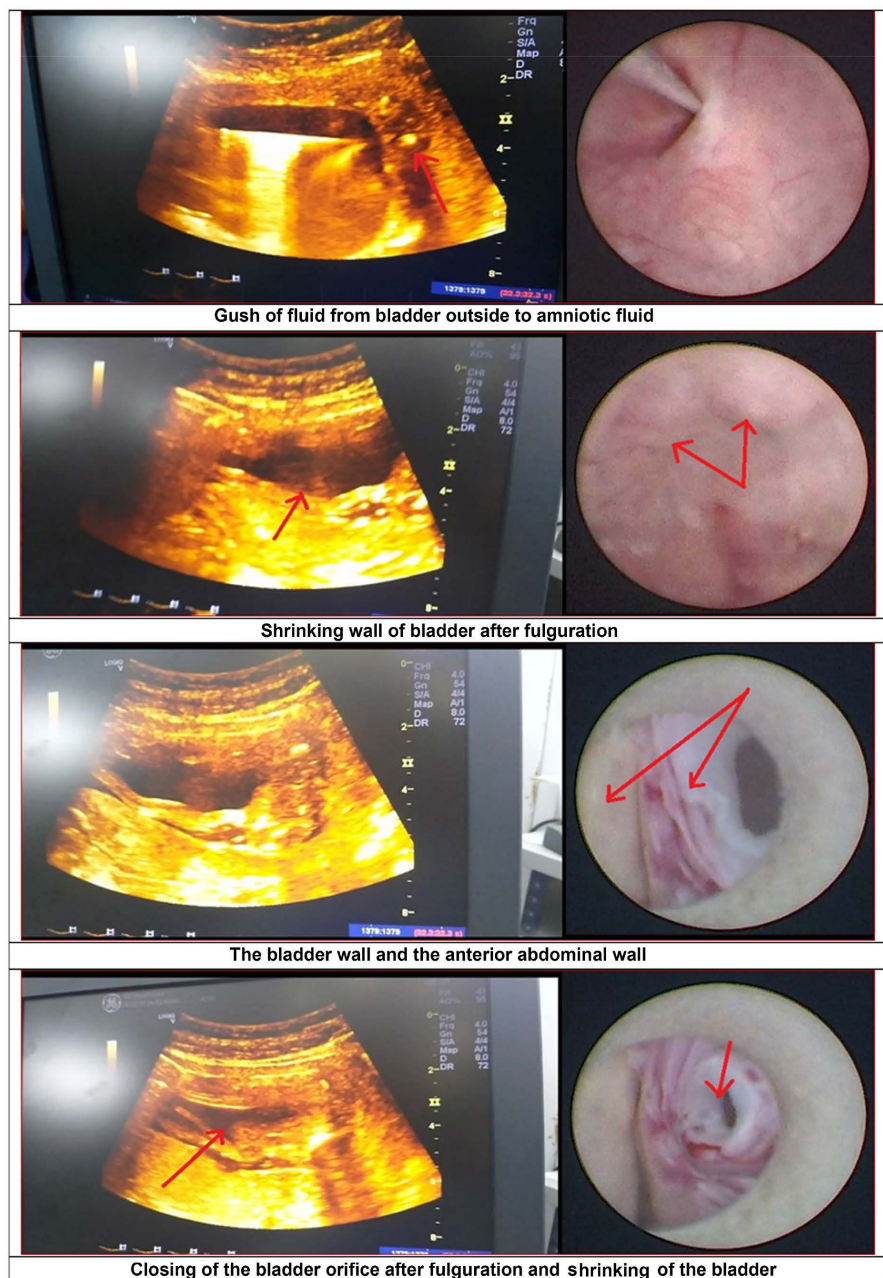


Figure 2. Posterior urethral valve (PUV): Steps of the procedure.

Besides, in PUV cases, fulguration by different tools; guide wires, graspers or laser; the achievement of urethral patency was immediately, and we can see the spell of the urine outside the bladder by the US and the bladder deflates its wall on fetoscopy, as shown in **Figure 2**. One of the best diagnostic sign for the fetoscopy in our study is the differentiation between PUV and atresia, which is consistent with other studies [25] [28].

Fetoscopy was very beneficial in one of our cases as we suspected cord anomaly by the US, but during fetoscopy, we can see a constricted coil around the fetal leg which was the reason behind the low blood flow (**Figure 1(a)**). Therefore, fetoscopy can help to confirm or disprove the diagnosis made by the US. However, this can be only made in early second trimester cases.

Although we have a small number of cases due to the nature of the study and the rarity of cases, we conclude from our study that fetoscopy is a safe tool. The overall maternal safety was excellent in our study. Fetoscopy was a safe tool for the cases. However, of course, it carries some risks to the mother and the fetus. We recommend conducting further detailed studies with a large sample for each indication in separate. In cases of hydrocephalus, we recommend doing new research studies for the innovation of flexible fetoscope appropriate for the endo-nasal route. Also, we recommend a multidisciplinary approach including the cooperation of pediatric neurosurgeons. In cases of LUTO, we recommend a further three-arm research study comparing the efficacy of laser, fulguration by wire or graspers, and shunting. In cases of TTTS, we recommend a further research study comparing the complete coagulation of the equatorial line (Solomn technique) versus the selective vessels coagulation technique. Finally, we recommend more studies in challenging entry such as in cases with the anterior placenta. We recommend comparing laparoscopic-assisted fetoscopy versus open surgery techniques.

5. Conclusion

Fetoscopy has the ability to diagnose and differentiate between PUV and atresia, and to manage well-selected cases of TTTS, and has a good survival rate in LUTO.

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Conflicts of Interest

All authors have no things to disclose.

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Condensation

In this study, we evaluated the Fetoscopy role in our region. It has shown to be a safe tool. Also, it has a powerful ability to diagnose and differentiate between diseases like PUV and atresia, and to manage some disease in well-selected cases such as TTTS, and have a good survival rate in LUTO cases.

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