Prenatally Diagnosed Congenital High Airway Obstruction Syndrome: Perinatal Management and Outcome—A Single Tertiary Care Center Experience

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Abstract

To report our experience with the management of prenatally diagnosed cases of congenital high airway obstruction syndrome (CHAOS) and the postnatal outcome of those who underwent an ex utero intrapartum treatment (EXIT) procedure. This is a single center, retrospective observational study of prenatally diagnosed CHAOS cases using two-dimensional ultrasound from December 2017 to December 2022 in a tertiary care facility. Of the total nine fetuses prenatally diagnosed with CHAOS, three (33.3%) were associated with multiple congenital anomalies, seven out of nine (77.8%) developed ascites, and one had fetal hydrops. Five (55.6%) underwent medical termination of pregnancy and two were lost to follow-up (22.2%). The remaining two continued pregnancy and required EXIT tracheostomy at the time of delivery (22.2%). Microarray was performed in both which was normal. Postnatally, both infants are tracheostomy dependent with one requiring frequent ventilator support. CHAOS even when isolated generally has poor prognosis without intervention. Performing an EXIT procedure at birth can significantly improve postnatal survival by minimizing hypoxic damage. However, the long-term medical and surgical challenges for survivors remain numerous especially speech disorders, even after lifesaving fetal intervention and surgical correction. Therefore, an accurate prenatal diagnosis is necessary to give the couple an option of continuing pregnancy after realistic counseling regarding the prognosis and postnatal outcome.

Keywords

- CHAOS
- prenatal diagnosis
- EXIT

Introduction

Congenital high airway obstruction syndrome (CHAOS) is a rare, lethal obstruction of the fetal upper airway due to deficient recanalization of the laryngotracheal tree at 10 weeks of gestation, first reported by Hedrick et al in the late 1900s.[1] It can either be complete laryngeal atresia, complete laryngeal atresia with an esophageal fistula, or a near-complete high upper airway obstruction. CHAOS is mostly sporadic with a reported incidence of 1/50,000.[2] The causes of CHAOS could be intrinsic, most commonly atresia or stenosis of the larynx or trachea, subglottic stenosis/atresia, tracheal or laryngeal web, completely occluding laryngeal cyst (rare), or extrinsic including

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lymphatic malformation, cervical teratoma, and vascular rings like a double aortic arch.[3]

Prenatal imaging recognition and evaluation of CHAOS have become increasingly important because of the recently described ex utero intrapartum treatment (EXIT) procedure aimed to improve the outcome by allowing safe airway control.[4] It is important to have a multidisciplinary involvement of the obstetrician, anesthesiologist, otolaryngologist, pediatric surgeon, and neonatologist for this type of procedure.[2] However, due to the rarity of the disease, only a few cases of CHAOS have been reported describing the postnatal management and long-term prognosis.[5,6]

This study aims to report our experience in CHAOS cases managed with the EXIT procedure and their postnatal follow-up.

Materials and Methods

This study is a retrospective observational study of all the prenatally diagnosed CHAOS cases on ultrasound (US) between December 2017 and December 2022 in the division of fetal medicine and perinatology in a single tertiary referral center.

Inclusion Criteria

1. All prenatally diagnosed CHAOS cases during the study period in the institution, detected by bilateral enlarged echogenic lungs, an everted/flattened diaphragm, and a dilated tracheobronchial tree on US (►**Fig. 1**).
2. And who had a postnatal follow-up of at least 6 months.

The US examination was performed using a GE Voluson E10 unit, using a transabdominal curvilinear transducer with a frequency of 3.5 to 5 MHz (C1-5-D) by a fetal medicine specialist. A detailed evaluation of fetal anatomy was done to rule out associated anomalies.

The institutional ethical committee approved the study and informed written consent was obtained from all women. All the patient details including maternal age, obstetric history, gestational age at diagnosis, results of prenatal imaging studies (fetal US and echocardiography), chromosomal studies, fetal management and surgical interventions, causes of airway obstruction, associated anomalies, maternal and fetal complications, clinical outcome and postnatal course including gestational age at delivery, birth weight, sex, mode of delivery, details of the EXIT procedure, duration

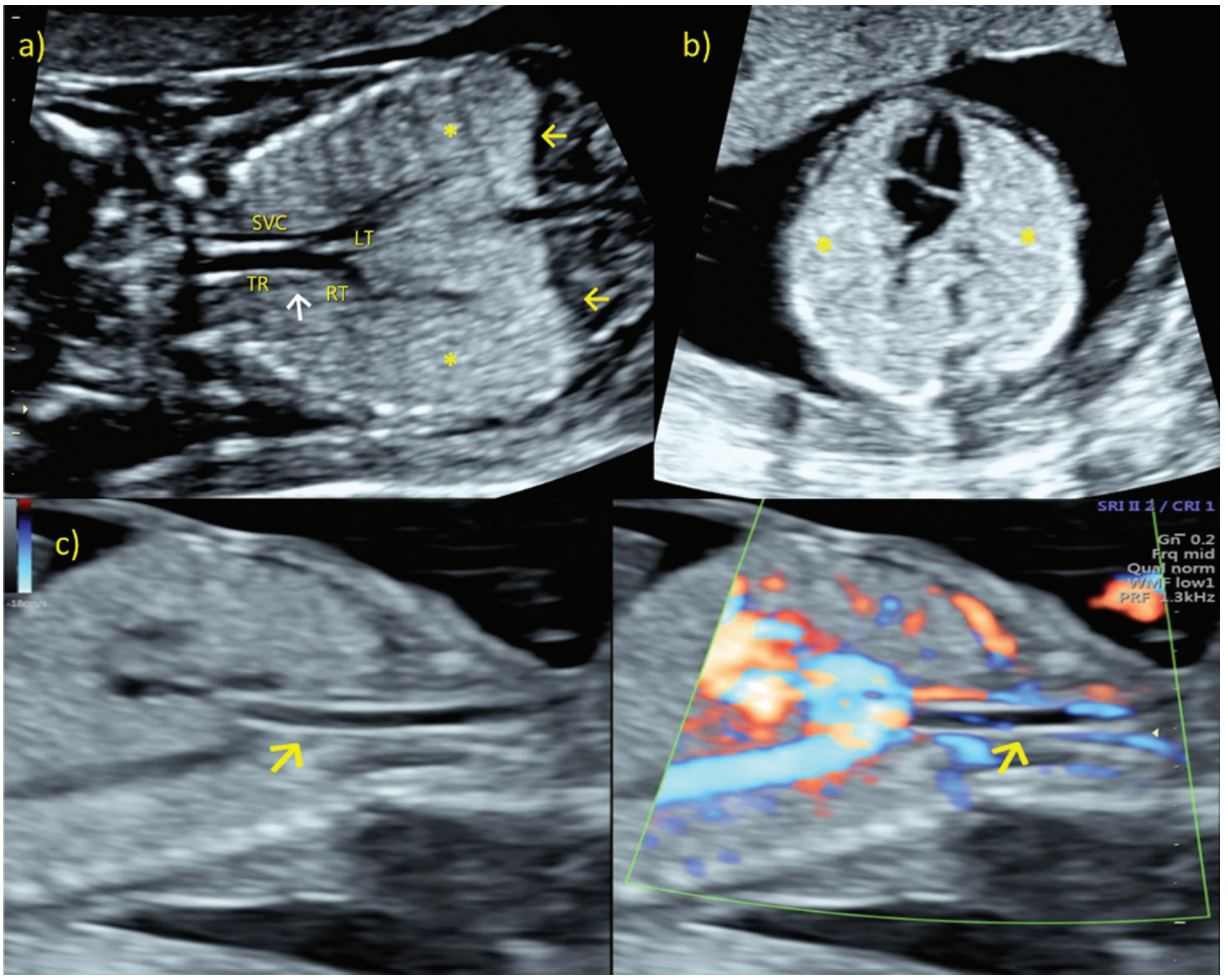

Fig. 1 US features of CHAOS. (**a**) Coronal section showing bilateral symmetrically enlarged ballooned out echogenic lungs (yellow asterisk), dilated trachea-bronchial tree (white arrow), flattened/everted diaphragm (yellow arrow). (**b**) Axial section showing bilateral symmetrically enlarged ballooned out echogenic lungs (yellow asterisk) with mesocardia. (**c**) Sagittal section—grayscale and color Doppler showing dilated trachea-bronchial tree (yellow arrow). CHAOS, congenital high airway obstruction syndrome; SVC, superior vena cava; TR, trachea; US, ultrasound.

of follow-up, and whether the surgical correction was performed were obtained from the hospital information system. Additional follow-up details were collected from the parents via telephonic interview. The demographic characteristics of the patients diagnosed with CHAOS in their fetuses with imaging details and outcomes of each are depicted in ►**Table 1**. All the families were counseled and managed by a multidisciplinary team involving an obstetrician, fetal medicine specialist, neonatologist, pediatric surgeon, anesthesiologist, otolaryngologist, and pediatric geneticist.

Patients who required the EXIT procedure at the time of delivery had normal genetic test results and prenatal imaging without evidence of other congenital anomalies apart from one which was associated with multiple congenital abnormalities but the parents opted to continue the pregnancy with the option of EXIT procedure despite counseling the couple regarding the postnatal outcome in detail.

Postnatally, all investigations were based on clinical indications. The management, including surgical corrections, was elective or depended on the clinical indication. The postnatal follow-up varied from 1 year to 4 years.

Results

Nine patients with CHAOS were identified between 2017 and 2022 at a gestational age ranging from $18+4$ to $22+4$ weeks. The average maternal age was 28.8 ± 4.8 years (24–36 years). In three of nine patients (33.3%), CHAOS was associated with other multiple congenital anomalies such as single umbilical artery (SUA), common arterial trunk, double superior vena cava (SVC), hemivertebrae, unilateral duplex kidney with suspicious bladder diverticula, tracheoesophageal fistula (TEF), aberrant right subclavian artery (ARSA), horseshoe kidneys, and features of Prune belly syndrome. Seven of nine (77.8%) had associated ascites and one had fetal hydrops with placentomegaly. The liquor volume was normal in five fetuses (55.6%), while two had anhydramnios (22.2%), one oligohydramnios (single vertical pocket—1.7cm) (11.1%), and one normal followed by polyhydramnios (amniotic fluid index—46 cm) (11.1%). Of the total nine cases, five (55.6%) underwent medical termination of pregnancy (MTP) and two were lost to follow-up (22.2%). The remaining two who continued the pregnancy required EXIT tracheostomy at the time of delivery (22.2%). ►**Fig. 2** and ►**Video 1** demonstrate the EXIT procedure being performed.

Amniocentesis for microarray was performed in both and was normal. One among these had associated double SVC, ARSA, horseshoe kidneys, atrial septal defect, and SUA with a suspicion of TEF on antenatal scans which was confirmed on postnatal evaluation and was diagnosed to have tracheal atresia of 9 mm on postnatal computed tomography (CT). This infant underwent surgery for a TEF and, unfortunately, also had a tracheostomy cannula accident while admitted to neonatal intensive care unit on postnatal day 2, and also developed gastroesophageal reflux disease, nonepileptic dyskinesia with infantile spasms on follow-up. Presently, the child is two and half years of age, tracheostomy dependent requiring frequent ventilator support has developed cooing but is still on percutaneous endoscopic gastrostomy (PEG) feeds. The other fetus who required the EXIT procedure was diagnosed to have laryngeal atresia of 5 mm postnatally without any other associated anomalies or complications. Presently, the child is four years of age, tracheostomy dependent, has attained developmental milestones for the age, can maintain a conversation, and is on oral feeds right from birth. ►**Table 2** describes the characteristics and the postnatal outcomes of the fetuses who underwent the EXIT procedure.

Discussion

Normal physiology of the fetal lung involves the absorption of secretions from the lung parenchyma through the tracheobronchial tree. Any mechanical obstruction disrupt this process, leading to increased intratracheal pressure and lung volume causing compression of the heart and mediastinal structures with diaphragmatic flattening and dysfunction, which is the pathology involved in CHAOS. The resultant cardiovascular dysfunction results in reduced venous return to the right side of the heart causing in utero heart failure manifesting as ascites, hydrops, and placentomegaly. This can be associated with polyhydramnios or oligohydramnios depending on alterations in fetal swallowing and gestational age at diagnosis.[7]

Some cases of CHAOS show spontaneous antenatal improvements, possibly due to spontaneous perforation or TEF. This leads to drainage of obstructed fluid, decreasing airway pressure, and reversing the pathology.[8] In a study by Roybal et al, involving 12 fetuses with CHAOS, 5 out of 6 who were delivered via the EXIT procedure survived the neonatal period, out of which 3 had less severe signs of CHAOS on prenatal imaging, with a tiny opening in the airway diagnosed postnatally on direct laryngoscopy in 2 of them.[5] One of our cases was also suspected to have associated TEF who eventually underwent an EXIT procedure and was operated on for the same postnatally. Thus, accurate prenatal US findings are highly predictive of postnatal outcomes and are a valuable guide to prenatal counseling and management.[5]

The typical prenatal sonographic findings of CHAOS are bilaterally enlarged hyperechoic lungs with dilated airways distal to obstruction and flattened or everted diaphragm. Bilaterally enlarged lungs can result in mesocardia, fetal ascites, and nonimmune hydrops.[9] Additionally, magnetic resonance imaging (MRI) can be used, especially if any fetal surgical intervention is planned, as it is more effective in detecting the exact level of obstruction which can help in decision-making regarding fetal versus neonatal intervention with the EXIT procedure.[10–12] However, none of our cases opted for prenatal MRI, but instead underwent CT postnatally (►**Fig. 3**).

CHAOS has been associated with genetic syndromes in more than 50% of the cases, the most common being Fraser's syndrome.[7] However, in our study, genetic testing was opted by only five patients, all of whom exhibited normal results. CHAOS may also be a part of Cri-du-chat syndrome, short-rib polydactyly syndrome, Velocardiofacial syndrome/DiGeorge syndrome, VACTERL (vertebral anomalies, anal atresia,

Table 1 Prenatal evaluation and outcome of patients with CHAOS from 2017 to 2022

Case no.	Age (y)	POG (wk) at diagnosis	Parity	US findings of CHAOS[a]	Ascites	Hydrops	Liquor	Other associated anomalies	Genetic study	Outcome
1	36	20 + 3	G2P1L1	+	Yes	No	Anhydramnios	Nil	Not opted	Lost to follow-up
2	24	20 + 2	Primi	+	Yes	Yes Placentomegaly+	Oligamnios (SVP—1.7 cm)	Nil	Karyotype—normal	MTP Expelled hydropic fetus (795 g) with the placenta (550 g) Fetal autopsy—low-set ears, depressed nasal bridge, large placenta, hyperplastic lungs consistent with CHAOS; however, the obstructive path could not be appreciated
3	27	19 + 4	Primi	+	No	No	Normal	Abdominal wall deficient below the umbilicus, B/L echogenic kidneys and urinoma on the right side, bladder distended and protuberant, suggestive of Prune belly syndrome	Karyotype—normal	MTP Fetal autopsy—confirmed the US findings
4	31	18 + 4	G3P1L1A1	+	Yes	No	Normal	Nil	Not opted	Lost to follow-up
5	32	21 + 2	G3P2L2	+ (in fetus A—MCDA twins)	Yes (fetus A)	No	Normal	Nil	Microarray—normal	MTP
6	29	22 + 4	Primi	+	Yes	No	Normal	Nil	Not opted	MTP
7	24	20 + 4	G2A1	+	Yes	No	Anhydramnios	SUA, B/L minimal pleural effusion, B/L SVC, common arterial trunk, suspicion of esophageal atresia, echogenic dilated bowel loops, hemivertebrae at S1, unilateral duplex kidney, dilated bladder with suspicious bladder diverticula (multisystem involvement—possibility of chromosomal/single gene disorder/VACTERL)	Not opted	MTP Expelled macerated dead infant of 320 g
8	28	20 + 2	Primi	+	Yes Resolved spontaneously at 35 wk	No	Normal	Nil	Microarray—normal	Elective LSCS with EXIT tracheostomy
9	29	20 + 5	G2A1	+	No	No	Normal f/b polyhydramnios (AFI—46 cm)	Persistent left SVC (B/L SVC), persistent right umbilical vein, ARSA, SUA, horseshoe kidneys, sluggishly filling stomach bubble with the possibility of esophageal atresia with TEF Fetal ECHO—ventricular disproportion, RV > LV, B/L SVC, persistent left SVC to coronary sinus with mesocardia	Microarray—normal	Amnioreduction at 33 + 5 wk because of polyhydramnios Elective LSCS with EXIT tracheostomy at 35 + 3 wk due to PPROM

Abbreviations: AFI, amniotic fluid index; ARSA, aberrant right subclavian artery; B/L, bilateral; CHAOS, congenital high airway obstruction syndrome; EXIT, ex utero intrapartum treatment; LSCS, lower segment cesarian section; LV, left ventricle; MCDA, monochorionic diamniotic twins; MTP, medical termination of pregnancy; POG, period of gestation; PPROM, preterm premature rupture of membrane; RV, right ventricle; SUA, single umbilical artery; SVC, superior vena cava; SVP, single vertical pocket; TEF, tracheoesophageal fistula; US, ultrasound; VACTERL, vertebral anomalies, anal atresia, cardiovascular anomalies, TEF, renal anomalies, and limb defects.

[a]Ultrasonographic findings of CHAOS: Bilateral symmetrically enlarged ballooned-out echogenic lungs, with the dilated trachea-bronchial tree, mesocardia with flattened/everted diaphragm.

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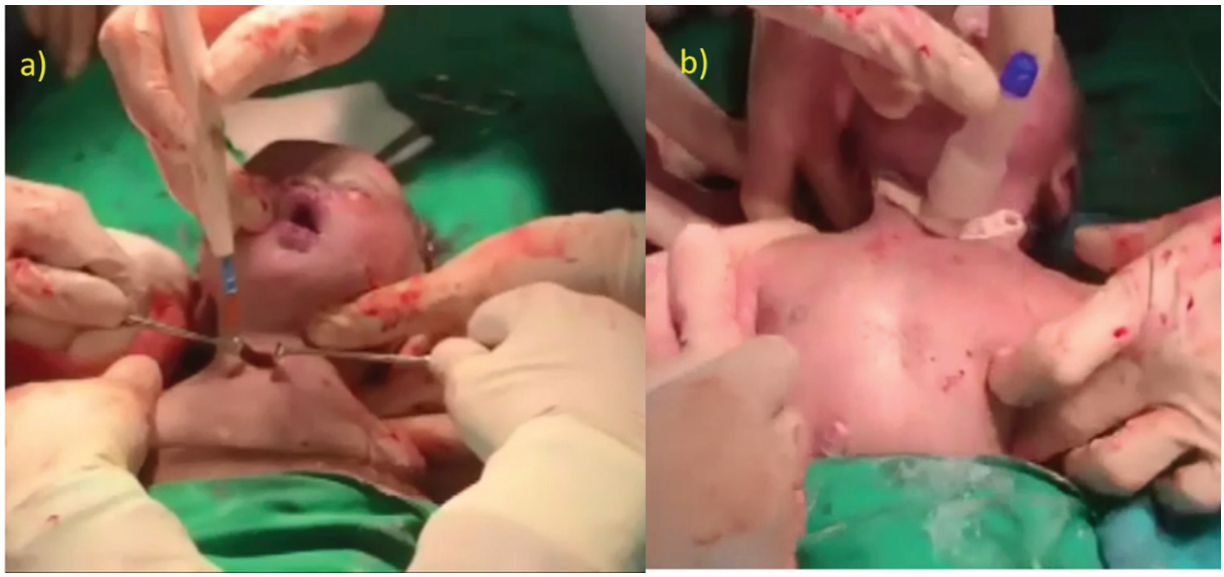

Fig. 2 (**a**) Ex utero intrapartum treatment being performed. (**b**) Tracheostomy tube in situ.

Table 2 The characteristics and postnatal outcomes of the fetuses who underwent the EXIT procedure

	Case 8	Case 9
POG at EXIT/delivery	36 + 2	35 + 3
Sex	Male	Female
Birth weight (kg)	2.38	1.8
Airway management	EXIT tracheostomy	EXIT tracheostomy
Postoperative complications	Nil	Nil
Final diagnosis	Type II laryngeal atresia (5 mm)	Tracheal atresia (9 mm), TEF, B/L SVC, ARSA, SUA, horseshoe kidneys
Postnatal complications	Nil	Underwent surgery for TEF with esophageal atresia on day 2 of life, had 7 mm large ASD and B/L SVC, had T-can accident, infantile spasms with nonepileptic dyskinesia, aspiration pneumonia, underwent Nissens fundoplication and gastrostomy because of GERD
The present age of follow-up	4 y	2 y 6 mo
Tracheostomy dependent	Yes	Yes
Ventilator dependent	Up to 1 wk of birth and on and off up to 1 y of age	Yes
Phonation	Conversation +	Cooing +
Feeding	On oral feeds from birth	On PEG feeds (Mic-Key button in situ)

Abbreviations: ARSA, aberrant right subclavian artery; ASD, atrial septal defect; B/L, bilateral; EXIT, ex utero intrapartum treatment; GERD, gastroesophageal reflux disease; PEG, percutaneous endoscopic gastrostomy; POG, period of gestation; SUA, single umbilical artery; SVC, superior vena cava; T-can, tracheostomy cannula.

cardiovascular anomalies, TEF, renal anomalies, and limb defects) and TARCD syndrome (tracheal agenesis, radial, cardiovascular malformations, duodenal atresia).[13] Therefore, a detailed evaluation of all CHAOS suspected cases with genetic workup is necessary due to the possibility of the coexistent genetic syndrome and the significant implications of inheritance in future pregnancies.

The delivery of a fetus with CHAOS involves the establishment of an immediate emergency airway (intubation or tracheostomy) by performing the EXIT procedure with partial delivery of the infant by cesarean section under deep maternal and fetal anesthesia, that remains attached to the placenta with fetoplacental circulation preserved while maintaining uteroplacental circulation through controlled uterine hypotonia.[4]

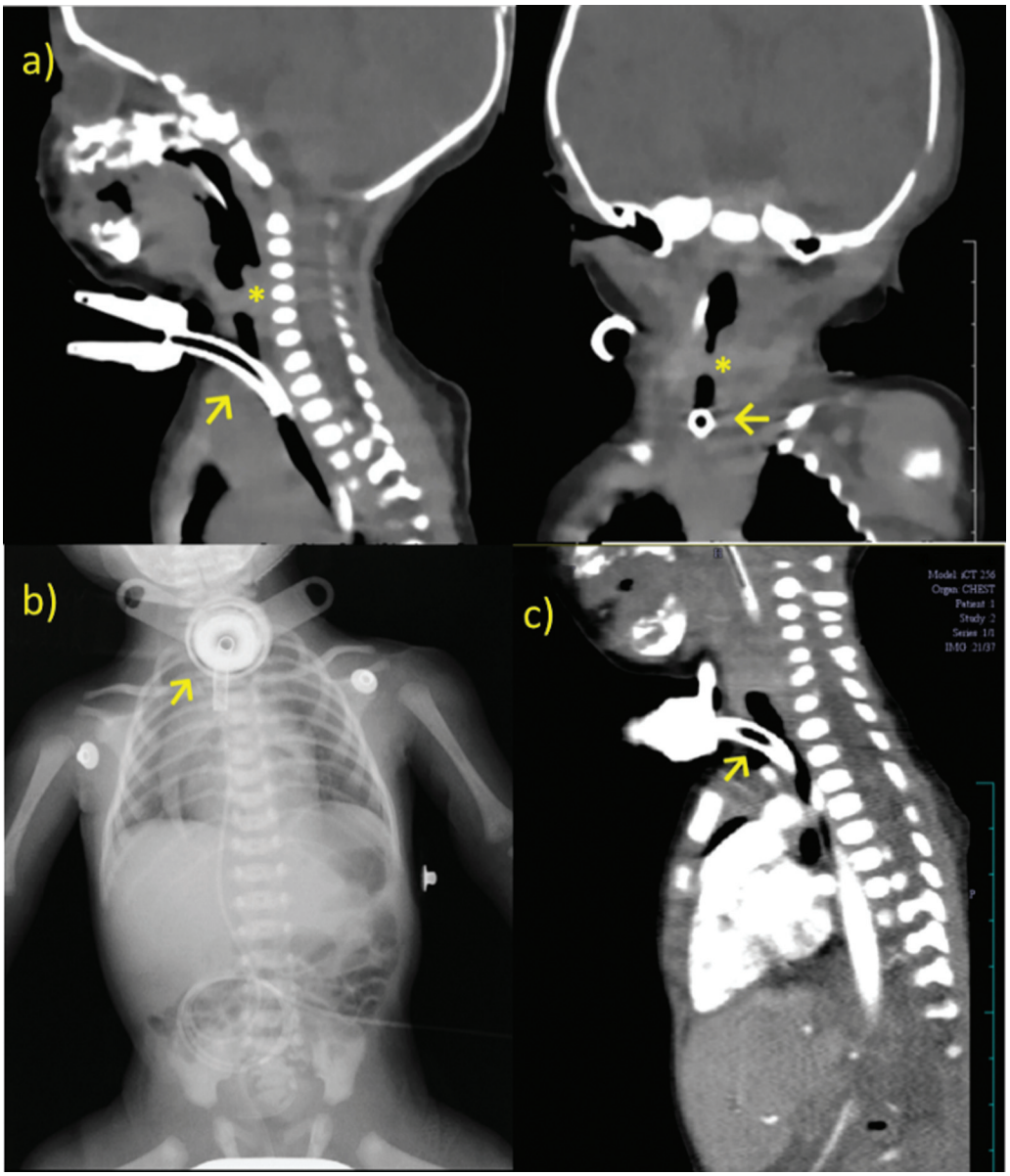

Fig. 3 Postnatal X-ray and CT of fetuses who underwent EXIT tracheostomy. (**a**) Case 8—sagittal and a coronal section on CT with a tracheostomy tube in situ (yellow arrow) and yellow asterisk showing the atretic segment, (**b**) Case 9—X-ray showing the tracheostomy tube in situ (yellow arrow), and (**c**) Case 9—CT showing the tracheostomy tube in situ (yellow arrow). CT, computed tomography; EXIT, ex utero intrapartum treatment.

Prenatal Prognostication in CHAOS

Early presentation with hydrops or associated anomalies indicates poor prognosis and survival, whereas isolated airway obstruction without hydrops or the prenatal resolution of sequence-related complications indicates a relatively favorable prognosis.[5] This is essential in counseling the family as well as planning the management and therapeutic intervention.

CHAOS diagnosed before viability may warrant close observation alone unless there is a pressing indication for fetal intervention which includes the rapid progression of hydrops, development of severe polyhydramnios, or signs of cardiac compromise. Various fetal interventions have been attempted such as percutaneous multiport fetoscopic tracheal decompression, single-incision fetoscopic laser ablation, and fetoscopy-assisted percutaneous tracheal needle decompression through the anterior neck of the fetus, all of which have resulted in the normalization of hemodynamics in hydropic fetuses with CHAOS from laryngeal atresia.[14–19] Anyhow, no such procedures were indicated in any of our cases. However, the algorithm followed in our institute for evaluating patients with CHAOS for fetal interventions is depicted in ►**Fig. 4**.

In a study by Jeong et al involving 13 prenatally diagnosed CHAOS cases, the EXIT procedure was performed in 6, resulting in 4 survivors with favorable outcomes.[20] Another study, including eight cases of fetal airway obstruction with successful EXIT procedures, reported six survivors at discharge, including five with long-term survival, two of whom had CHAOS.[21] Both studies concluded that the EXIT

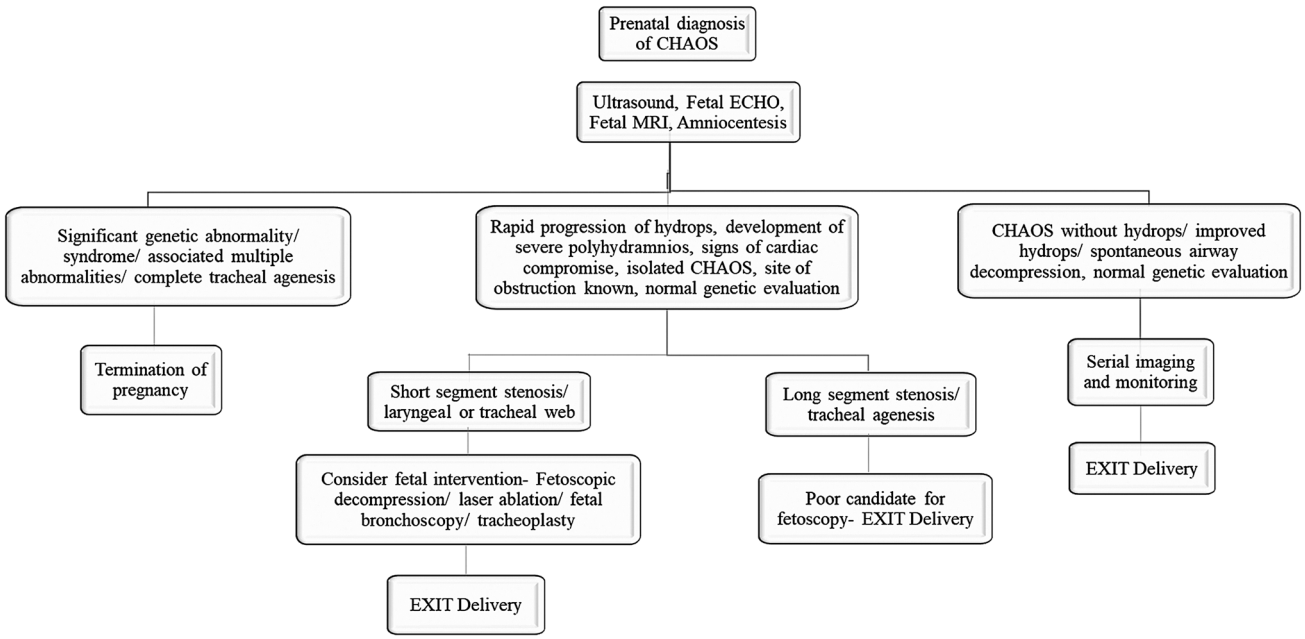

Fig. 4 An algorithm followed at our institute for evaluating patients with CHAOS for fetal intervention. CHAOS, congenital high airway obstruction syndrome; EXIT, ex utero intrapartum treatment; MRI, magnetic resonance imaging.

procedure is safe and effective for managing fetal airway obstruction with better survival rates. In our study as well, both the fetuses who underwent the EXIT procedure survived, are 4 and 2.5 years old, respectively, and both have attained normal developmental milestones as per the respective ages.

Even with an effective EXIT delivery, fetuses with CHAOS are likely to experience morbid postnatal sequelae, such as profound respiratory distress syndrome and severe diaphragmatic stretch injury with subsequently reduced diaphragm function.[6] Also, the EXIT procedure may have its difficulties such as inappropriate uterine entry, maternal hemorrhage, early placental separation, the inability to establish an airway, and mechanical failure of surgical instruments. However, despite longer operating times and increased blood loss, there have been no reported emergency hysterectomies, thromboembolic events, or maternal deaths from EXIT procedures yet, and neither did we face these in any of our cases. Fetus-related complications involve compromised uteroplacental exchange from inadequate uterine relaxation requiring discontinuation of the procedure, cord compression which may cause fetal bradycardia, risk of a malpositioned endotracheal tube, failure to secure an airway (requiring emergent neonatal surgery), and fetal death.[6] The postnatal complications of CHAOS often take weeks or months of intense supportive therapy before stability can be achieved.

Although fetuses with CHAOS can survive after an EXIT procedure, long-term postnatal outcomes have not been well documented so far. Among the studies, including our own, involving a total of 34 fetuses with CHAOS who underwent EXIT procedure, with a minimum of 12-month follow-up, 3 died due to unsuccessful EXIT procedures, while 10 deaths resulted from respiratory complications, yielding a survival rate of 61.8%. The predominant cause of death was the accidental removal of the tracheostomy cannula during sleep, underscoring the necessity for vigilant posttracheostomy supervision. Among the survivors, seven individuals underwent reconstructive surgery at a median age of 24 months (range: 16–48 months). Twenty of the 21 survivors remained tracheostomy dependent during follow-up. Only 10 (47.6%) were able to be fed orally and 4 (19%) were able to phonate/maintain a conversation. ►**Table 3** provides an overview of various studies addressing perinatal management and postnatal outcomes of CHAOS cases.

Postnatally, complete airway patency is difficult to obtain on follow-up due to the risk of restenosis and bilateral vocal fold paralysis. The increase in the tracheal diameter and length is not always proportional to the patient's age. Thus, an adequate age for reconstructive surgery remains unestablished. However, it is generally deferred until the child is at least 2 years of age.[2] In our study among the two who underwent EXIT tracheostomy, the child who is now 4 years old is planned for reconstruction surgery soon, while the other who is now 2 years 6 months is still on follow-up with the plan of reconstruction surgery only after 3 to 4 years of age. Options for surgical reconstruction involve using a T-tube, cartilage graft reconstruction, cricotracheal resection, and tracheal homografts.[2] Reconstructive surgery can restore the anatomy of the airway, but in the absence of vocal cords or vocal cord mobility, speech cannot be restored and sign language may have to be taught. For patients with subglottic stenosis or tracheal atresia, recovery of speech may be possible with the capping of the tracheostomy, but speech therapy is essential. Postoperative complications involve airway restenosis requiring dilatation and the development of airway polyps or granulation tissue that postpones potential decannulation. Oral feeding in these patients

Table 3 Summary of studies done on perinatal management and postnatal outcomes of CHAOS

Reference (year)	No. of cases	MTP/IUD	EXIT cases	Associated abnormalities	POG at diagnosis (wk)	POG at EXIT (wk)	Pathology	Outcome/survival	Morbidity
Our study (2023)	9	7	Case 1	Nil	20 + 2	36 + 2	Laryngeal atresia	Alive	Tracheostomy dependent, on oral feeds, maintains conversation
			Case 2	TEF, B/L SVC, ARSA, SUA, horseshoe kidneys	20 + 5	35 + 3	Tracheal atresia	Alive	Tracheostomy and ventilator dependent, on PEG feeds
Mong et al[12] (2008)	10	7	Case 1	Nil	22	30	Laryngeal atresia	Died due to tracheostomy complication at 13 mo	
			Case 2	Nil	22	37 + 4	Laryngeal atresia	Reconstruction done at 4 y	Tracheostomy and ventilator dependent
			Case 3	Nil	21	31	Tracheal atresia	Reconstruction done at 16 mo with costocartilage graft	Tracheostomy-dependent
Guimaraes et al[11] (2009)	7	3	Case 1	Micrognathia and club feet	27	NA	Tracheal atresia	Death at 4 mo	
			Case 2	Microphthalmia, horseshoe kidneys, two-vessel cord	23 + 4	NA	Laryngeal atresia	VACTERL syndrome	Tracheostomy-dependent
			Case 3	Micrognathia, small kidneys	26 + 2	NA	Laryngeal atresia	Death at 30 min	
			Case 4	Nil	26	NA	Laryngeal atresia	Death at 2 mo	
Roybal et al[5] (2010)	12	6	Case 1	Nil	22	37	Subglottic stenosis	Reconstruction done at 2.5 y	Tracheostomy-dependent, on oral feeds
			Case 2	Nil	22	37	Laryngeal web	Reconstruction done at 2 y	Tracheostomy-dependent and nonverbal
			Case 3	Nil	22	34	Laryngeal atresia	Reconstruction done at 2 y	Tracheostomy dependent
			Case 4	Mandibular hypoplasia and omphalocele	19	29	Laryngeal atresia	Died at 13 mo due to tracheostomy complications	
			Case 5	Nil	20	31	Tracheal atresia	Reconstruction done at 16 mo	Tracheostomy dependent, on oral feeds
			Case 6	Nil	20	31	Tracheal agenesis	Died due to failed EXIT	

Table 3 (*Continued*)

Reference (year)	No. of cases	MTP/IUD	EXIT cases	Associated abnormalities	POG at diagnosis (wk)	POG at EXIT (wk)	Pathology	Outcome/survival	Morbidity
Saadai et al[6] (2012)	12	8	Case 1	Nil	23	23	Laryngeal atresia	Prune belly syndrome	Tracheostomy dependent, on oral feeds at 14 y
			Case 2	Cardiac defects	21	30	Tracheal atresia	Reconstruction done at 2 y	Tracheostomy free at 3 y, on oral feeds, able to phonate
			Case 3	Nil	21	34	Tracheal web	Alive	Tracheostomy and Ventilator dependent
			Case 4	Cardiac defects	24	35	Laryngeal atresia	Prune belly syndrome, fragile X syndrome	Tracheostomy and ventilator dependent, on PEG feeds
Nolan et al[14] (2019)	15	10	Case 1	Nil	23 + 5	33 + 5	Laryngeal atresia	Alive	Tracheostomy and ventilator dependent, on oral feeds
			Case 2	Nil	24 + 2	31 + 1	Laryngeal atresia	Alive	Tracheostomy and ventilator dependent, on PEG feeds
			Case 3	Nil	25 + 2	31 + 6	Laryngeal atresia	Died due to failed EXIT	
			Case 4	Nil	21 + 5	37	Laryngeal atresia	Died due to failed EXIT	
			Case 5	Nil	26 + 1	33 + 2	Laryngeal atresia	Died due to multi-system organ failure	
Masahata et al[21] (2019)	NA	NA	Case 1	Duodenal atresia, anorectal malformation	22	30	Laryngeal atresia	Died due to respiratory failure	
			Case 2	Nil	20	37	Laryngeal atresia	Died due to respiratory failure	
			Case 3	Nil	24	37	Laryngeal atresia	Alive	NA
			Case 4	Nil	21	34	Laryngeal atresia	Alive	NA
Jeong et al[20] (2021)	13	7	Case 1	Cardiac defect (CCTGA)	22 + 3	39 + 5	Laryngeal atresia	Alive	Tracheostomy dependent, on oral feeds
			Case 2	Nil	21 + 1	37	Tracheal atresia	Alive	Tracheostomy dependent, on oral feeds, maintains conversation
			Case 3	Nil	20 + 1	38 + 2	Laryngotracheal agenesis	Alive	Tracheostomy dependent, on oral feeds

(*Continued*)

Table 3 (*Continued*)

Reference (year)	No. of cases	MTP/IUD	EXIT cases	Associated abnormalities	POG at diagnosis (wk)	POG at EXIT (wk)	Pathology	Outcome/survival	Morbidity
			Case 4	Cardiac defect (DORV)	23 + 3	38 + 2	Laryngeal atresia	Died due to a T-can accident	
			Case 5	Nil	29 + 6	38 + 4	Subglottic stenosis	Alive	Tracheostomy dependent, on oral feeds
			Case 6	Nil	22 + 3	31	Laryngeal atresia	Died due to a T-can accident	

Abbreviations: ARSA, aberrant right subclavian artery; B/L, bilateral; CCTGA, congenitally corrected transposition of great arteries; CHAOS, congenital high airway obstruction syndrome; DORV,double outlet right ventricle; EXIT, ex utero intrapartum treatment; IUD, intrauterine demise; MTP, medical termination of pregnancy; NA, not available; PEG, percutaneous endoscopic gastrostomy; SUA, single umbilical artery; SVC, superior vena cava; T-can, tracheostomy cannula; TEF, tracheoesophageal fistula; VACTERL, vertebral anomalies, anal atresia, cardiovascular anomalies, TEF, renal anomalies, and limb defects.

is possible but is often delayed.[2] However, one of our cases on follow-up was started on oral feeds right from birth, whereas the other infant is still on PEG feeds, both awaiting reconstruction surgery. Therefore, even in the best case scenarios, CHAOS patients may have to face certain functional limitations affecting their quality of life. These issues should be addressed during prenatal counseling.

Despite many studies on CHAOS, its prenatal diagnosis, prognostication, and various treatment options including the EXIT procedure, there is still a paucity of literature, and the overall treatment efficacy is yet to be proven. Further studies are necessary to confirm the efficacy of prenatal interventions.

Limitations of the Study

The limitation of our study is the retrospective nature of our research and the small number of prenatal cases, making it difficult to generalize the data for prognostication.

Conclusion

Unfortunately, due to the postnatal complications of CHAOS with their implications on the quality of life and intensive care required, most patients opt for MTP. CHAOS even when isolated, generally has a poor prognosis without intervention; however, larger studies are required to prognosticate this condition. Performing an EXIT procedure at birth can significantly improve postnatal survival by minimizing hypoxic damage. However, the long-term medical and surgical challenges for survivors remain numerous, especially speech disorders, even after lifesaving fetal intervention and surgical correction. Thus, future efforts should focus on prenatal identification of prognostic markers that differentiate the less morbid survivor from a more morbid survivor. One should also consider detailed prenatal counseling with adequate information given to the parents for a mutual agreement on an appropriate treatment plan also considering the infant's quality of life, and have a multidisciplinary team for the optimum care of prenatally diagnosed CHAOS cases and a successful EXIT procedure.

Video 1

EXIT procedure being performed.
Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0044-1786361.

Consent to Participate and Consent to Publish

Written informed consent was obtained from the patients for participation and publication of this study.

Ethical Approval

This retrospective study was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later

amendments or comparable ethical standards. The institutional ethics committee approved this study.

Authors' Contribution

All authors contributed to the study's conception and design. All authors have read and approved the final manuscript.

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Conflict of Interest

None declared.

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