# WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

# IMAGISTIC CORRELATIONS BETWEEN ULTRASOUND AND MRI EXAMINATION OF THE FETUS WITH CONGENITAL DIAPHRAGMATIC HERNIA

**Erick Nestianu*[1], Cristina Guramba Bradeanu[2], Ioana Dragan[3] and Radu Vladareanu[1,4]**

[1]University of Medicine and Pharmacy "Carol Davila" Bucharest, Romania.
[2]Affidea Fundeni Imaging Center Bucharest Romania.
[3]Columna Medical Center, Bucharest, Romania.
[4]Obstetrics and Gynecology Department of the Emergency University Hospital Elias of Bucharest, Romania.


***Corresponding Author: Erick Nestianu**

University of Medicine and Pharmacy "Carol Davila" Bucharest, Romania.

## ABSTRACT

**Aims:** We wanted to find correlations between the ultrasound examination of pregnancies with diaphragmatic hernia and the MRI examination that followed in these cases. Fetal MRI is used to confirm, complete and make the differential diagnosis in difficult cases. In some cases, it can also bring forth now information regarding the prognosis. **Methods:** This was a retrospective study of 6 pregnancies that were recommended to a third-degree maternity from multiple diagnosis centers. The ultrasounds and MRI examinations were performed in specialized fetal medicine study centers. The information obtained about the progression of pulmonary hypoplasia helped decide the prognosis and treatment of these cases. **Results:** The diagnosis was made in the second trimester in 4 cases and in the third trimester in the other 2 cases. We described the herniated organs, the dimensions of the hernia and the remaining lung capacity so that we could correctly evaluate the prognosis. We also used the Lung to Head Ratio (LHR) to try and better determine the degree of lung hypoplasia. **Conclusions:** Considering diaphragmatic hernia as solitary malformation, the localization (on the left side, right side or bilateral) corresponds with international statistics. High quality ultrasound followed by an MRI examination helped correctly appreciate the prognostic, treatment possibilities and the total affected lung volume. With the expansion of highly specialized fetal medicine study centers, there will be an increase in the diagnosis capacity. The MRI follow up will increase the certainty of the diagnosis and improve the overall quality of the medical care.

**KEYWORDS:** Fetal diaphragmatic hernia, fetal abnormalities, prenatal diagnosis, ultrasound examination, fetal MRI.

## INTRODUCTION

Congenital diaphragmatic hernia is a malformation that can cause severe consequences in the development of the new born, that will usually be admitted in the neonatal ICU, rising the morbidity and mortality during this period. Modern ultrasound techniques improved the diagnosis of this pathology, which complemented by the MRI examination offer an increased diagnostic accuracy.[1]

For the last 30 years, the intrapartum diagnosis of the diaphragmatic hernia has been made using ultrasound. It is recognized as a syndrome that includes pulmonary hypoplasia, pulmonary immaturity, hypoplasia of the left heart and neonatal PPHN.[2]

Our goal is to identify the malformation as soon as possible, and based on the individual characteristics of the pregnancy, to guide the patients to a competent and specialized hospital (a level III intensive care nursery with neonatal and pediatric surgery support), that has all the necessary equipment and a well-trained team of doctors and nurses that can offer the best chance of survival for the newborn.[3]

Such complicated cases require a team of doctors, from numerous specialties, such as pediatric surgeons, neonatologist, gynecologists, pediatric radiologist, infantile pneumologist, genetics expert, fetal medicine expert, etc.

There is a different approach based on the severity of the hernia, as such, cases where the diaphragmatic defect is small do not require such ample intervention. The real problems appear when the defect is large, when the newborn usually needs very skilled intensive care. These cases can be helped by high frequency ventilation, NO administration and even ECMO (extracorporeal membrane oxygenation).

Recently, new in-utero treatments have been developed, such as FETENDO and FETO. In the case of diaphragmatic hernia, the goal is to implant a balloon in the trachea and obstruct it, so that the lung can expand to the thoracic wall. These new techniques use a combination of ultrasound and real time video imagery.[4]

## Incidence

Prayer et al found the incidence of diaphragmatic hernias to be situated between 1/2500-1/5000 births, while The Fetal Medicine Foundation found the incidence to be approx. 1/4000 births.[5,6]

The most recent study was made by The Kings College Hospital in London. They surveyed 100.000 pregnancies and found 1.720 cases of non-chromosomal malformations. Out of these, 24 were diaphragmatic hernias. 7 Cases were diagnosed in the first trimester, 14 in the second trimester, 2 in the third trimester and the last one was observed postpartum.[7]

Ample studies in the last 30 years made on lots of over ten million pregnancies found an incidence of diaphragmatic hernia at approx. 2,3/10.000.[5,8] They also concluded that it represents about 8% of the total malformation that affect the fetus.[9]

Other studies made by The Central-Eastern France Birth Defects Registry, and ISUOG (International Society of Ultrasound in Obstetrics and Gynecology) show similar incidence and an average prenatal detection rate of approx. 59%, which is considered acceptable.[10,11]

Many other studies, from all over the world; from Europe (The Catholic University of Rome) that used MEDLINE and Cochrane Central Register of Controlled Trials data.[12,13] as well as other studies from the United States of America, India and Australia are in consensus, all of them describing an incidence of around 1/2000-4000 births.[14,15,16]

An Australian study shows that the majority of cases were delivered at term (70%) and had a survival rate of 64% while the other 30% were born prematurely and had only a 35% survival rate.[17]

As expected, most of the cases come from single pregnancies, and in about 40% of all cases, the diaphragmatic hernia is also associated with another genetic syndrome.[5,8] The most common are 21, 18 1nd 13 trisomy, but also 12p tetrasomy.[6,18] Other anomalies include syndromes such as: Fryns, Lange, Marfan, Pallister-Killian and Donnai-Barrow.[6,19]

The mother age over 40 years, Caucasian race, smoking and alcohol use are cited among the risk factors.

There is an apparent 1/0,69 male to female ratio of the malformity.[20]

The mean detection age is 24,2 weeks.[21,22] A higher incidence of premature birth, intra-uterine growth restriction and death (antepartum as well as postpartum) has also been noted. The mortality of this cases at 1 year of age is around 45.8%.[23]

It is believed that the true mortality of this anomaly is sub estimated all over the world, mainly because not all births take place in specialized centers.[24]

Congenital diaphragmatic hernia appears as a result of a diaphragmatic defect. The defect appears in the embryonic stage and can be the cause for pulmonary hypoplasia and persistent fetal pulmonary hypertension.[9,25] In most cases, it affects the left diaphragm, but it can also be localized on the right diaphragm or even bilaterally.[14]

From a clinical standpoint, 70% are posterolateral (Bochdalek hernia), and approx. 25-30% are on the anterior side (Morgagni hernia). The central part is rarely affected.[25]

Usually, the lung on the affected side is hypoplastic, while the lung on the contralateral side is only partially affected. As such the bronchial tree and the alveoli are not properly developed, all while the epithelium is also being affected. This can lead to the apparition of the hyaline membrane syndrome as well as a surfactant deficiency.[26]

## MATERIAL AND METHODS

We are trying to find correlations between the ultrasound description and the MRI examination results, that are suggestive for diaphragmatic hernia. The article is based on a retrospective study that began in the middle of in 2019.

The inclusion criteria were as follows: pregnant women that underwent second trimester fetal morphology ultrasound in specialized diagnosis centers, pregnant women that had a follow-up MRI examination to confirm or to complete de ultrasound diagnosis and lastly patients in which the diaphragmatic hernia was the only observable malformation.

The patients were rigorously monitored throughout the pregnancy, as the ISUOG protocols dictate, with follow up ultrasound in the second as well as in the third trimester, respecting all the guideline parameters.[27]

The ultrasound examination was performed on high-end devices, with a dedicated software for the obstetrics examination. They can use mode B eco-doppler, and are equipped with a convex transducer with a wide band and frequency between 2 and 8 Mhz. We adapted the power as needed, generally using a lower setting so that we can obtain a good image depth and special resolution (so we could better describe the existing lesions).

After the original ultrasound diagnosis was made, the patients were advised to undertake a follow-up MRI examination. This is made using an 1,5 Tesla MRI machine, without the use of gadolinium contrast agents, as are the current international recommendations. We used body coils to enhance the image and the following sequences: Fast Imaging Employing Steady State Acquisition (FIESTA, FOW de 450/500 mm, TR of 5,2 ms, TE of 2,4 ms), Single Shot Fast Spin Echo (SSFSE, FOW de 450/500 mm, TR of 534.4 ms, TE of 160.2 ms), Diffusion Weighted Image (DWI, FOW de 450/500 mm, TR of 6.2 ms, TE of 3.1ms) and Liver Acquisition with Volume Acceleration (LAVA, FOW de 450/500 mm, TR of 6.2 ms, TE of 3.1ms). The slice thickness was between 4 and 6 mm.[28]

The investigation was made with the mother in the supine or lateral position, without de administration of sedation, as per the ISOUG recommendations.[29]

We obtained approval from the Ethical Committee of the examination center prior to conducting this study. All the patients have also signed an informed consent prior to the inclusion in this study.

We started to enroll patients in our study since mid-2019. The mothers were examined by ultrasound a specialized third-degree maternity.

The prognosis was evaluated using the LHR ratio that was corelated with the gestational age, using the procedures recommended by Jani et al.[5]

We enrolled 6 patients, 4 were of gestational age between 21,3 and 26,3 weeks and the other 2 between 33,1 and 34,2 weeks. All of them performed an MRI scan. We were most interested in the size of the defect, what organs herniated in the thorax and the impact on the lungs; we took all this in to consideration when we decided the prognosis and the treatment procedures.

## RESULTS AND DISCUSSION

The ultrasound finding compatible with diaphragmatic hernia were: an excess of amniotic fluid (polyhydramnios) and/or the presence of abdominal structures in the thoracic cavity. Polyhydramnios is also an indicator of premature delivery. The diaphragm is visualized as an echo-free space between the abdominal and thoracic cavity on sagittal and coronal slices. Just viewing the diaphragm is not enough to make the diagnosis of diaphragmatic hernia. The ultrasound diagnosis is made only after objectifying direct signs, such as: stomach, intestines or liver that have ascended in the thoracic cavity, and indirect signs, such as: mediastinal shifting on the contralateral side, and cardiac axis shifting.[22]

The diagnosis is easier if the herniation takes place on the left side (80-90% of cases) because, the stomach and intestines contain liquids with a characteristic ultrasound aspect, that are discordant with the normal lung image. In the transversal slices, we have 2 major signs that help with the diagnosis: the presence of the stomach or intestines in the thoracic cavity, as stated above and the sifting of the mediastinum. The abdominal circumference is smaller, and we can observe the absence of the normal organization of the herniated organs. We can also observe in some cases polyhydramnios, hydrothorax (in 5%of cases) and rarely hydrops.[22]

Diagnostic problems appear when the liver herniates through the defect because of the similar aspect of the liver and lung of the fetus. The stomach can also herniate along with the left liver lobe, in which case the examiner has an easier job differentiating the structures. If the right hepatic lobe herniates, the gallbladder can help with the diagnosis, as it is seen separately from the stomach. By using Doppler examination, the hepatic veins and port system can also be identified.[22,30,31] These cases benefit the most from an MRI follow-up examination, as even with the assistance of the Doppler effect, sometimes the examination can be inconclusive due to the high similarity between the lung and the liver at this stage of development.

Bilateral diaphragmatic hernia is rarely present (1-2% of cases), and has both of the characteristics discussed above; mainly stomach and intestines that occupy the left hemithorax and liver that ascend in the right hemithorax. Ultrasound can also observe cardiac suffering caused by the pressure that the herniated organs put on it. Ultrasound follow-up should be made every 4 weeks, in accordance to The Fetal Medicine Foundation protocols.[6]

The differential diagnosis should be made with pulmonary cystic disease, cystic adenomatous malformations, or mediastinal cystic process (pulmonary sequestration, bronchogenic cyst or thymic cysts.

The main limitation remains the correct evaluation of pulmonary hypoplasia.[32] This is the most important prognostic factor when talking about the survival rate of the newborn. Ultrasound prediction factors include: the ratio between the left and right ventricle, the ratio between the pulmonary diameter and the thorax circumference, the amount of amniotic fluid, shifting of the normal mediastinal and stomach positions.[5]

Some authors suggest the use of a Lung and Head circumference Ratio (LHR). The lung can be measured on the transversal 4 chambers ultrasound slice.[9] The lungs develop 4 times as much as the head between the 12'th and 32'th week, and as such the LHR ratio must be adapted in accordance with de gestational age so that it can correctly predict the amount of lung hypoplasia. There are multiple techniques used to measure this ratio; such as the one used by the University of San Francisco, in Europe, the one proposed by Jani et al. is more commonly see, and it is also the one we used.[3] The

quality of the prediction improves if we also take in to account the presence of the liver in the thorax.[5]

The cutoff values of his ratios between 22 and 28 weeks of pregnancy are as follows: 0,4-0,5 there is a 0% survival rate, 0,6-0.7 there is a 30% survival rate, 0,8-0,9 there is a 32% survival rate, 1,0-1,1 there is a 74% survival rate, 1,2-1,3 there is a 38% survival rate, 1,4-1,5 there is a 72% survival rate and finally, over 1,6 there is an 88% survival rate.[5]

Extrapolating from this, it is estimated that an LHR value lower than 15% of the normal value represents an extreme stage of pulmonary hypotrophy, with no chances of survival, a value between 15-20% (severe pulmonary hypoplasia) has a 20% survival rate, a value between 26-35% (moderate pulmonary hypoplasia) has a survival rate of 30-60% and a value between 36-45% (light pulmonary hypoplasia) has a survival rate of over 75%.[22]

Another sign of pulmonary suffering can be objectified by measuring the pulmonary artery blood pressure. This is done using ultrasound, and can show evidence of tissue perfusion abnormalities.

MRI can differentiate lung from liver and other herniated structures from the mediastinum. Early examinations are performed to identify what organs have ascended through the defect, but also to try and identify any other possible malformation that the ultrasound might have missed. MRI examinations are performed at a more advanced age, generally to evaluate the pulmonary volume and the pulmonary hypoplasia.[22]

MRI can determine how much of the liver is herniated.[5] (the volume of the herniated liver is another indicator of the lung suffering) and also make the differential diagnosis with other diseases, such as: congenital pulmonary airway malformation (CPAM), pulmonary

sequestration, congenital lobar emphysema, pleural effusions, tumoral masses and skeletal dysplasia.[6] It is also an important tool to asses the lung on the herniated side, as it is difficult to make such measurements in the case of ultrasound, thus providing an accurate evaluation.[5]

Another attempt to better measure the lung capacity is by analyzing the lung volume, using MRI volumetry (TLV or TFLV).[22] This is a technique that has been in use since the 90'. An innovative method to approximate the total lung capacity is by using the percent predicted lung volume (PPLV). In this care we measure the total thoracic volume from which we subtract the mediastinal volume, thus giving us an estimated lung volume.[22]

3D reconstruction of the fetal diaphragm defect and the surrounding organs is a relatively new method to determine the impact of the hernia. With this we can more clearly see the localization and size of the hernia and quantify it better. The surgical planning can be made using these reconstructions, as well as developing a personalized therapeutic plan (personalize patch design based on 3D-printable templates).[33]

In all of the 6 cases, the ultrasound biometry was in concordance with the MRI biometry.
1 case was from a twin pregnancy, while the other 5 were single pregnancies.

In 5 cases the defect was on the left side, and in 1 case it was on the right side. We didn't have any bilateral hernias.
4 cases were diagnosed in the second trimester and 2 in the third trimester.

The stomach herniated in 5 out of the 6 cases, and was the most frequently involved organ. The left liver lobe was more or less herniated in 3 cases. Fig 1, Fig 2.



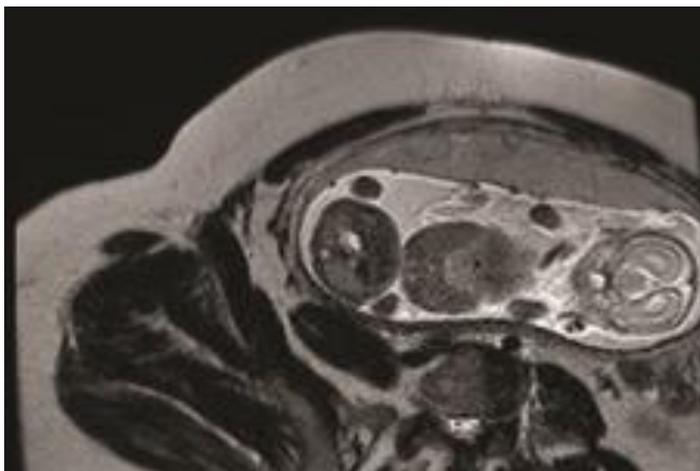**Fig. 1: Transverse section of the thorax reveals the 4-chamber view of the fetal heart.**

**Fig 2: SSFSE aquisition T2 weighted axial section of a twin pregnancy.**

In 1 case the right liver lobe was the one that herniated. Fig 3, Fig. 4



**Fig 3: Transverse section of the thorax. The heart is displaced to the left hemithorax.**
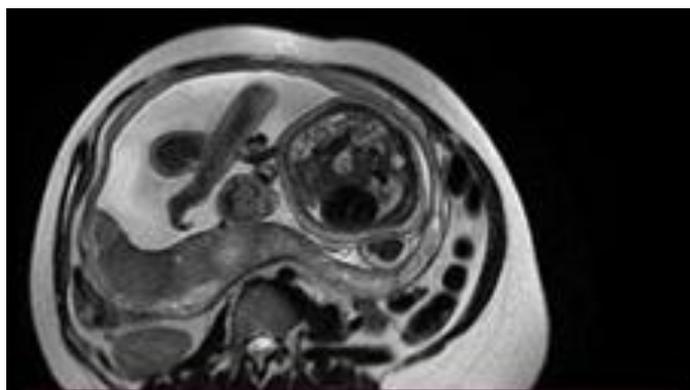


**Fig 4: SSFSE aquisition T2 weighted axial image. It clearly shows the herniation of the right liver lobe and the gallblader.**

Intestinal loops were seen in the thorax in 4 cases, and in
2 cases we even observed parts of the colon. Fig 5.

**Fig. 5: Transverse section of the thorax reveals the 4-chamber view of the fetal heart, in which we observe a left diaphragmatic hernia.**

In 1 of those 2 cases, segments from all the colonic regions were herniated. The MRI examination also helped differentiate between the intestinal loops and the colonic segments, Fig 6.
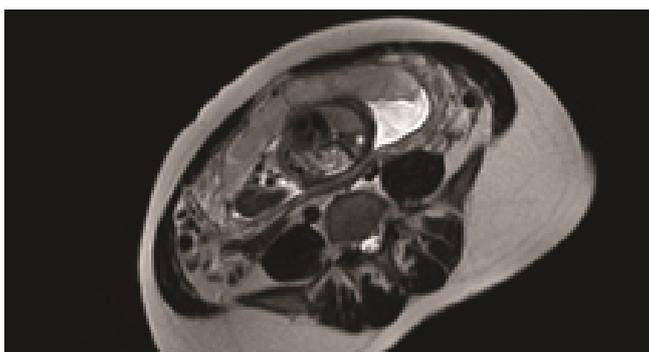


**Fig. 6: SSFSE aquisition T2 weighted axial image in which we can identify the stomach, small bowel loops, and a part of the colon.**

Two times the MRI examination differentiated the lung from the liver, something which the ultrasound examination was not able to. Fig.6 Fig. 7, Fig. 8, Fig. 9. One of them was the case with the right hernia, in which the right lung was collapsed and pushed to the left by the liver.



**Fig. 7: Transverse section of the thorax that reveals a hipoplasic right lung, a partialy collapsed left lung and the heart that is placed in the right hemithorax.**
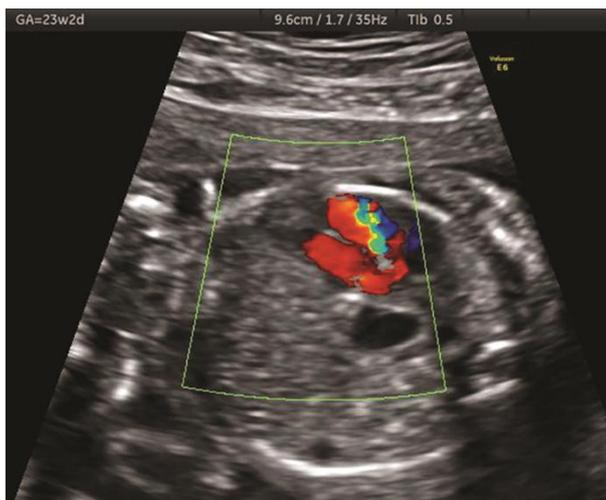
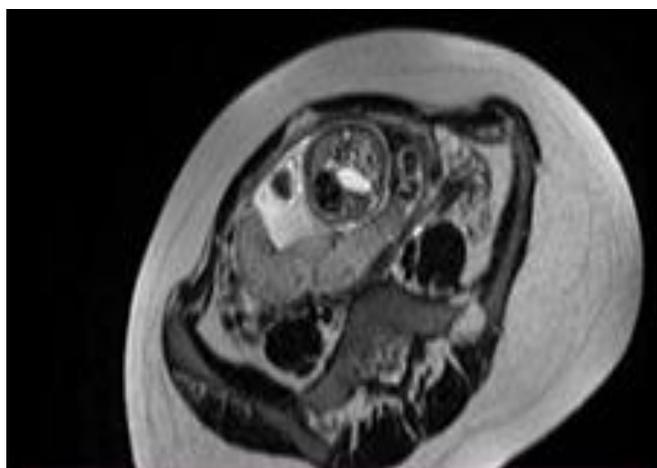**Fig. 8: The same image as Fig 7, but with collor doppler included.**



**Fig. 9: SSFSE aquisition T2 weighted axial image.**

The ultrasound scan was not able to determine if the lung had shrunk in volume, but fortunately, the MRI investigation provided the answers, and confirmed a reduction in total lung volume. It also showed the herniation of the left kidney. Fig 10, Fig. 11. In the second case, it differentiated the lung and liver of a left sided defect, in which the liver ascended in the thorax. Fig. 11, Fig. 12, Fig. 5.
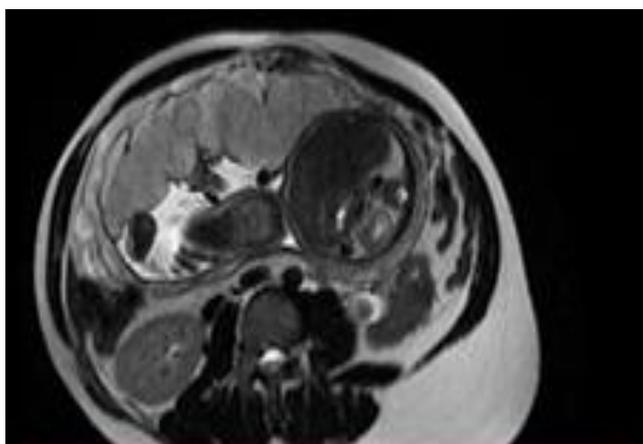


**Fig. 10: SSFSE aquisition T2 weighted axial image that sows the herniation of the left kidney.**
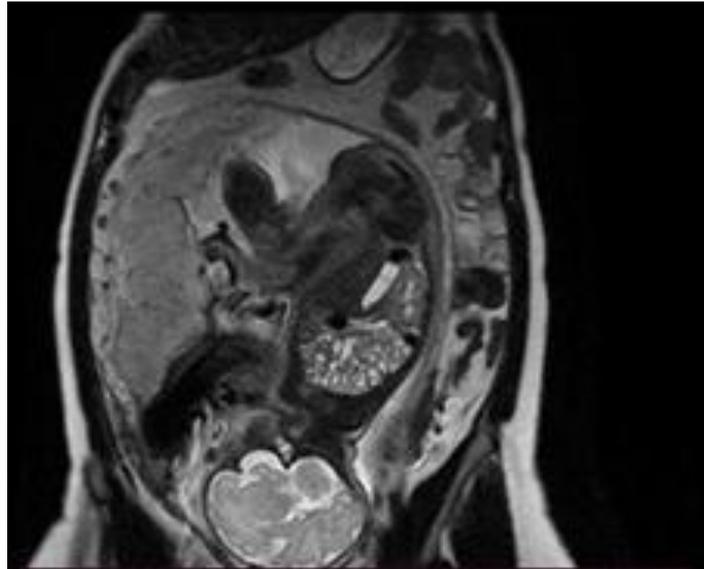
**Fig. 11: SSFSE aquisition T2 weighted sagital image of the same case as Fig 10.**



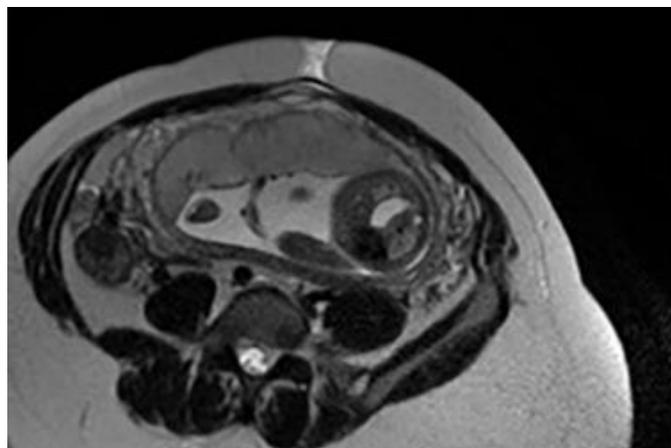**Fig. 12: Left diaphragmatic hernia.**



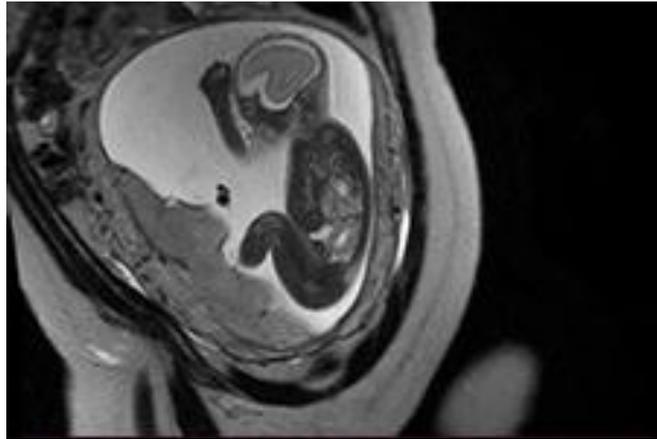**Fig. 13: SSFSE aquisition T2 weighted axial image.**

**Fig. 14: SSFSE aquisition T2 weighted safital image of the same case as Fig 13.**

If only the small bowel was herniated, the remaining healthy lung volume was significantly larger than in the cases where the colon also herniated.

When we calculated the LHR, we found 2 situation in which it was 1,5 (good prognosis with 72% survival rate), 2 cases where it was 1,2 (a good prognosis, but with only 68% survival rate), and the last 2 cases had an LHR of 0.9 respectively 1.0 (bad prognosis, with only about 32% survival rate).

The ratio between the calculated LHR and the estimated one adapted to the gestational age was between 60-60,8% (good prognosis) in 4 cases, respectively 55% (relatively good prognosis) and 14% (very bad prognosis) for the last 2 cases.

All the mothers were guided to third degree medical centers at the due date, and all the surviving babies needed specialty neonatal ICU treatments, as well as pediatric and pediatric surgery evaluation.

We studied all the cases that we found during a year, which didn't represent a numerous lot, but considering the low incidence of these malformation, it is within the expected parameters.

Findings were consistent with specialty literature, and as such, most of the cases (5 out of 6) presented with a left side herniation, and also this was the sole malformation detected. The most common herniated structures were the stomach and the small bowel. Three cases also presented herniation of the liver – 2 cases had the left liver lobe herniated n the thorax, whilst the last one presented herniation of the right liver lobe along with the gall bladder. Only one of the 6 patients had a kidney displaced through the herniation defect.

We calculated the LRH in all cases, so that we can better appreciate the level of lung hypoplasia, from which we then estimated the survival rate. Naturally, better results were observed when only the defect was smaller and only small bowel, stomach and a little bit of liver was discovered in the thoracic cavity, as opposed to the cases

when a larger part of the liver and even a kidney was seen to migrate through the defect.

In our study, the MRI examination has provided some extra information when comparing it to the ultrasound as follows:

- In one case it could correctly differentiate between the collapsed lung and the liver lobe that ascended in the thorax, thus allowing a much better evaluation of the LHR and the remaining pulmonary volume
- In another case it revealed that a kidney also ascended in the thoracic cavity through the diaphragmatic defect. Even though this was the case, pulmonary volumetry was not as bad as it would have been expected, revealing moderate lung hypoplasia.
- In 4 cases it distinguished between the small bowel and the segments of the colon that herniated through the defect.
- In one case it confirmed the herniation of the right liver lobe, along with the gall bladder. The ultrasound was not able to correctly identify the gall bladder and the small bowel that herniated.

Calculating the LHR and the ratio between the calculated LHR and the estimated value corresponding to the age of the pregnancy proved useful in determining the prognosis and the degree of pulmonary hypoplasia.

All the mothers were guided to specialized third degree hospitals, that had infantile surgery and specialized ICU staff and equipment for the delivery.

We believe that with the expansion of specialized medical centers, the discovery rate of such pathologies will increase. The correlation between the ultrasound findings and the MRI examination will improve the final outcome of the patients. The family must be counseled to complete the necessary investigations and to approach specialized healthcare so that we can offer the best chances of survival to the newborn. The lack of developed medical centers will mean that some cases will be missed, and this can lead to a more complex and difficult postpartum treatment.

Finally, we consider that if the delivery isn't made in a specialized medical center that does not have a specialized ICU and infantile surgery ward the newborn might not be able to get the needed medical attention in time.

## CONCLUSIONS

The training of ultrasound specialists and also the improving technology that the ultrasound machines offer will undoubtably lead to an increase of anomaly detection. This coupled with the ever-growing accessibility to MRI examinations will guarantee that the diagnosis is made correctly and that it can be thoroughly characterized.

This means that the at-risk mother can be more carefully monitored throughout the pregnancy and that they can be led to specialized third-degree hospitals that have all the necessary equipment and staff to rapidly intervene if need be. This allows even for in-utero procedure to be made at relatively low risks.

Through this collaboration between gynecologists and radiologist, we believe that a real step forward has been made towards a better quality of healthcare for the mother and baby.

## REFERENCES
1. Fernández PY, García DL, Sánchez J,Antiñolo G, Borrego S Ultrasound, Echocardiography, MRI, and Genetic Analysis of a Fetus with Congenital Diaphragmatic Hernia and Partial 11q Trisomy. *Case Rep Obstet Gynecol,* 2017.
2. Shripati AJ, Gowdra A, Javaregowda D, Jadhav V, Narendra BM., Sahadev R. Hernia in Neonates: Our Institutional Experience. *J Indian Assoc Pediatr Surg,* 2018; 23[3]: 131–139.
3. UCSF University of California, San Francisco. *https://fetus.ucsf.edu/cdh.* [Online] Benioff Children*s Hospitals. [Cited: Jan 25, 2021.] https://fetus.ucsf.edu/cdh.
4. Deprest J, Gratacos†, Nicolaides KH, Fetoscopic tracheal occlusion (FETO) for severe congenital diaphragmatic hernia: evolution of a technique and preliminary results. *Ultrasound Obstet Gynecol,* 2004; 24.
5. Cannie M, Jani J. Diagnosis of Congenital Diaphragmatic Hernia. [book auth.] D. Prayer. *Fetal MRI.* Berlin - Haidelberg : Springer - Verlag, 2011; 229 - 339.
6. The Fetal Medicine Foundation. https://fetalmedicine.org/education/fetal-abnormalities/thorax/diaphragmatic-hernia. *fetalmedicine.org.* [Online] [Cited: Jan 19, 2021.] https://fetalmedicine.org/education/fetal-abnormalities/thorax/diaphragmatic-hernia.
7. Syngelaky A., Hammami A., Bower S., Zidere V.,Akolekar R. Diagnosis of fetal non-chromosomal abnormalities on routine ultrasound examination at 11-13 weeks' gestation. *Ultrasound Obstet Gynecol,* Oct 2019; *468-476.*
8. McGivern MR, Best KE, Rankin J , et al. Epidemiology of congenital diaphragmatic hernia in Europe: a register-based study. *Arch Dis Child Fetal Neonatal Ed,* Mar 2015.
9. Points, Key. Congenital Diaphragmatic Hernia. [book auth.] Timothy M. Crombleholme, Mary E, D"Alton, Fergal D. Malone Diana W. Bianchi. *Fetology Diagnostic and Management of the Fetal Patient.* second. New York : Mc Graw Hill, 2010, 37.
10. Gallot D, Boda C, Ughetto S , et al. Prenatal detection and outcome of congenital diaphragmatic hernia: a French registry-based study. *Ultrasound Obstet Gynecol,* Mar 2007; *29[3]: 276-283.*
11. Clementi, E. Garne M. Haeusler I. Barisic R. Gjergja C. Stoll M. Congenital diaphragmatic hernia: evaluation of prenatal diagnosis in 20 European regions. *Ultrasound in Obstetrics & Gynecology,* 2002; 19(4).
12. Logan JW, Rice HE , Goldberg RN, Cotten CM. Congenital diaphragmatic hernia: a systematic review and summary of best-evidence practice strategies. *J Perinatol,* 2007; 27[9].
13. Caruso L. Masini M. De Santis G. et al. Congenital diaphragmatic hernia: prenatal evaluation and outcome. *Ultrasound in Obstetrics & Gynecology.* April 30, 2002; 18(1).
14. Woodbury JM., Bojanić K, Grizelj R, et al. Incidence of Congenital Diaphragmatic Hernia in Olmste Country, Minnesota: A Population-Based Study. *J Matern Fetal Neonatal Med.* Oct 29, 2017.
15. Lin EC, Hekmatnia , Ali McHugh K. Congenital Diaphragmatic Hernia (CDH) Imaging. *Medscape.* [Online] May 07, 2020. [Cited: Jan 17, 2021.] https://emedicine.medscape.com/article/407519-overview.
16. Emrah Aydin, Lim Foong-Yen, Kingma Paul, Foong-Yen, Haberman Beth, et al. Congenital diaphragmatic hernia: the good, the bad, and the tough. *Pediatr Surg Int.,* 2019; 35[3]: 303-313.
17. Levison John, Halliday Robert, Holland Andrew J A, et al. A population-based study of congenital diaphragmatic hernia outcome in New South Wales and the Australian Capital Territory, Australia, 1992-2001. *J Pediatr Surg,* Jun 2006; 41[6]: 1049-53.
18. Witters I, Legius E, Moerman P, et al. Associated malformations and chromosomal anomalies in 42 cases of prenatally diagnosed diaphragmatic hernia. *Am J Med Genet.* Nov 1, 2001; 103[4]: 278-82.
19. Tovar, Juan A. Congenital Diaphragmatic Hernia. *Orphanet Journal of Rare Diseases.* Jan 03, 2012.
20. McGivern MR, Best KE, Rankin J. Epidemiology of congenital diaphragmatic hernia in Europe: a register-based study. *Arch Dis Child Fetal Neonatal Ed.,* Mar 2015.
21. Clementi M, Garne E. Haeusler M. Barisic I. Gjergja R. Stoll C. Congenital diaphragmatic hernia:

evaluation of prenatal diagnosis in 20 European regions. *Ultrasound in Obstetrics & Gynecology.* December 12, 2002.

22. Beth M, Kline-Fath. Congenital Diaphragmatic Hernia. [book auth.] Dorothy I. Bulas, Ray Bahado-Singh Beth M. Kline-Fath. *Fundamental and Advanced Fetal Imaging Ultrasound and MRI.* s.l. : Wolters Kluwer Health, 2015; 17(2): 583-595.

23. Balayla J, Abenhaim HA. Incidence, predictors and outcomes of congenital diaphragmatic hernia: a population-based study of 32 million births in the United States. *J Matern Fetal Neonatal Med.* Sep 27, 2014.

24. Harrison MR, Bjordal RI, Langmark F, Knutrud O. Congenital diaphragmatic hernia: the hidden mortality. *J Pediatr Surg,* Jun 1978; 13[3].

25. Franzcog JM, Franzcog JT, A review of congenital diaphragmatic hernia. *Australiasian Journal of Ultrasound in Medicine.* December 31, 2015; 16(1).

26. Moya FR, Thomas VL, Romaguera J, et al. Fetal lung maturation in congenital diaphragmatic hernia. *Am J Obstet Gynecol,* Nov 1995; 173[5]: 1401-5.

27. ISUOG. Performance of the routine mid-trimester fetal ultrasound scan,. *ISUOG. org.* [Online], January 2011; 1(37): 116-126. [Cited: Jan 31, 2021.] https://www.isuog.org/resource/performance-of-the-routine-pdf.html.

28. Taylor G, Mojisola AO, Estroff J, Imaging of congenital diaphragmatic hernias. *Pediatric Radiology,* Aug 2009; 1-16.

29. Prayer D, Malinger G, Brugger PC et al. ISUOG Practice Guidelines: performance of fetal magnetic resonance imaging. *Ultrasound Obstet Gynecol.* April 6, 2017; 49: 671-680.

30. SRUOG. www. sruog.ro. [Online] [Cited: Jan 20], 2021.

31. *Ghidurile de practică medicală pentru evaluarea ecografică fetală de.* Salomon L. J., Alfirevic Z. , Berghella V. et al. s.l. : wileyonlinelibrary.com, Ultrasound Obstet Gynecol, 2010.

32. Gianluigi P, Kypros H. Nicolaides. *Diagnosis of fetal abnormalities - The 18-23 week scan.* New York, london : The Parthenon Publishing Group, 1999. ISBN 1-85070-492-9.

33. Kasprian, F. Prayer M. Metzelder W. Krois P. C. Brugger G. M. Gruber M. Weber A. Scharrer A. Rokitansky G. Langs D. Prayer E. Unger G. Three-dimensional reconstruction of defects in congenital diaphragmatic hernia: a fetal MRI study. *Ultrasound in Obstetrics & Gynecology.* April 15, 2019.