Özgün Araştırma / Original Article

Jinekoloji - Obstetrik ve Neonatoloji Tıp Dergisi
The Journal of Gynecology - Obstetrics and Neonatology

DOI: 10.38136/jgon.1276563

Konjenital Diyafragma Hernisi Tanılı Fetüslerde Prognostik Marker Olarak Mide Pozisyonu

Stomach Position as a Prognostic Marker in Fetuses with Congenital Diaphragmatic Hernia

MERVE ÖZTÜRK AĞAOĞLU [1] Orcid ID: 0000-0002-1283-4032
ATAKAN TANAÇAN [1] Orcid ID: 0000-0001-8209-8248
ZAHİD AĞAOĞLU [1] Orcid ID: 0000-0001-8726-1075
ZÜMRÜT ÇALIŞKAN ŞENAY [1] Orcid ID: 0000-0001-5608-060X
ÖZGÜR KARA [1] Orcid ID: 0000-0003-1569-4474
DİLEK ŞAHİN [1] Orcid ID: 0000-0003-1569-4474

[1] Ankara Şehir Hastanesi, Perinatoloji Kliniği, Ankara, Türkiye

ÖZ

Amaç: Konjenital diafragma hernisinde (KDH) mide pozisyonu ile neonatal sağkalım arasındaki ilişkiyi incelemek

Metod: Aralık 2019- Aralık 2022 tarihleri arasında Ankara Şehir Hastanesi Perinatoloji kliniğine başvuran 18-45 yaş ve 22-39 gebelik haftaları arasında, fetal KDH tanılı toplam 36 gebe retrospektif olarak analiz edildi. Gebelikler yenidoğan sağkalımına göre iki gruba ayrıldı. Sağkalan (n=8) ve canlı doğup ölen (n=22) gruplar arasında demografik özellikler, klinik özellikler ve kontralateral akciğer boyutu / baş çevresi (LHR) oranı, mide pozisyonu ve diğer prognostik faktörler karşılaştırıldı.

Bulgular: Ortalama anne yaşı 29,30 ± 1,02 (17-40 aralığında) olup, hastaların %36'nin (13/36) ilk gebeliğiydi. Tanı anındaki median gebelik haftası 25,10 (13.5-37,6) idi. Parite, tanı anındaki medyan gebelik haftası, KDH tipi, karaciğer pozisyonu, median LHR açısından sağkalan ve doğum sonrası kaybedilen gruplar arasında istatistiksel olarak anlamlı fark bulunmadı. Grade 2 mide pozisyonu sağkalan grupta istatiksel olarak anlamlı olacak şekilde daha yüksek saptandı (p=0,01). neonatal operasyon oranı ve 1.-5. dakika apgar skorları doğum sonrası kaybedilen gruba göre daha yüksek saptandı (p=0,02, p=0,01, p=0,00 sırasıyla).

Sonuç: KDH'de mide pozisyonu derecelendirmesi, neonatal sağkalım ile ilişkili olabilecek, pratik ve uygulanabilir bir yöntemdir ve grade 2 mide pozisyonu, LHR'den bağımsız olarak KDH'li fetüslerde artmış sağkalım ile ilişkili bir belirteç olabilir. Bu yöntem, neonatal prognozun değerlendirilmesinde ve fetal müdahalelerin mevcut olduğu üçüncü basamak merkeze maternal transfer gibi perinatal yönetimin planlanmasında yararlı olabilir.

Anahtar Kelimeler: Konjenital diafragma hernisi, mide, prognoz

ABSTRACT

Objective: To examine the relationship between stomach position and neonatal survival in congenital diaphragmatic hernia (CDH).

Study Design: A total of 36 pregnant women with a diagnosis of fetal CDH, aged between 18-45 years and 22-39 weeks of gestation, who applied Ankara City Hospital Perinatology clinic between December 2019 and December 2022, were analyzed retrospectively. Pregnancies were classified into two categories based on neonatal survival. Demographic characteristics, clinical features and contralateral lung size/head circumference (LHR) ratio, stomach position, and other prognostic indicators were evaluated among the survivor (n=8) and non-survivor (n=22) groups.

Results: The mean maternal age was 29.30 ± 1.02 (range 17-40), and 36% (13/36) of the patients were primigravid. The median gestational week at diagnosis was 25.10 (13.5-37.6). There was no statistically significant difference between the survivor and non-survivor groups in terms of CDH type, liver position, gestational week at diagnosis, and median LHR. Grade 2 stomach position was found to be statistically significantly higher in the survivor group (p=0.01). Operation rate and 1st-5th minute Apgar scores were higher than in the non-survivor group (p=0.02, p=0.01, and p=0.00, respectively).

Conclusion: Stomach position grading in CDH is a practical and applicable method associated with neonatal survival, and grade 2 stomach position may be a marker associated with increased survival in fetuses with CDH regardless of LHR. It may be useful in assessing neonatal prognosis and planning perinatal management, such as maternal transfer to a tertiary center where fetal interventions are available.

Keywords : Congenital diaphragmatic hernia, prognosis, stomach

Sorumlu Yazar/ Corresponding Author: Merve Öztürk Ağaoğlu
Adres: Department of Obstetrics and Gynecology, Division of Perinatology, Turkish Ministry of Health, Ankara City Hospital, 1604th Street, No: 9, Cankaya/Ankara, 06800 Turkey
E-mail: drmerveozturk@hotmail.com

Başvuru tarihi: 04/04/2023
Kabul tarihi: 12/08/2023

INTRODUCTION

Congenital diaphragmatic hernia (CDH) is a developmental disorder of the diaphragm that results in herniation of the abdominal organs into the fetal thorax. CDH is a relatively common anomaly with an incidence of 1 in 2500 live births (1). While in the postpartum period, the diaphragmatic defect can be repaired surgically, pulmonary hypoplasia caused by CDH and pulmonary hypertension can increase morbidity and mortality in the neonatal period (2). Postpartum mortality rates can range from 15% to 50% in isolated cases (3, 4).

Several prenatal variables influence the survival of newborns with CDH (5, 6). Numerous prognostic factors are used for survival prediction, clinical decision-making, and counseling (7). The most commonly used parameters are the ratio expressed as the ratio of the contralateral lung area to the fetal head circumference (LHR), obtained in a cross-section of the fetal thorax, and the determination of the intrathoracic liver position. Fetal LHR is used to indirectly measure lung volume in postnatal prognosis. Patients with right-sided CDH, chromosomal abnormalities, severe congenital anomalies, liver herniation, hydrops fetalis, and low fetal LHR have a poor prognosis. (6, 8).

More recent studies have begun investigating the predictive role of stomach position on neonatal survival in CDH, and various grading systems have been developed (9, 10). A study by Cordier et al. found that prenatal stomach position grades could potentially predict neonatal survival, the need for neonatal mesh repair, the need for extracorporeal membrane oxygenation (ECMO), and the need for long-term respiratory support (9). However, there is a paucity of data in the literature on this topic, for which there needs to be more studies.

The aim of our study is to investigate the relationship between fetal stomach position and neonatal survival in pregnancies with CDH and to evaluate obstetric outcomes.

MATERIALS AND METHOD

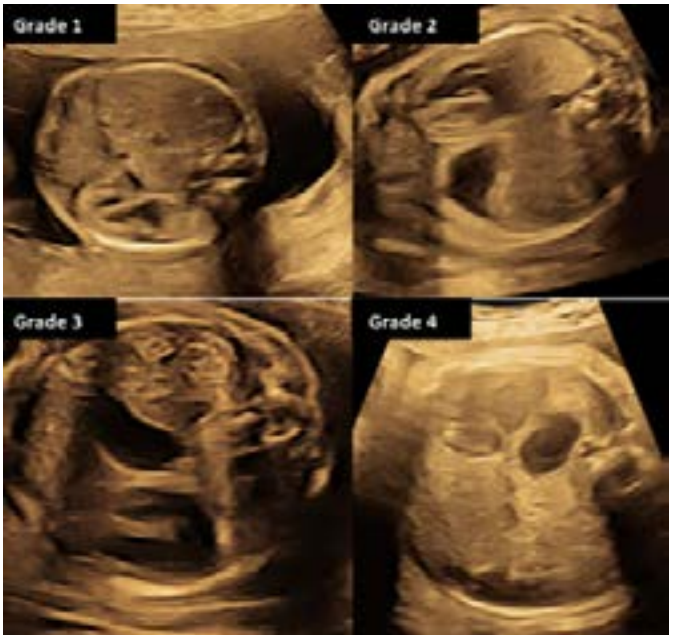
A total of 36 pregnant women diagnosed with fetal CDH who presented to the perinatology clinic of Ankara City Hospital between December 2019 and December 2022 were retrospectively analyzed. The study protocol was approved by the Ethics Committee of Ankara City Hospital (Decision No: E2-23-3737). The general principles of the Declaration of Helsinki were followed, and informed consent was obtained from all patients.

A total of 36 pregnant women between the ages of 18 and 45 years who were diagnosed with CDH and were between 22 and 39 weeks pregnant were included in the study. Cases with premature rupture of membranes and multiple pregnancies were excluded from the study. Cases were evaluated for demographic and clinical characteristics, ultrasound findings, and obstetric and neonatal outcomes. Pregnancy termination rate, invasive prenatal diagnostic tests, chromosomal abnormalities, and concomitant congenital anomalies were recorded. According to neonatal survival, patients were divided into two groups. Maternal age, gravida, parity, median week of gestation at diagnosis, CDH type, fetal stomach position, presence of liver and intestinal herniation, LHR, median week of gestation at delivery, birth weight, 1-5. Minute Apgar score, mode of delivery, and neonatal operation rate were compared. The percentages of liver and intestinal herniation, LHR, and neonatal operation rates were examined between groups according to stomach position.

Prenatal ultrasonography

A maternal-fetal medicine specialist performed all prenatal ultrasound examinations using transabdominal sonography (Voluson E8; GE Medical Systems). LHR was defined as the ratio of the product of the two longest vertical measurements of the contralateral lung area to the fetal head circumference in a four-chamber transverse section of the fetal thorax. The stomach position was graded as suggested by Cordier et al., in the four-chamber transverse section of the fetal heart used for LHR measurement (9): Grade 1: stomach cannot be visualized, grade 2: stomach is anterior, visualized at the level of the apex of the heart, there is no structure between stomach and apex, grade 3: abdominal organs are present anterior and posterior to the stomach, the stomach is mostly anterior according to the level of the atrioventricular valves, and grade 4: most of the stomach is behind the level of the atrioventricular valve (Figure 1).

Figure 1. Ultrasonography images. Prenatal stomach position. Grades 1–4, Cordier et al. According to the rating system. Grade 1: abdominal, no stomach is observed in the thorax. Grade 2: anteriorly located stomach in the thorax, Grade 3: stomach in the mid-posterior thorax. Grade 4: retrocardiac.



Statistics

The Statistical Package for the Social Sciences was used to conduct statistical analyses. (IBM SPSS Statistics for MAC, version 22.0). Visual (histograms, probability plots) and analytic methods (Shapiro-Wilk test) were used to determine whether variables were normally distributed. In descriptive analyses, the median was used for variables that were not normally distributed. The Mann-Whitney U test was used for comparison between groups when continuous variables were not normally distributed. The Kruskal-Wallis test was used to test the significance of the difference between three or more groups for non-normally distributed groups. If applicable, the chi-square and Fisher's exact tests were used to compare categorical variables. $P < 0.05$ was considered statistically significant.

RESULTS

The mean maternal age was 29.30 ± 1.02 years (range, 17-40 years), and 39% (14/36) of pregnant women were primiparous.

The median gestational week at diagnosis was 25.1 (13.5-37.6). Amniocentesis was used to analyze the fetal karyotype in 12 cases (33%), and it was reported that 9 of them had a normal karyotype. Of the three abnormal karyotypes, one fetus was found to have trisomy 12, one fetus was found to have a 15q13.3 duplication, and the other fetus was found to have Matthew Wood syndrome. Left-sided CDH was present in 28 (78%) fetuses and right-sided CDH in 5 (19%) fetuses, posterolateral hernia in 2 fetuses (6%), and posterior hernia in 1 fetus (3%). Congenital structural anomalies were found in 14 (39%) fetuses. Cardiovascular (21%) and genitourinary (6.1%) were the most common system anomalies. Intestinal herniation was present in 57.6%, and liver herniation in 42% of patients. After appropriate counseling, three families requested termination of pregnancy. In addition to CDH, one fetus had holoprosencephaly, one had a clenched hand and aberrant right subclavian artery (ARSA), and the other had a neural tube defect. The median week of termination was 22 weeks.

While 3 (9%) of 33 fetuses with CDH died intrauterine, 8 (24%) of 30 live births survived after birth. No significant difference was found between the survivor group (n=8) and the non-survivor group (n=22) in maternal age, week of diagnosis, type of CDH, LHR values, week of birth, and birth weight ($p > 0.05$) (Table 1).

Table 1. Comparison of demographic obstetric and neonatal outcomes among neonatal survival groups

	Survivor (n= 8)	**Non-survivor (n= 22)**	**p-value**
Maternal age (year)	26.5 (26-36)	30 (18-42)	0.48
Gravida (n)	1.5 (1-6)	2 (1-6)	0.71
Parity (n)	0.5 (0-4)	1 (0-4)	0.71
Gestational week at the time of diagnosis	29.9 (16-37)	24.7 (13-37)	0.32
CDH type			0.30
Left	8 (100%)	18 (81%)	
Right	0 (0%)	2 (9%)	
Posterolateral	0 (0%)	1 (5%)	
Posterior	0 (0%)	1 (5%)	
Intestinal herniation			0.70
present	7 (88%)	15 (6%8)	
none	1(12%)	7 (32%)	
Liver position			0.05
Thorax	2 (25%)	14 (64%)	
Abdomen	6 (75%)	8 (6%)	
Additional anomaly			0.20
Izole	6 (75%)	11 (50%)	
Non-izole	2 (25%)	11 (50%)	
LHR	1.7 (0.8-2.8)	0.8 (0.2-2.3)	0.07
Week of birth	37.9 (36-39)	38.4 (25-39)	0.60
Birth weight	3065 (2800-3440)	2640 (770-3790)	0.08
Mode of delivery			0.18
Vaginal delivery	1 (12.5%)	6 (62.5%)	
Cesarean section	7 (87.5%)	16 (37.5%)	
1.min apgar score	5 (4-8)	2 (0-6)	0.01
5.min apgar score	7.5 (6-9)	4 (0-8)	0.00
Neonatal operation			0.02
present	8 (100%)	4 (18%)	
none	0 (0%)	18 (81%)	

CDH, congenital diaphragmatic hernia; LHR, lung-to-head ratio

Values were presented as median (min-max), number, percentile (n, %)

$p < 0.05$ was considered statistically significant

It was found that 100% of the surviving neonates underwent surgery in the neonatal period, and it was observed that Apgar scores were higher in the first to fifth minutes (p=0.01 and p=0.00, respectively). The rate of herniation of the liver and intestines into the thorax was similar in the survival groups. When compared by stomach position, grade 2 stomach position was statistically significantly higher between survival groups (p=0.01) (Table 2).

Table 2. Comparison of stomach position degrees among neonatal survival groups

	Survivor (n=8)	Non-survivor (n=22)	p-value
Stomach position			
Grade 1	2 (25%)	10 (55%)	0.38
Grade 2	4 (50%)	1 (5%)	0.01
Grade 3	1 (12.5%)	7 (32%)	0.23
Grade 4	1 (12.5%)	4 (18%)	0.77

Values were presented as number, percentile (n, %)

p < 0.05 was considered statistically significant

Chi-square test

While neonatal surgery rates were higher for grade 2 stomach position, LHR and liver and intestinal herniation rates were similar (Table 3).

Table 3. Comparison of the clinical and ultrasonographic features of the groups formed according to the degrees of stomach position

	Stomach position				
	Grade 1 (n=12)	Grade 2 (n=6)	Grade 3 (n=9)	Grade 4 (n=6)	p-value
LHR	1.7 (0.2- 2.8)	1.8 (0.5-2.8)	1.3 (0.7-6.6)	0.7 (0.3-3.1)	0.13
Liver herniation	5 (45%)	3 (50%)	4 (57%)	4 (80%)	0.60
Intestinal herniation	7 (70%)	5 (100%)	5 (71%)	3 (100%)	0.21
Neonatal operation	3 (25%)	6 (50%)	2 (17%)	1 (8%)	0.03
Izole CDH	7 (58%)	4 (66%)	4 (44%)	4 (68%)	0.79

CDH, congenital diaphragmatic hernia; LHR, lung-to-head ratio

Values were presented as median (min-max), number, percentile (n, %)

p < 0.05 was considered statistically significant

Kruskal-Wallis test, chi-square test

DISCUSSION

In our study, stomach position ratios were examined among the survival groups were investigated. Whereas the LHR ratio was similar, Grade 2 stomach position was found to be higher in neonates who survived postnatally. These results suggest that prenatal grade 2 stomach position may be a marker associated with increased survival in CDH independent of LHR.

Advances in prenatal diagnosis and the discovery of predictive factors in CDH have led to improved fetal and neonatal management in appropriate tertiary centers. There are limitations in measuring LHR, the most commonly used parameter, such as variations among physicians performing ultrasound and difficulties in determining the border of the hypoplastic lung in severe forms of CDH (7, 11). In addition, uncorrected LHR has been demonstrated to increase with gestational age (12-14). For this reason, studies on using organs herniated into the thorax as direct and indirect markers have come to the forefront. There are publications in which the location and volume of the stomach and liver in CDH have been studied by MRI (9, 15).

In recent years, prenatal stomach position has been recommended for predicting neonatal prognosis (16-18). Some publications in the literature use different methods to evaluate fetal stomach position in pregnancies with CDH. A study by Kitano et al. described a 4-level grading system for stomach position; the classification was made according to the rate of stomach herniated to the thorax (10). Cordier et al., on the other hand, classified the stomach according to its position in the thorax relative to the atrioventricular valve plane and studied the correlation between the liver position detected on MRI and the stomach position grades (9). They showed that grading stomach position on prenatal ultrasound is a very reliable and simple method for indirectly assessing liver herniation to thorax in left-sided CDH. Using the stomach position grading method by Cordier et

al., our study found that grade 2 stomach position was associated with long-term neonatal survival. The fact that the LHR ratio was statistically similar among the survivor and non-survivor groups also suggests that this method may be a practical and reproducible predictor independent of LHR.

Tanacan et al. similarly classified the location of the stomach in their study of 44 pregnant women with CDH. They found that the stomach was in the abdomen in more than 50% of the surviving neonates, second most commonly in the anterior left thorax (19). Our study found a grade 2 stomach position in 50% of the surviving infants, suggesting an increased survival rate. Another recent study compared groups with similar LHR ratios in infants with left-sided CDH without liver herniation and found that neonatal morbidity was lower in infants with stomach in the abdomen than in infants with gastric hernia (20).

Prenatal estimation of neonatal respiratory morbidity in CDH is not entirely possible because the lungs are not functional until after birth. Both the degree of stomach position and LHR can be considered indicators of pulmonary hypoplasia, reflecting the likelihood of survival and the degree of respiratory morbidity. The study performed by Weller et al. showed that the time to resolution of pulmonary hypertension on echocardiography increased with increasing degree of prenatal stomach position(15). The increased neonatal survival seen in our study may be related to decreased respiratory morbidity. Studies in the literature indicate a linear correlation between the need for ECMO and the degree of stomach position(17). The advantages of our study are that the cases had homogen obstetric characteristics, and the same physician investigated the stomach position using prenatal ultrasound data. Limitations are the retrospective design and the criteria for long-term survival in assessing neonatal prognosis, and morbidities such as pulmonary hypertension and chronic lung disease that develop in the postnatal period were not included in the analysis. Therefore, further studies are needed for definitive conclusions.

CONCLUSION

Stomach position grading in CDH is a practical and applicable method associated with neonatal survival, and grade 2 stomach position may be a marker associated with increased survival in fetuses with CDH regardless of LHR. It may be useful in assessing neonatal prognosis and planning perinatal management, such as maternal transfer to a tertiary center where facilities such as fetal interventions are available.

REFERENCES

1. Langham MR, Kays DW, Ledbetter DJ, Frentzen B, Sanford LL, Richards DS. Congenital diaphragmatic hernia. Epidemiology and outcome. Clin Perinatol. 1996;23(4):671-88.

2. Leeuwen L, Fitzgerald DA. Congenital diaphragmatic hernia. J Paediatr Child Health. 2014;50(9):667-73.

3. Gallot D, Coste K, Francannet C, Laurichesse H, Boda C, Ughetto S, et al. Antenatal detection and impact on outcome of congenital diaphragmatic hernia: a 12-year experience in Auvergne, France. Eur J Obstet Gynecol Reprod Biol. 2006;125(2):202-5.

4. Colvin J, Bower C, Dickinson JE, Sokol J. Outcomes of congenital diaphragmatic hernia: a population-based study in Western Australia. Pediatrics. 2005;116(3):e356-63.

5. Bouchghoul H, Senat MV, Storme L, de Lagausie P, Begue L, Khen-Dunlop N, et al. Congenital diaphragmatic hernia: does gestational age at diagnosis matter when evaluating morbidity and mortality? Am J Obstet Gynecol. 2015;213(4):535.e1-7.

6. Sperling JD, Sparks TN, Berger VK, Farrell JA, Gosnell K, Keller RL, et al. Prenatal Diagnosis of Congenital Diaphragmatic Hernia: Does Laterality Predict Perinatal Outcomes? Am J Perinatol. 2018;35(10):919-24.

7. Metkus AP, Filly RA, Stringer MD, Harrison MR, Adzick NS. Sonographic predictors of survival in fetal diaphragmatic hernia. J Pediatr Surg. 1996;31(1):148-51; discussion 51-2.

8. Spaggiari E, Stirnemann JJ, Sonigo P, Khen-Dunlop N, De Saint Blanquat L, Ville Y. Prenatal prediction of pulmonary arterial hypertension in congenital diaphragmatic hernia. Ultrasound Obstet Gynecol. 2015;45(5):572-7.

9. Cordier AG, Cannie MM, Guilbaud L, De Laveaucoupet J, Martinovic J, Nowakowska D, et al. Stomach position versus liver-to-thoracic volume ratio in left-sided congenital diaphragmatic hernia. J Matern Fetal Neonatal Med. 2015;28(2):190-5.

10. Kitano Y, Okuyama H, Saito M, Usui N, Morikawa N, Masumoto K, et al. Re-evaluation of stomach position as a simple prognostic factor in fetal left congenital diaphragmatic hernia: a multicenter survey in Japan. Ultrasound Obstet Gynecol. 2011;37(3):277-82.

11. Laudy JA, Van Gucht M, Van Dooren MF, Wladimiroff JW, Tibboel D. Congenital diaphragmatic hernia: an evaluation of the prognostic value of the lung-to-head ratio and other prenatal parameters. Prenat Diagn. 2003;23(8):634-9.

12. Usui N, Okuyama H, Sawai T, Kamiyama M, Kamata S, Fukuzawa M. Relationship between L/T ratio and LHR in the prenatal assessment of pulmonary hypoplasia in congenital diaphragmatic hernia. Pediatr Surg Int. 2007;23(10):971-6.

13. Jani J, Nicolaides KH, Keller RL, Benachi A, Peralta CF, Favre R, et al. Observed to expected lung area to head circumference ratio in the prediction of survival in fetuses with isolated diaphragmatic hernia. Ultrasound Obstet Gynecol. 2007;30(1):67-71.

14. Peralta CF, Cavoretto P, Csapo B, Vandecruys H, Nicolaides KH. Assessment of lung area in normal fetuses at 12-32 weeks. Ultrasound Obstet Gynecol. 2005;26(7):718-24.

15. Weller K, Peters NCJ, van Rosmalen J, Cochius-Den Otter SCM, DeKoninck PLJ, Wijnen RMH, et al. Prenatal stomach position and volume in relation to postnatal outcomes in left-sided congenital diaphragmatic hernia. Prenat Diagn. 2022;42(3):338-47.

16. Burge DM, Atwell JD, Freeman NV. Could the stomach site help predict outcome in babies with left sided congenital diaphragmatic hernia diagnosed antenatally? J Pediatr Surg. 1989;24(6):567-9.

17. Basta AM, Lusk LA, Keller RL, Filly RA. Fetal Stomach Position Predicts Neonatal Outcomes in Isolated Left-Si-

ded Congenital Diaphragmatic Hernia. Fetal Diagn Ther. 2016;39(4):248-55.

18. Mann PC, Morriss FH, Klein JM. Prediction of survival in infants with congenital diaphragmatic hernia based on stomach position, surgical timing, and oxygenation index. Am J Perinatol. 2012;29(5):383-90.

19. Tanacan A, Orgul G, Aydin E, Kayki G, Celik HT, Yalcin S, et al. Antenatal management and outcomes of pregnancies with congenital diaphragmatic hernia. J Neonatal Perinatal Med. 2020;13(3):323-30.

20. Didier RA, Oliver ER, Rungsiprakarn P, Debari SE, Adams SE, Hedrick HL, et al. Decreased neonatal morbidity in 'stomach-down' left congenital diaphragmatic hernia: implications of prenatal ultrasound diagnosis for counseling and postnatal management. Ultrasound Obstet Gynecol. 2021;58(5):744-9.