




# Role of Predictive Mortality Calculator in Antenatal Assessment of Congenital Diaphragmatic Hernia

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**Abstract** Congenital diaphragmatic hernia (CDH) is one of the most common major congenital anomalies. In utero visceral organ herniation into the thoracic cavity can result in lung hypoplasia and pulmonary hypertension may ensue. Post-natal mortality rates in isolated CDH remain high reaching up to 80% in severe cases. Several prenatal predictors of morbidity and mortality have been proposed. Reliable predictive markers can aid clinicians in providing effective family counselling, prediction of survival, and propose therapeutic options. Decreased total fetal lung volume (TFLV) via magnetic resonance imaging (MRI) has been reported to be significantly associated with mortality. We report on 2 cases of CDH, with fetal MRI performed at third trimester, focusing on the TFLV and

observed-to-expected TFLV. We would like to highlight the importance of predictive mortality calculator which provides statistical data for healthcare providers in counselling families and aids in risk-stratification.

**Keywords** Total fetal lung volume (TFLV) · Congenital diaphragmatic hernia · Fetal MRI

## Introduction

Congenital diaphragmatic hernia (CDH) is a developmental diaphragmatic defect allowing abdominal visceral herniation into the thoracic cavity. It is considered one of the most common major congenital anomalies with an incidence of 1 in 2,500–3,000 live births. Although CDH is surgically correctable, in utero visceral herniation can result in pulmonary hypoplasia leading to pulmonary hypertension, which is the primary causes of postnatal morbidity and mortality [1]. Despite the advancement in neonatal management, post-natal mortality rates in isolated CDH remain high, reaching up to 80% depending on severity [2]. Considering high mortality rates associated with CDH, many studies have been carried out to determine prenatal predictors of morbidity and mortality, particularly those relating to fetal development. Decreased total fetal lung volume (TFLV) has been reported to be significantly associated with mortality [3]. We report on 2 cases of CDH related perinatal deaths and how magnetic resonance imaging (MRI) can predict survival outcome.

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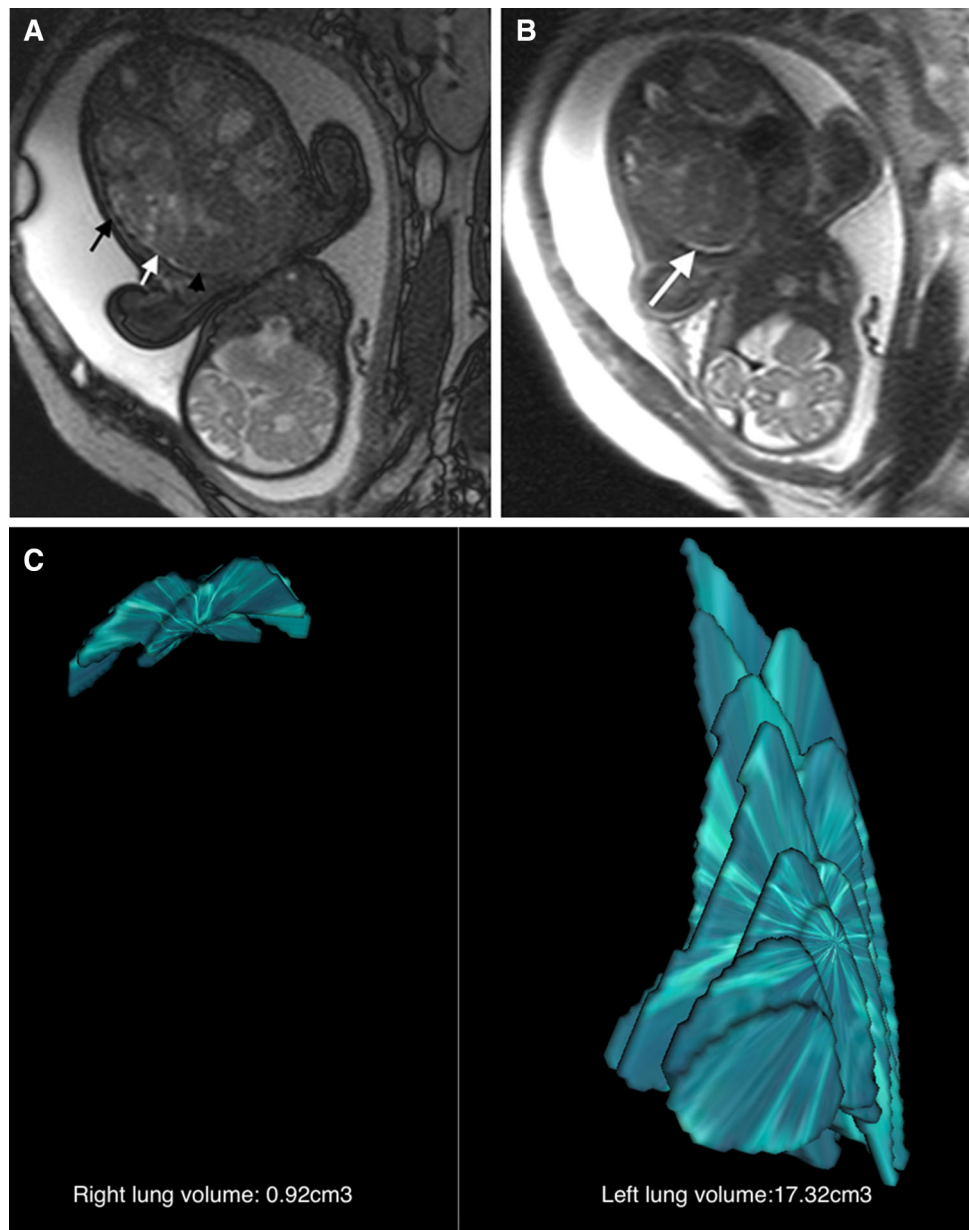
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**Fig. 1** **a** Herniated right lobe of liver (black arrowhead), loops of small bowel (black arrow) and hepatic flexure (white arrow) into the right hemithorax. **b** Right lung (white arrow) was barely visible, as it was compressed and displaced superiorly. **c** Post-processing MRI measurement of the right and left lung volumes



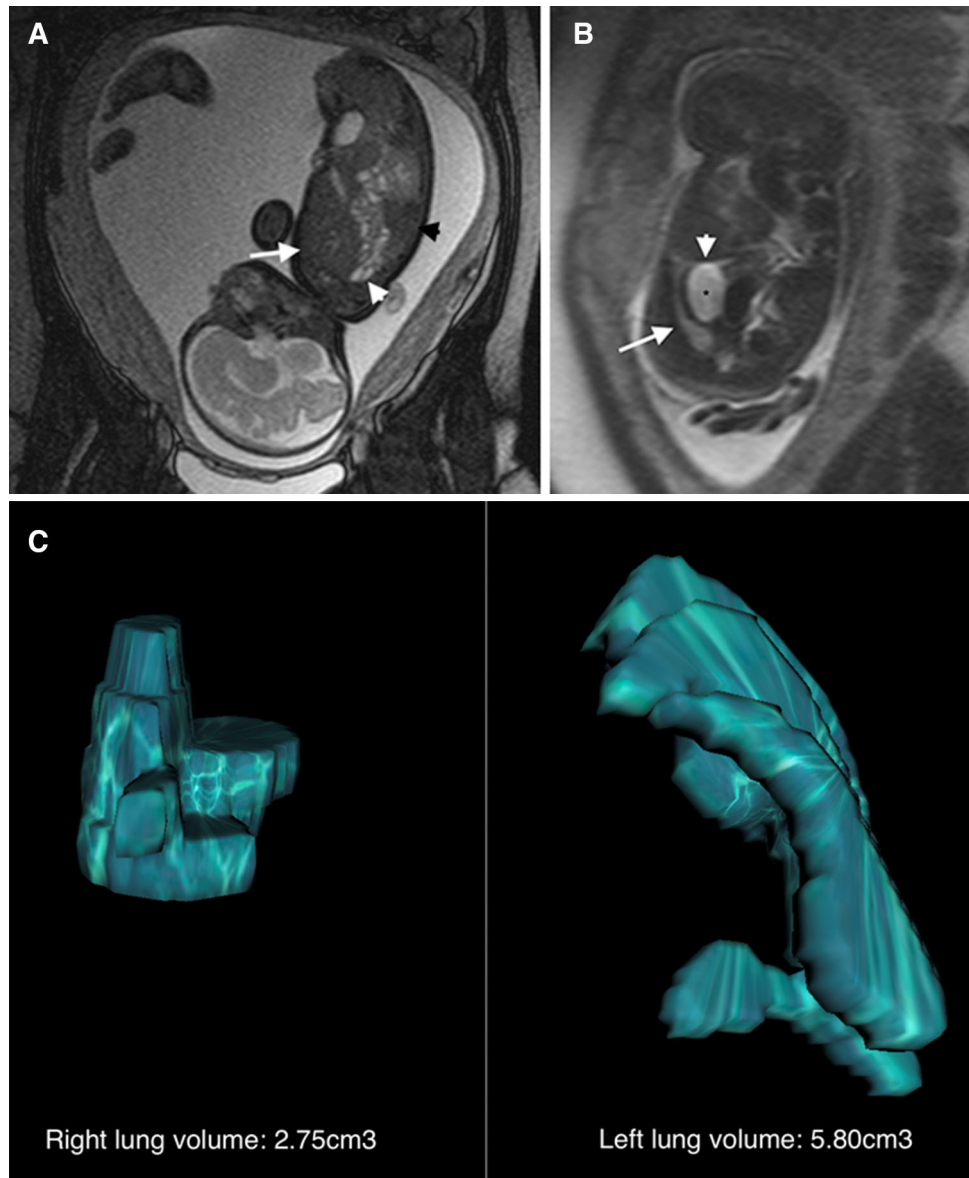
## Case Presentation

### Case 1

A 29-year-old lady was referred at 35 weeks of gestation for elective lower cesarian section due to 2 previous scars. An antenatal ultrasound scan revealed polyhydramnios and cystic lesions in the right side of the thoracic cavity. A subsequent fetal MRI demonstrated absent right

hemidiaphragm with herniation of right lobe of liver, loops of small bowel and hepatic flexure into the right hemithorax (Fig. 1a). The right lung was barely visible and displaced superiorly (Fig. 1b). The left hemidiaphragm was otherwise intact. Using OsiriX MD12.0, a post-processing MRI measurement of right and left lung volumes were 0.92mls and 17.32mls respectively (Fig. 1c). The fetus was diagnosed with right diaphragmatic hernia with associated right lung hypoplasia. An elective cesarian section was

**Fig. 2** **a** Herniation of liver (white arrow), as well as small bowel (white arrowhead) and large bowel (black arrowhead) into the right hemithorax **b** Hiatal stomach hernia (asterisk) in the left hemithorax compressing the ipsilateral lung (white arrow). Note that the diaphragm is intact (white arrowhead). **c** Post-processing MRI measurement of the right and left lung volumes



performed at 37 weeks of gestation. Intramuscular dexamethasone was administered for fetal lung maturation. Upon delivery, the newborn had poor breathing effort, was cyanosed and subsequently intubated. Despite optimum intensive care, the baby succumbed at day 3 of life.

## Case 2

A 30-year-old primigravida, was referred to a tertiary hospital at 26 weeks of gestation for suspected right diaphragmatic hernia on antenatal scan. Amniocentesis

performed at 15 weeks of gestation to check for aneuploidy, was normal. A recent detailed obstetric scan at 30 weeks showed congenital bilateral diaphragmatic hernia with intrathoracic liver, bowel and stomach herniation. The lungs were small. There was associated polyhydramnios. MRI was performed at 30 weeks of gestation showing herniation of liver, as well as small and large bowel into the right hemithorax (Fig. 2a). The left hemidiaphragm was well delineated. There was, also, hiatal stomach hernia into the left hemithorax (Fig. 2b). Both lungs were compressed and small in volume. The right and left lung volumes were

2.75ml and 5.8ml respectively (Fig. 2c). Following a planned and controlled delivery via an elective cesarian section at 37 weeks of gestation, the baby succumbed at day 3 of life, despite optimum intensive care.

## Discussion

Failure of the pleuroperitoneal folds to close during fourth to tenth weeks post conception results in a diaphragmatic defect and allows herniation of visceral content into the thoracic cavity. This in turn, interferes with normal lung development. The severity of these adverse effects vary, depending on the gestational age when the viscera herniate [4].

Over 60 percent of CDH cases are initially suspected on a routine sonographic fetal anatomic survey at 18 to 22 weeks of gestation [5]. Mild cases may not be identified until later in life as these present with mild gastrointestinal or respiratory symptoms or are first suspected on a chest radiograph [6].

Prenatal diagnosis of CDH is based on the visualization of abdominal organs in the fetal thoracic cavity [7]. CDH may be accompanied by polyhydramnios or rarely hydrops. A wide range of sensitivity of ultrasound in detecting CDH has been reported with higher sensitivity when the defect is large, with advancing gestational age, presence of associated abnormalities and with experienced sonographers performing the examination [8].

CDH is associated with a spectrum of morbidity and mortality. High survival is expected in neonates with mild physiologic consequences of CDH. Severe cases however, despite advancement of neonatal management, are still associated with significant mortality. In these cases, Brown et al. [1] reported mortality rate between 30 and 50%, while another study by Yokoi et al. [2], reported mortality rate as high as 70 to 80%. Prenatal diagnosis of CDH allows parents to obtain a prognosis and treatment options via multidisciplinary counselling. These include prenatal intervention or expectant prenatal management, postnatal intervention or postnatal palliative care, as well as pregnancy termination in those cases with poor prognosis [9].

Several prognostic factors have been of significant interest which could assist in optimizing treatment options, with pulmonary hypoplasia having the utmost importance. This is calculated by measuring both lung sizes and estimating fetal lung volume. Several studies have reported that magnetic resonance imaging (MRI) is superior to 2-dimensional or 3-dimensional ultrasound in both diagnosis of CDH and outcome prediction, as it is not affected by oligohydramnios, fetal position and allows visualization and measurement of fetal lung volume irrespective of maternal body mass index (BMI) [3].

MRI measurement of observed-to-expected total fetal lung volume (O/E-TFLV) is a recognized independent predictor of neonatal mortality and morbidity. A study conducted by Düttemeyer et al. [3] calculated lung volume using T2 HASTE sequences in the transverse plane which allowed complete lung imaging without motion-induced artifacts. The area of the lungs was determined on each section by using free-form regions of interest (ROI). The measured areas were added and subsequently multiplied by inter-gap and slice thickness to determine the entire volume of the right and left lung. Summation of the right and left lung volume provided the TFLV. The authors expressed each TFLV measurement as a percentage of appropriate normal mean for gestational age (O/E ratio of TFLV  $\times$  100), which was based on a study of 215 fetuses with normal lung development at 21–38 weeks of gestation [10]. A recent study with bigger sample size, derived a best fit formula for TFLV according to gestation (from 18 to 38 weeks gestation) [11], which were similar to values predicted by Rypens [10].

MRI for our first case was performed at 35 weeks of gestation with isolated right sided CDH and liver herniation. The TFLV was 18.24ml. Based on a study performed by Meyers et al. [11], the expected mean TFLV for a 35 weeks gestation is 93.6ml ( $\pm$  27.0). The O/E-TFLV was 19.5%. The second case was also a right sided CDH but complicated by a hiatal gastric hernia into the left hemithorax. MRI was performed at 30 weeks gestation and showed herniated liver and bowel into the right hemithorax. Both lungs were compressed and hypoplastic. The TFLV was 8.55ml. The expected mean TFLV at 30 weeks gestation is 63.3ml ( $\pm$  14.0) and the O/E-TFLV for the fetus was 13.5%. Both fetuses were delivered via planned cesarian section but succumbed on day 3 of life despite optimum intensive care.

Brown et al. [1] showed that the O/E-TFLV was significantly associated with mortality. A mean O/E-TFLV in non-survivors was reported at 24%. Stomach position in the intrathoracic cavity was also significantly associated with mortality ( $P = 0.049$ ) [1]. In other studies, both O/E-TFLV and liver herniation were significantly associated with neonatal mortality and morbidity [3]. Le et al. developed the congenital diaphragmatic hernia congenital prognostic index (CDH-CPI) based on 10 prenatal parameters which encompass genetic, cardiac, hernia and lung factors [12]. Meanwhile, Brown et al. [1] used the multi-variable model to assign weights for different fetal MRI imaging factors and came up with a prediction model for mortality, where mortality (%) =  $1 / (1 + e^{-X})$ . For O/E-TFLV of less than 24%,  $X = -1.63 + 2.7 \times$  (stomach herniation) +  $0.94 \times$  (liver herniation), where 1 and 0 denote presence and absence of herniation respectively [1].

Based on this prediction model, the mortality rates for both of our cases were 33.4% and 88.2% respectively.

This predictive mortality calculator utilized information which was easily obtained from fetal MRI and subsequently provided statistical data for healthcare providers in counselling families and aids in risk-stratification. Severity scoring can influence perinatal management. Affected parents can make early preparation physically, financially, and emotionally considering prolonged hospital stay, several surgical interventions, medications, chronic lung disease and possible death. In cases where the child is ineligible for postnatal intervention or imminently fatal, the care team could provide appropriate counseling and delivery arrangements with palliative care in mind [1].

Such predictive mortality calculators are still underutilized in our local setting. Fetal MRI was performed at 30–35 weeks of gestation in both cases. Style et al. [13] concluded that accuracy of MRI lung volumes to predict outcome is dependent on the gestational age at the time of examination with the second trimester lung volume to be strongly correlated with mortality [13]. Based on this evidence, we propose early scheduling of fetal MRI at second trimester for suspected CDH so that the parents can be counseled earlier of the fetal outcome.

## Conclusion

In conclusion, we would like to highlight the importance of utilizing such predictive mortality calculator in fetuses diagnosed with CDH. Early counseling of parents about outcome anticipation and the necessary preparations as well as planned delivery with neonatal intensive care unit and pediatric surgical backup can be accomplished. Furthermore, fetal MRI, which is underutilized in our country, should be developed, and fully utilized as an adjunct examination to ultrasonography, to provide better three-dimensional information.

**Author's contribution** All authors have accepted responsibility for the entire content of this manuscript and approved its submission. All authors contributed to the study conception and design. Material preparation and analysis were performed by Azril Ishak and Hasyma Abu Hassan. The first draft of the manuscript was written by Azril Ishak and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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## Declarations

**Conflict of interests** Authors state no conflict of interest.

**Ethical Approval** The local Institutional Review Board deemed the study exempt from review.

**Informed Consent** Informed consent was obtained from all individuals included in this study. The subjects have given their written informed consent to publish their cases and can be made available upon request.

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