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Prenatal Diagnosis of Congenital Diaphragmatic Hernia Improve the Outcome: A Local Experience

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Abstract— Background: Management of congenital diaphragmatic hernia (CDH) remains a challenging problem, as to date, uniform standards for management have not existed.

Objective: To assess the influence of prenatal diagnostic modalities for CDH on postnatal management and outcome in a developing country.

Methods: This is a retrospective study of 32 neonates with CDH without other associated congenital anomalies admitted to Neonatal Intensive Care Unit (NICU) during an 8 years' period from December 2013 to November 2021. Identified cases were classified into 2 groups; Group I included 17 infants who were prenatally diagnosed with CDH and continuous prenatal follow-up were available. Group II included 15 infants with no records for continuous prenatal follow-up. A particular resuscitation protocol for the neonates was adopted. Recorded operative data, morbidity and mortality were statistically analyzed.

Results: The overall male to female ratio was 1.4: 1. The mean gestational age at postnatal diagnosis was 37.1±1.2 weeks. Twenty-four infants had left-sided, and 8 had right-sided CDH. In group I, the mean gestational age at prenatal diagnosis was 25.4 weeks. However, those in group II, who had the perinatal diagnosis and lost for follow-up, showed mean gestational age of 21.6 weeks. The overall survival was 14 patients out of 32 (43.8%). Group I showed survival of 11 neonates out of 17 (64.7%). Three patients expired post-operatively, while the remaining 3 did not undergo any surgery. In group II, 5 neonates out of 15 survived with a survival rate of (33.3%), with a statistically significant difference between the two groups.

Keywords— Congenital diaphragmatic hernia (CDH), prenatal diagnosis, neonatal assisted ventilation.

1. Introduction

Congenital diaphragmatic hernia (CDH) is a significantly challenging neonatal emergency pathology. It usually occurs due to a defect of the posterolateral diaphragm. This results in intrathoracic herniation of abdominal organs and various degrees of pulmonary hypoplasia and hypertension [1]. However, the so-called late-presenting CDH cases may present beyond the neonatal period (Late-CDH) [2-4]. It occurs in 1 out of 2000 to 4000 live birth [5-6]. A detailed prenatal sonographic examination is considered as the main

pivot in elucidating most fetal congenital anomalies [7-8].

In developing countries, pregnant ladies are not privileged to have proper and good quality prenatal care that focuses on congenital anomalies scanned by experienced and qualified personnel. This perplexing abnormality is riddled with flawed and sometimes conflicting reports. Congenital diaphragmatic hernia (CDH) occurs in 1 out of 2000 to 4000 live birth [1-4]. In a report from a developing country, the CDH survival rate was 50% [5].0 CDH is a lethal birth defect in which the diaphragm fails to form entirely in the developing fetus [6]. This allows the bowel to enter the thoracic cavity resulting in pulmonary hypoplasia and pulmonary hypertension [7]. However, CDH is often missed on routine ultrasonography that assesses the fetal size [8]. The definitive sonographic diagnosis of fetal CDH relies on visualizing abdominal organs in the fetal chest. The sonographic hallmark of a left-sided CDH is a fluid-filled stomach just behind the left atrium and ventricle in the lower thorax, as seen on a transverse view. Other sonographic features that imply the presence of left-sided CDH include the absence of the stomach below the diaphragm, mediastinal shift to the right, and a small abdominal circumference. Right-sided CDH is more frequently missed or misdiagnosed because the herniated viscera consist predominantly of the liver's right lobe, which may have similar echogenicity to the lung, or be confused with a solid mass in the chest [9]. Nevertheless, fetal diagnosis of CDH has revolutionized postnatal care by educating families and preparing the health care teams towards eventual delivery of the CDH patient [6]. In a previous work by the author from a low resource nation, the fetal diagnosis showed a well-recognized effect on neonatal surgical outcome [10]. In cases where the presence of CDH is known prenatally, it is imperative that the team in the delivery room consist of personnel experienced in the immediate resuscitation and stabilization of critically ill neonates [11-12]. Many affected patients will require positive pressure ventilation in the delivery room. To prevent distension of the gastrointestinal tract and further compression of the pulmonary parenchyma, a nasogastric tube of the large caliper is placed to act as a vent [13]. Early intubation is preferable to bag-mask ventilation or continuous positive airway pressure via a mask or nasal prongs. Positive pressure ventilation must be applied with great skill because the presence of pulmonary hypoplasia is associated with an increased risk of pneumothorax [14].

As the hidden neonatal mortality of undiagnosed CDH cases remains a challenging problem in low-resource nations, the current study aimed to assess the effect of different prenatal diagnostic modalities for CDH on postnatal management and outcome in a developing country, addressing the prognostic prenatal predictors that should be included in any detailed fetal anomaly scan.

2. Patients and Methods

This is an 8 years' retrospective study of CDH patients with no other associated congenital anomalies-admitted to the Neonatal Intensive Care Unit (NICU). The study aimed to test the influence of the different available prenatal diagnostic modalities for CDH on postnatal management and outcome. It also aimed to highlight the prenatal predictors of postnatal outcome of this elusive developmental anomaly. After approval of the concerned Institutional Review Boards for the bioethical eligibility. The study started in December 2013 till November 2021. When data collection was complete, processing and analysis extended to December 2021.

CDH neonates were classified into two groups; group I included those were prenatally diagnosed and followed up till having a special care delivery as CDH. Group II were those who did not undergo any sort of prenatal diagnosis as well as others who initially underwent prenatal diagnosis but were lost for follow-up during pregnancy although appeared at delivery.

Those babies had not undergone any special care for delivery or postnatal care as their prenatal diagnosis were missed. The available prenatal ancillary aids for final diagnosis were Ultrasonography (US) and

Magnetic Resonance Imaging (MRI). Detailed ultrasound examination was done for fetuses suspected of CDH using ultrasonography machine, TOSHIBA SONOLAYER SSA-260A with 2D probe-type TOSHIBA PVF-375MT (3.75MHz). In addition to the basic ultrasound biometric parameters, the definitive sonographic diagnosis of CDH relied on the presence of fluid-filled stomach in the lower chest, mediastinal and/or cardiac shift, small abdominal circumference, and diaphragmatic eventration. Pulmonary hypoplasia associated with CDH was estimated in the US using a measurement known as the Lung-Head Ratio (LHR) [15]. This measurement was used to assess the relative size of the contralateral lung by expressing the lung cross-sectional area measured at the level of the cardiac atria (in square millimeters) to the head circumference in millimeters. Also, a detailed review of other fetal body systems was done to search for associated congenital malformations. MRI was done for 11 fetuses using a phased-array body coil of 1.5 tesla super-conducting imaging system Gyroscan ACS.NT power track 6000 PHILIPS Magnetic Resonance scanner. This ultrafast fetal MRI measured fetal lung volumes, calculating the Percentage of Predicted Lung Volume (PPV). It was determined by subtracting measured mediastinal volume from total measured thoracic volume [16]. Fetal Lung volume values were adjusted to the fetal gestational age at scan time. The PPV was correlated with postnatal outcomes. Also, liver protrusion into the fetal chest and the degree of that protrusion was evaluated. Mothers subjected to MRI examination were after 18 weeks gestation, and verbal informed consent was obtained to explain the safety of this complimentary procedure.

When the diagnosis was settled, breaking the news to the family was done respecting the mother's psychological condition. However, the family was clearly informed about the potential bad outcome of this developmental anomaly. This counseling helped get parents' involvement in decision-making and compliance for the subsequent visits and delivery planning. Pregnant women diagnosed with CDH fetuses (group I) had been scheduled for biweekly visits until 30 weeks, then check-up visits were weekly until the planned delivery date. Fetal echocardiography was arranged for the possible association of structural cardiac abnormalities. In addition, genetic amniocentesis was performed for group I mothers once the CDH diagnosis was established to detect any genetic disorders. Pregnant women were informed that they would have a planned delivery where the multidisciplinary team responsible for managing their neonates had the necessary preparedness. The multidisciplinary team pillars were the anesthesiologist, neonatologist, and pediatric surgeon. Group II CDH neonates were either not diagnosed during pregnancy or undergone initial sonographic assessment (Figs 1,2) but missed for follow-up. All patients whether, prenatally diagnosed and had special care plus those who did not have similar care, as they were not prenatally diagnosed, were admitted to the NICU with the final diagnosis of CDH after having plain and contrast x-ray films (Fig 3). They arranged to meet neonates' families to explain treatment options and potential outcomes and answer any family's questions. Immediately after the planned delivery of group I neonates, stabilization and special ventilation through immediate endotracheal intubation and mechanical volume membrane ventilation to avoid the risk of pulmonary barotrauma and intestinal distension. Bag-valve-mask or pressure ventilation were avoided. Also, an adequate-sized nasogastric tube was placed, connected to continuous suction to allow intestinal decompression. At the NICU, continuous pre-and post-ductal-pulse oximetry was used to assess the degree of Persistent Pulmonary Hypertension of the Newborn (PPHN) via right-to-left shunting at the level of the ductus arteriosus. Moreover, umbilical arterial and venous catheters were placed to allow for continuous blood pressure monitoring, blood gas sampling, fluid administration, and to give any required inotropic support. For all studied neonates, the type and timing of surgical intervention were determined according to baby progress until there was hemodynamic stability ($PaCO_2 < 60$ mm Hg, $PaO_2 > 40$ mm Hg, $SatO_2 > 85\%$ with a $FiO_2 < 50\%$) for at least 48 consecutive hours after stabilization. The diaphragmatic defect was approached through a subcostal incision or median incision. The viscera were reduced gently from the chest and eviscerated from the abdomen after the defect was visualized. A hernia sac was presented in 4 patients and was excised. Diaphragmatic reconstruction with a prosthetic material (Gortex®) was

adopted in 8 patients as inadequate diaphragmatic tissue was not present to accomplish a primary repair. Post-operatively, meticulous attention was given to ventilator management to ensure adequate tissue oxygenation avoiding hypercarbia and acidosis. Postoperative fluid requirements were properly calculated to prevent hypotension, maintaining blood pressure above 50 mmHg. Narcotic analgesia and sedation with fentanyl (2 mg/kg/dose, IV) were routinely used for at least 24 hours after surgery. However, 12 patients had this medication for 72 hours. Systemic antibiotics (3rd generations Cephalosporins plus Metronidazole) were routinely administered preoperatively. Regarding hospital stay, the postoperative course of 14 days extended to 21 days in 4 neonates who underwent the usage of a prosthetic patch. However, the remaining babies stayed less than 14 days (11 ± 2.3). Follow-up care after discharge took place by a detailed record kept with parents, stressing the necessity of follow-up, which was scheduled with concerned pediatric clinics. Descriptive statistics, frequency, and percentage were used to describe the characteristics of the parents. Student's *t*-test and chi-square test were used to compare the postnatal outcome in the 2 study groups. A *P*-value of less than 0.05 was considered significant. Spearman correlation coefficients were used to measure the univariate association between radiological measures and outcome severity rank. The adjustment was made for gestational age at delivery and birth weight since these factors might have affected outcome and severity rank. Severity rank was the dependent variable in the regression analysis. Gestational age at delivery, birth weight, and radiological measures were the independent variables.

3. Results

Thirty-two CDH neonates were studied in the period from December 2013 to November 2021. They were classified into two groups: Group I included 17 neonates prenatally diagnosed as CDH. They were 10 males and 7 females with a ratio of 1.4 :1. Group II included 15 who did not undergo any sort of comprehensive prenatal care. There were 9 males and 6 females with a ratio of 1.5:1 and a total male to female preponderance ratio of 1.4:1. Maternal age ranged from 18 to 42 years with an average of 29.5 ± 4.6 years. Characteristics of the studied mothers are presented in table 1. In group I, in 12 pregnant women (70. 6%), CDH discovery was between 28 and 34 weeks of gestational age (average = 30.6 ± 1.87), while 5 cases were diagnosed before 28 weeks (28.1%). Thirteen fetuses showed a left CDH, and 4 had a right CDH. While in group II, 11 patients had left CDH with 4 right-sided hernias. The prenatal imaging findings in the studied mothers are shown in Table II. Table 3 showed risk stratifications of CDH fetuses based on imaging findings. Surgical findings in both groups are clarified in Table 4. Out of the total studied 17 patients in group I, 11 patients survived with the percentage of 64.7%. While in group II, only 5 babies out of the total 15 studied cases in this group, the percentage of survival was 33% (table 5).

For group I fetuses, the lung area had a circumference ratio (LHR) ranging from 0.36 to 0.23 and was obtained at 19 to 36 weeks. Only 3 fetuses had ultrasound examinations at 23 to 25 weeks (Figs.3, 4). The contra-lateral lung was too small to be visualized in one case. Polyhydramnios was reported in all patients. In group I, 11 babies were delivered after 38 weeks of gestation (GA), 3 at 37 weeks and another 3 at 35.2. While in group II, the GA was seen to be beyond 38 weeks in 4 cases, 37.5 in 5 cases, and below 37 weeks GA in the remaining 6 cases with a mean GA 37.4±2.3 weeks. All of the prenatally diagnosed infants were delivered via a cesarean section. Meanwhile, 8 infants in group II were delivered through a normal vaginal delivery (53.3%), and the rest 7 infants were also delivered through cesarean section (46.7%). The birth weight ranged from a low of 2 kg up to 3.1 kg in group I and from 1.9 kg up to 3.3 kg in group II with an overall mean, in both groups, of 2653±500g. The mean APGAR score after 5 minutes was calculated in both groups. It was 7.1 in group I and 6.1 in group II. In group I, all infants were intubated and mechanically ventilated with a maximum of 20 minutes (5±3.2, mean ± SD) after birth while infants of group II had

undergone intubation and mechanical ventilation within the first six hours of age (240±50, mean ± SD). The timing of surgery ranged from 48 hours after delivery up to more than 120 hours with an overall mean of 63.6±20. The analysis of arterial blood gases showed that a pH of less than 7.3 (4 patients in group I and 9 patients in group II). This was associated with high mortality in comparison to a pH of 7.3 or more (58.8% and 15%, respectively, *P*=0.01). Furthermore, PaCO2 of more than 45 mmHg was associated with high mortality (55.5%), compared to a PaCO2 of 45 mmHg or less (16.6%, P=0.03). In addition, peak inspiratory pressure (PIP) of more than 25 cm H2O at presentation was associated with high mortality, compared to PIP of 25 cm H2O or less (90% and 11%, respectively, P=0.001). The operative findings are shown in table 4. Analysis of other variables revealed no significant difference among the survivors and the non-survivors in the two groups regarding the 5-minute APGAR score, sex, mode of delivery, and initial PaO2. A statistically significant difference in survival rate was noted between the two groups. In group I, 11 patients out of 17 survived with a rate of 64.7%. In group II, only 5 infants out of 15 survived with a rate of 33.3%.

4. Discussion

Controversy exists concerning the factors influencing outcomes in infants with CDH [17]. The newborn with CDH remains one of the most intriguing patients in the newborn period. Not only is this patient a challenge for the pediatric surgeons in the newborn and preoperative period, but they may remain one of the most complex situations to care for throughout their infancy and childhood. Despite increased prenatal diagnostic capability and significant advances in the preoperative care of critically ill neonates, CDH still has an unacceptably high mortality rate [18]. Management of CDH has changed dramatically over the last three decades. Surgical correction over congenital diaphragmatic hernia is no longer an emergent procedure. Rather, it can wait until the patient is stabilized concerning respiratory distress and associated pulmonary hypertension. The basis for this change in CDH treatment has been the realization that; it is not the defect that causes respiratory distress but the hypoplastic lungs and associated pulmonary hypertension. Building on these theories, several groups have advocated prolonged preoperative stabilization and delayed surgery to avoid vascular vasospasm [19], and interference of the surgical procedures on the respiratory complaints [20-21]. The best ventilation mode for infants with CDH has not yet been proven conclusively in the literature. However, avoiding iatrogenic barotrauma is the strategy most widely used and has resulted in an improved survival rate [1,22]. In our current work, a total of 32 patients with CDH have been evaluated prospectively, comparing infants who had undergone an in-utero diagnosis of CDH (group I) with those who did not have the diagnosis (group II). The overall survival rate in group I was 64.7%, significantly higher than those in group II with a survival rate of 33.3%. This may be due to the fact that the prenatally diagnosed cases might have the expert personnel waiting for an immediate resuscitation at the delivery room with the avoidance of positive pressure ventilation using an Ambu® bag (Bag-mask). Still, only free flow O2 was used until the endotracheal tube was placed and mechanical ventilation was initiated. All infants had a wide nasogastric tube to low intermittent suction inserted to prevent abdominal distension and respiratory compromise. On the other hand, those infants of group II were not diagnosed with CDH. Still, as management of respiratory distress at the delivery room, Ambu® bag ventilation was used for many of them.Although surfactants were administrated as a single dose upon endotracheal intubations among 6 of our CDH infants, it does not show any improvement in the results. This coincides with the report of the CDH study group [23]. Surgical intervention was not an emergent repair in our current study. The mean time of performing surgery was 63.6±20 after birth, coinciding with the data in the literature. This delay aims to wait for the "honeymoon period" to elapse [17,24-25].

The survival rate in group I patients was higher than in group II. Yet, it is low compared to that in the literature for those patients who underwent prenatal diagnosed [2,3,6,17,26-29]. This difference might be because we neither adopt the nitric oxide nor the oscillatory ventilation system in our center. However, our results in group I simulate some published data from similar centers in the area [28-32].

It was noted that the mortality rate has gradually decreased in our late cases (4 patients with a survival rate of 100%) where chest tubes were not used. This is consistent with other data [10,27,33-38], who advocated that iatrogenic lung injury can result from sources such as chest tubes and thoracotomy.

It is concluded that prenatal diagnosis with qualified personnel, taking care of not causing iatrogenic barotraumas to the lung during early resuscitation, may help in improving the postoperative results of CDH infants, thoracotomy, and chest tubes insertion should be avoided except in very limited cases.

Although the number of studied patients is not much, it is hoped that the results may give a clue about how to improve the management of CDH infants in the future for better survival and less morbidity in developing countries.

5. Conclusion:

Prenatal diagnosis of CDH has a better influence on the survival outcome. It should be considered in any health programs to improve the materno-fetal outcome in developing countries.

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3. **Table 3.** Risk Stratifications of CDH fetuses based on imaging findings
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5. **Table 5.** Survival rates of the studied neonates (*n =32*)

Figures:

Fig 1: A longitudinal section taken at 35 weeks' gestation, the spine is up.

The fetal small bowel (S) is dilated and extends into the fetal chest posterior to the heart. S: Small bowel, RV: right ventricle, RA: right atrium.

Fig 2: On this longitudinal section taken at 37 weeks' gestation, the sternum is up. The fetal stomach (S) is seen in the chest, posterior to the right ventricle (RV). S: stomach, RV: right ventricle, D: diaphragm.

Fig 3: Plain & Contrast Anteroposterior (AP) view of the chest shows a left-sided Bochdalek Hernia.

Table 1

N= 32 mothers	***n***	***%***
Primipara	5	15.6
Multipara	27	84.4
History of early pregnancy loss	4	12.5
History of Intrauterine Fetal Demise (IUFD)	2	6.25
History of child with congenital anomaly	0	0
History of Diabetes	1	3.1
History of any medical disorder during pregnancy like hypertensive disorders, thyroid disorders, etc..…,	4	12.5
History of a child with a medical disorder with genetic etiology	0	0
History of consanguineous marriage	5	15.6
History of smoking, passive or active	8	25
Compliance with prenatal visits	17	53.1
The current pregnancy was planned	28	87.5
The current pregnancy was unplanned	4	12.5

Table 2

Ultrasound Findings n=17		*Complimentary MRI Findings n=11*	
Item	***n & (%)***	***Item***	***n & (%)***
Query right-sided CDH	4 (23.5)	Definite Right-sided CDH	4 (36.4)
Definite Left-sided CDH	13 (76.5)	Definite Left-sided CDH	7 (63.6)
LHR less than 25%	6 (35.3)	Low " gestational-age based" PPV	2 (18.2)
LHR more than 25%	8 (47.1)	PPLV within normal range	9 (81.8)
Right Mediastinal shift	9 (52.9)		10 (90.9)

Stomach behind fetal heart	5 (29.4)	7 (63.6)
Polyhydramnios	17 (100)	11 (100)

Table 3

Risk Order	*Imaging Finding*			
	Low PPLV	***LHR less than 25%***	***Intrauterine Growth Restriction (IUGR)***	***Right-sided CDH with liver up position***
High Risk	4	3	3	5
Guarded Prognosis	0	3	4	2
Low Risk	0	2	-	-

Table 4

Surgical findings	Group I	Group II	*P* Value
Small or large intestines in chest	17	15	NS*
Spleen	4	6	NS*
Stomach in chest	3	4	NS*
Left kidney	1	-	NS*
Liver	7	6	NS*
Use of Gortex® patch	4	4	NS*
Postoperative infection	3	5	NS*
Age at repair by hours (mean ± SD)	53 ± 15	71 ± 20	*P*< 0.002

NS=No significance

Table 5

Prognosis	**No. of cases No. (%)**		**Total survival No. (%)**	
	G I	G II	G I	G II

Sever	8 (47.1)	9 (60)	3 (37.5)	0
Intermediate	5 (29.4)	3 (20)	4 (80)	2 (66.7)
Good	4 (23.5)	3 (20)	4 (100)	3(100)
Total Outcome	17 (100)	15 (100)	11/17* (64.7)	5/15** (33%)

*G I=17, ** GII=15

Fig. 1

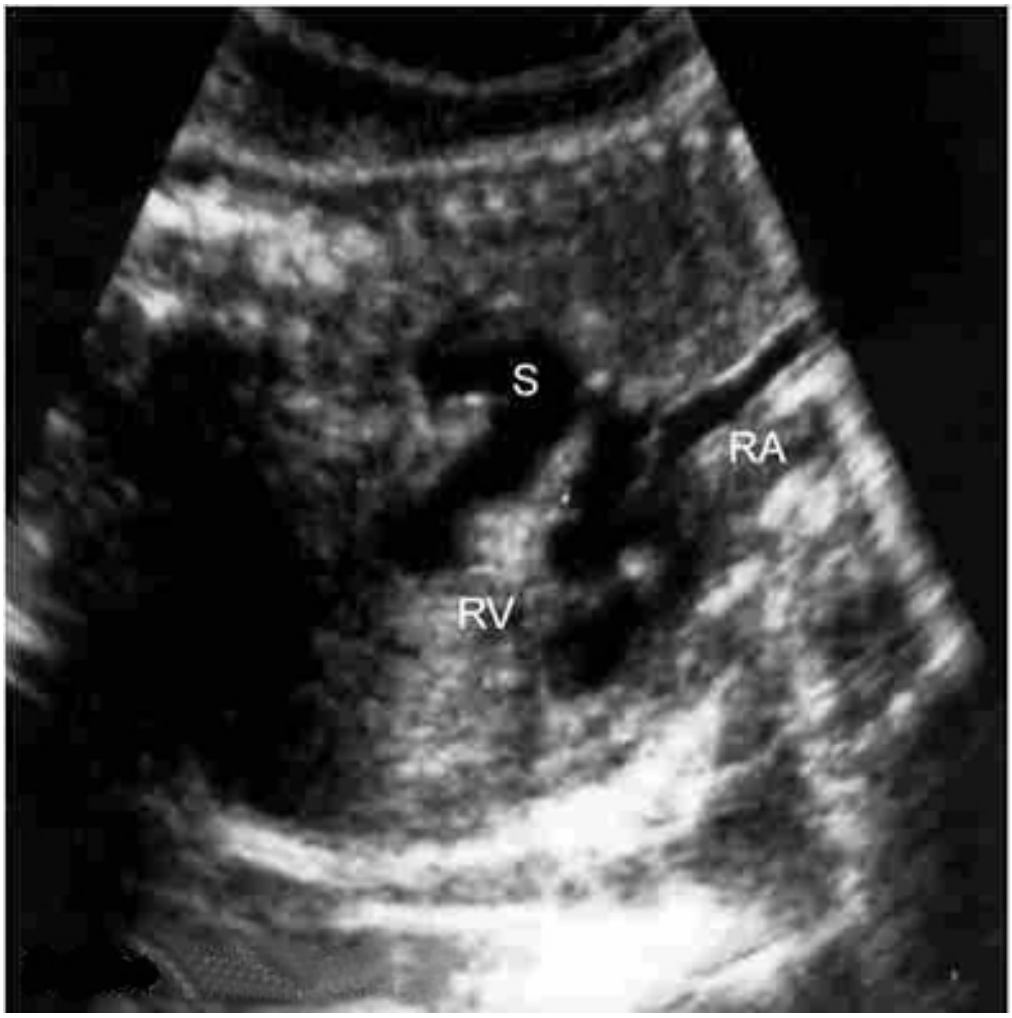

Fig.2

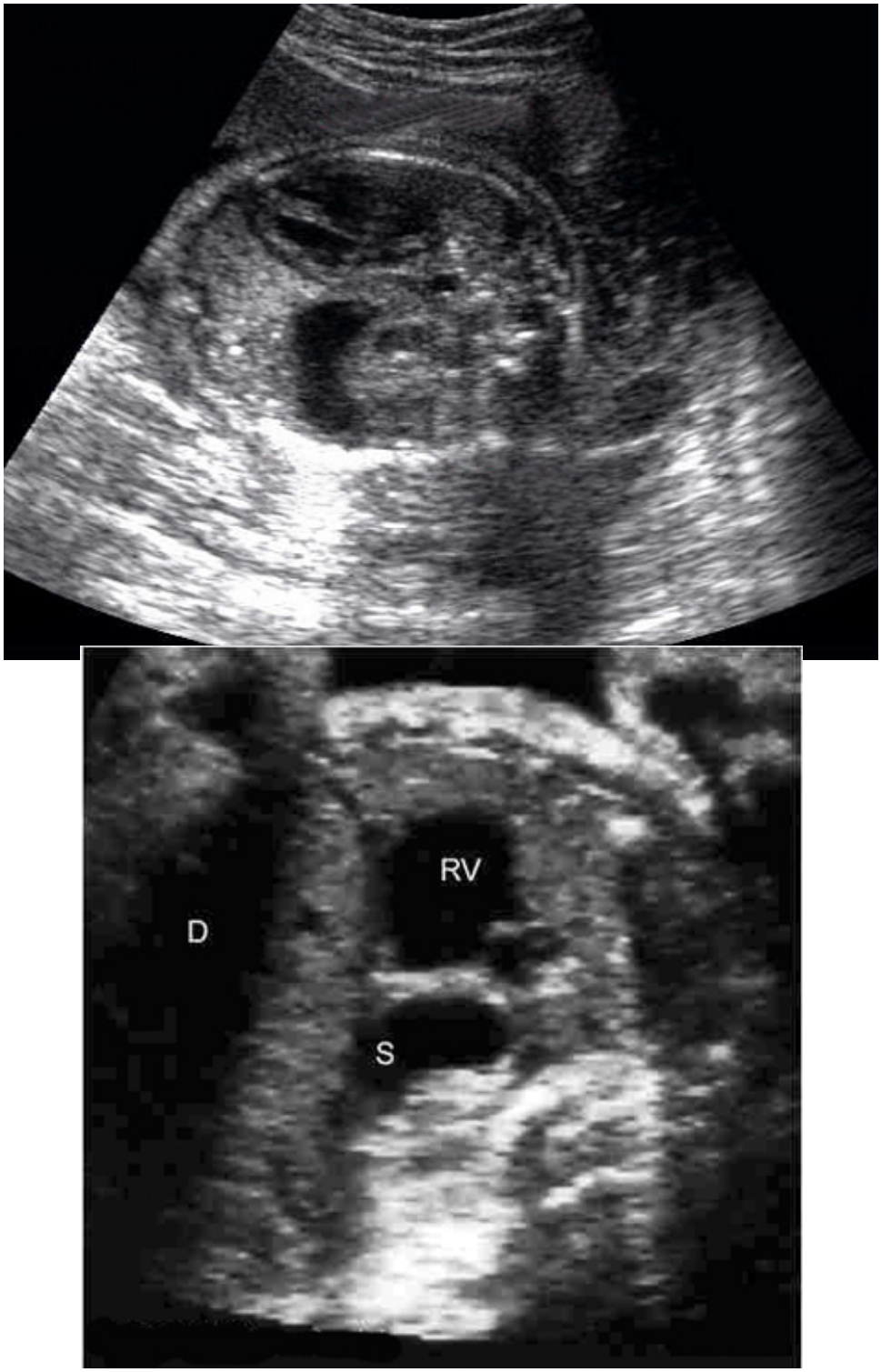

Fig. 3