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Right to privacy and informed consent: A coded and restricted database was created with the data collected, to which only the researchers had access. Data collection was retrospective and based on medical records. No direct or indirect contact was made with pregnant women or their newborns; therefore, informed consent was not used in this study.

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Prenatal diagnosis and perinatal outcomes in newborns with esophageal atresia

Diagnóstico prenatal y resultados perinatales en recién nacidos con atresia esofágica

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ABSTRACT

Introduction: Esophageal atresia is a rare congenital malformation of the digestive system. Early diagnosis is essential to plan adequate medical and surgical treatments. Objective: To evaluate the diagnosis of esophageal atresia using prenatal ultrasound and to describe the perinatal outcomes associated with this pathology. Methods: Descriptive, retrospective study of newborns with confirmed esophageal atresia seen at the Instituto Nacional Materno Perinatal (INMP) between 2019-2021. Data were collected on medical and ultrasound diagnoses, as well as maternal and neonatal variables. The procedures were approved by the institution's ethics committee. The information was kept confidential using alphanumeric codes, and a coded and restricted database was created for analysis. Results: There were 46,301 births at the INMP. Eighteen cases of confirmed esophageal atresia were identified (3.9 per 10,000 births). It was found that 66.7% of cases with esophageal atresia had some other associated malformation, cardiac being the most frequent. Intrauterine growth restriction (66.6%) and polyhydramnios (55.5%) were the most common findings in prenatal ultrasounds. Mortality was 50%, but only 20% when excluding fetuses with malformations. Conclusions: In neonates with confirmed esophageal atresia, intrauterine growth restriction was the most frequent ultrasound finding. Polyhydramnios and small or absent stomach were observed in about 50% of the cases, so their absence does not exclude the possibility of this pathology. The incidence of associated malformations was similar to that reported in other publications, but infant mortality was higher even after excluding malformed fetuses.

Key words: Esophageal atresia, Ultrasonic prenatal diagnosis, Neonate, Indicators of morbidity and mortality

RESUMEN

Introducción. La atresia esofágica es una rara malformación congénita del sistema digestivo. Es esencial diagnosticarla tempranamente para planificar tratamientos médicos y quirúrgicos adecuados. Objetivo. Evaluar el diagnóstico de atresia esofágica usando ecografía prenatal y describir los resultados perinatales asociados con esta patología. Métodos. Estudio descriptivo y retrospectivo que incluyó recién nacidos con atresia esofágica confirmada atendidos en el Instituto Nacional Materno Perinatal (INMP) entre 2019 y 2021. Se recopilaron datos de diagnósticos médicos y ecográficos, así como las variables maternas y neonatales. Los procedimientos fueron aprobados por el comité de ética de la institución y la información se mantuvo confidencial mediante códigos alfanuméricos. Resultados. Hubo 46,301 nacimientos en el INMP. Se identificaron 18 casos de atresia esofágica confirmada (3,9 por 10,000 nacimientos). Se encontró que el 66,7% de los casos con atresia esofágica presentó alguna otra malformación asociada, siendo la cardiaca la más frecuente. La restricción del crecimiento intrauterino (66,6%) y el polihidramnios (55,5%) fueron los hallazgos más frecuentes en las ecografías prenatales. La mortalidad fue del 50%, pero de solo 20% al excluir los fetos con malformaciones. Conclusiones. En neonatos con atresia esofágica confirmada, la restricción de crecimiento intrauterino fue el hallazgo ecográfico más frecuente. El polihidramnios y el estómago pequeño o ausente se observaron en alrededor del 50% de los casos, por lo que su ausencia no excluye la posibilidad de esta patología. La incidencia de malformaciones asociadas fue similar a la hallada en otras publicaciones, pero la mortalidad infantil fue elevada aún después de la exclusión de los fetos malformados.

Palabras clave. Atresia esofágica, Diagnóstico prenatal, Neonato, Indicadores de morbimortalidad

Introduction

Esophageal atresia (EA) is a rare and severe congenital malformation of the digestive system affecting approximately 2.3-2.4 cases per 10,000 births[1]. Characterized by the interruption or abnormal closure of the esophagus, this condition can present in different forms, with esophageal atresia with tracheoesophageal fistula being the most common, with 86%[2].

Esophageal atresia can have serious consequences for the health and survival of the newborn, so its accurate and early diagnosis is crucial for planning appropriate medical and surgical interventions[3]. Mortality is mainly related to associated anomalies and genetic syndromes that reduce survival by up to 51%[1,4].

In recent years, prenatal ultrasound has become a fundamental tool in the detection and evaluation of fetal anomalies. High level ultrasound has low sensitivity (29.4%) but very good specificity (80%) for the diagnosis of EA[5,6]. Only 40% of the cases of esophageal atresia can be suspected before birth, since in more than 80% there is an associated tracheoesophageal fistula that can make the stomach look normal in size[7] and that there is no polyhydramnios.

Prenatal detection by ultrasound is based on the finding of a small or absent gastric chamber and polyhydramnios in 44%-56%. When one or both of these are coupled with the presence of the so-called 'pouch sign' - the presence of a cystic pocket in the neck or upper fetal mediastinum especially visible in the third trimester (after 26 weeks of gestation)-, its predictive value increases to 100% with 80% sensitivity[1,8].

Due to its low prevalence, there is limited evidence in the national literature regarding the sensitivity of prenatal diagnosis of esophageal atresia and perinatal characterization of newborns. The present study aimed to evaluate the diagnosis of esophageal atresia using prenatal ultrasound and to describe the perinatal outcomes associated with this pathology.

Material and methods

This descriptive and retrospective study included newborns with suspected and/or postnatally confirmed prenatal esophageal atresia attended at the Instituto Nacional Materno Perinatal (INMP) in Lima, Peru, between 2019-2021. Inclusion criteria were high-risk and low-risk newborns with an ICD 10 discharge diagnosis of esophageal atresia or with suspected prenatal esophageal atresia by ultrasound through evaluation for the presence of polyhydramnios (ILA > 25 cm), absent or reduced gastric chamber and/or presence of an esophageal pouch. When a fetal weight estimated by ultrasound was found to be below the 10th percentile, Doppler of the umbilical, middle cerebral and uterine arteries was performed and the INMP Guidelines[9] for the diagnosis of intrauterine growth restriction (IUGR) were applied. We excluded stillbirths or cases with no record of variables of interest in the clinical history. All newborns born between 2019-2021 who met the aforementioned criteria were entered into the study.

Information was collected on the diagnosis of esophageal atresia confirmed in the newborn by a specialist physician's record or with a diagnosis of suspected esophageal atresia based on ultrasound findings. Fetal ultrasound data were obtained (normal visible stomach and small visible stomach, polyhydramnios, intrauterine growth restriction) and other variables such as maternal age measured in years, gestational age in weeks, presence of maternal comorbidities (such as arterial hypertension, cancer, stroke, epilepsy or other affected organs), obstetric morbidity (preeclampsia, eclampsia, hemolysis syndrome, elevated liver enzymes, thrombocytopenia (HELLP), chorioamnionitis, maternal sepsis, hyperemesis gravidarum, pneumonia, placenta previa, placental accretism, placental abruption, among other pathologies that were recorded in the maternal medical record), route of delivery (cesarean or vaginal), Apgar at one minute and five minutes after birth, stay in the neonatal intensive care unit, type of fetal malformations and condition of discharge of the newborn.

The procedures were performed after evaluation by the research ethics committee of the INMP and their respective authorization for the development of the present study. The pregnant women with prenatal ultrasound scan registered in the electronic database of the fetal medicine service, attended between 2019-2021, were identified. Likewise, the statistics and informatics office determined the births occurring in that period with the ICD 10 diagnosis of esophageal atresia.

Subsequently, based on the identification of the electronic record number, the medical records of the mother and the newborn were reviewed, selecting the participants who met the selection criteria. The study variables were collected on a data sheet prepared for this purpose, indicating the presence, absence or missing data on the variables of interest.

The information collected from each pregnant woman and her newborn was kept confidential by assigning an alphanumeric code to each participant in the collection of information for the sole purpose of this study. A coded and restricted database was created with the data collected, to which only the researchers had access.

Results

A total of 46,301 births were registered in the INMP between 2019 and 2021[10,11]. Of these newborns, 18 had a confirmed diagnosis of esophageal atresia, which represented 3.9 cases per 10,000 live newborns. Eight cases had suspected esophageal atresia by ultrasonography with subsequent confirmation at birth and 10 had no ultrasonographic suspicion of esophageal atresia, but later the diagnosis was confirmed at birth.

Among the maternal sociodemographic characteristics of the 18 cases, 55% were between 19-34 years old and 40% were 35 years old or older. Most of the participants (72%) had secondary education, 22% higher education and 6% elementary education; most of the women were cohabitants (72%) (Table 1).

Regarding the prenatal ultrasound findings, of 8 newborns with suspected esophageal atresia, 7 (87.5%) had small or absent stomach, polyhydramnios, or intrauterine growth restriction. In newborns without suspected esophageal atresia, normal and visible stomach was more frequently observed, followed by intrauterine growth restriction. In newborns with confirmed esophageal atresia, the most frequent finding was intrauterine growth restriction (66.6%) followed by polyhydramnios (55.5%) (Table 2).

In newborns with confirmed esophageal atresia, 66.7% had some other malformation, mainly heart (38.9%) and musculoskeletal diseases (33.3%). There were chromosomopathies in 27.7% and malformations were observed more frequently in those with no previous suspicion of esophageal atresia (Table 3).

Table 1. Maternal sociodemographic characteristics of newborns who presented with a confirmed diagnosis of esophageal atresia.

Maternal sociodemographic characteristics	N = 18 n (%)
Maternal age	
19-34 years old	11 (55%)
35 and over	7 (45%)
Level of education	
Elementary school	1 (6%)
Secondary school	13 (72%)
High school	4 (22%)
Marital status	
Single	2 (11%)
Married	3 (17%)
Cohabitant	13 (72%)
Employment	
Housewife	15 (83%)
Self-employed	1 (6%)
Student	2 (11%)

Of the 18 confirmed cases, eight had prenatal suspicion and ten did not. The median gestational age was 36 weeks, with a minimum of 29 and a maximum of 41 weeks. The median birth weight was 1,957.2 g +/- 676.7 and a median Apgar score of 6 points at 1 minute and 8 points at 5 minutes. The most frequent type of delivery was cesarean section (83.3%), especially in those without suspected prenatal atresia. All the newborns with esophageal atresia were admitted to the ICU, with a median of 42 days of hospitalization in the ICU, greater in those who had not presented with suspected prenatal esophageal atresia

Table 2. Description of ultrasound findings of newborns who presented with suspected esophageal atresia and/or confirmed esophageal atresia.

Ultrasound findings*	Newborns with confirmed esophageal atresia (N= 18)		
	With suspected atresia (n=8)	No suspicion of atresia (n=9**)	Confirmed atresia (n=18)
Normal and visible stomach	1 (12.5%)	7 (77.7%)	8 (44.4%)
Small or absent stomach	7 (87.5%)	2 (22.2%)	9 (50.0%)
Polyhydramnios	7 (87.5%)	3 (33.3%)	10 (55.5%)
Intrauterine growth restriction	7 (87.5%)	5 (55.6%)	12 (66.6%)

**A single newborn may present more than one prenatal ultrasound finding.*
***In one of 10 newborns with no suspected atresia, no ultrasound data were available.*

(47 days of hospitalization in the ICU). Mortality of newborns with confirmed esophageal atresia was 50% including fetal anomalies, and 20% not including fetal anomalies (Table 4).

Likewise, of the 18 confirmed cases of esophageal atresia, 13 cases underwent surgery, 5 of them died, with cardiovascular malformations and 2 had some malformation of the nervous system. Of the eight cases that did not die and that underwent surgery, none had another malformation.

Among the 18 cases of esophageal atresia, 5 cases did not undergo surgery and 4 of them died, 3 with cardiovascular and nervous system malformation and one was referred to a pediatric hospital after a 9-day stay in the ICU.

Discussion

The frequency of esophageal atresia in our study was 1 in 2,572 live births, which is twice the worldwide prevalence of 1 in 4,166 to 1 in 4,347 according to the study by Pardy et al[1]. Our Institute is a reference center for obstetric pathology at the national level. We confirmed an increase in its appearance at older maternal age, with almost 40% in patients over 35 years of age, despite having fewer births in this population, almost double the 22% found by Cassina et al[12]. The sex was male in 55%, similar to the 52% found by Galarreta et al. in California[13].

Table 3. Description of malformations in newborns with confirmed esophageal atresia.

Malformations	Confirmed esophageal atresia (n=18)		
	With suspected atresia (n=8)	No suspicion of atresia (n=10)	Total (n=18)
Associated malformations			
- Yes	5 (41.7%)	7 (58.3%)	12 (66.7%)
- No	3 (50%)	3 (50%)	6 (33.3%)
Type of malformation			
Chromosomopathy	2 (66.7%)	3 (33.3%)	5 (27.7%)
- Trisomy 18	1 (100%)	0	1 (5.6%)
- Trisomy 21	1 (33.3%)	2 (66.7%)	3 (16.7%)
- Polymorphism	0	1 (100%)	1 (5.6%)
Nervous system	3 (100%)	0	3 (16.6%)
Cardiopathy	3 (42.9%)	4 (57.1%)	7 (38.9%)
Genitourinary	1 (25%)	3 (75%)	4 (22.2%)
Musculoskeletal	3 (50%)	3 (50%)	6 (33.3%)
Other	2 (66.7%)	1 (33.3%)	3 (16.6%)

Table 4. Perinatal characteristics of newborns with confirmed esophageal atresia.

Perinatal characteristics	Confirmed esophageal atresia (n= 18)		
	With suspected atresia (n=8)	No suspicion of atresia (n=10)	Total (n=18)
Gestational age (wk)	36 (32-38)	35 (29-41)	36 (29-41)
Type of delivery			
- Vaginal	3 (100%)	0	3 (16.7%)
- Cesarean section	5 (33.3%)	10 (66.7%)	15 (83.3%)
Sex			
- Male	3 (30%)	7 (70%)	10 (55.6%)
- Female	5 (71.4%)	2 (28.6%)	7 (38.9%)
- Ambiguous	0 (0%)	1 (100%)	1 (5.6%)
Birth weight (g) †	1,954 ±708.4	1,978.6 ± 727.1	1,957.2 ± 676.7
- Apgar 1' *	5 (1 a 8)	6 (3 a 8)	6 (1 a 8)
- Apgar 5" *	8 (4 a 9)	8 (7 a 9)	8 (4 a 9)
Admission to NICU	8 (44.4%)	10 (55.6%)	18 (100%)
Days in NICU *	39 (1-143)	47 (10-176)	42 (1-176)
Total days hospitalized *	39 (1-143)	47 (10-176)	42 (1-176)
Crude infant mortality	5 (55.6%)	4 (44.6%)	9/18 (50%)
Adjusted infant mortality **	1/3 (33.3%)	0/3 (0%)	1 /5 (20%)

** Median (minimum, maximum)*
† Mean, standard deviation
*** Adjusted mortality in fetuses without associated anomalies*

Of the 18 cases confirmed postnatally, 55% were detected prenatally by ultrasound, higher than expected in the literature (31.7%). Polyhydramnios was present in 55.5% of the confirmed cases and absent or with small stomach in 50%, similar to Pardy et al[1]. IUGR was found in 66% of the cases, higher than that reported by Tatjana et al.[14] who, after a 20-year follow-up in Germany, found 40.7% of small for gestational age. This could be taken into consideration to broaden the signs of suspected esophageal atresia when associated with polyhydramnios, even when the gastric chamber is of normal size, since up to 80% of esophageal atresias may be accompanied by tracheal fistulas[7]. Prenatal detection of these fistulas is very difficult[15], since prenatal ultrasound has low sensitivity but very good specificity for diagnosis[5].

Infant survival was 50%, although in the population with esophageal atresia not associated with other malformations it was 80%. These figures are lower than those published in the literature, which mention 84.5% overall survival in the first

year of life and 97% when esophageal atresia is isolated (16). It is even lower than the national finding in a third level center dedicated exclusively to the care of the pediatric population, which found an overall survival of 89.2%[17].

Cassina et al. in a 25-year follow-up showed that the highest mortality occurs in the first months of life, with 79% survival in children with non-isolated esophageal atresia[12]. One of the factors that may explain this finding is the high rate of prematurity (70%) in the newborns in our study, with weights less than 2 kg in more than half of the cases (12/18). Likewise, the presence of malformations associated with esophageal atresia.

Another factor that could explain the increased mortality in our study could be the underdiagnosis of genetic syndromes, as karyotype information was not available in most of the newborns due to the limited attention of the genetic service of the institution during the years of the COVID 19 pandemic.

These findings lead us to prioritize the evaluation of the conditions that may influence the alarming mortality rate of these infants and to carry out additional studies to improve their survival.

Among the limitations of the present study are those inherent to the design, due to the retrospective collection of information and the short follow-up of the cases with esophageal atresia. Nevertheless, the information collected corresponds to evaluations performed by specialist physicians, review of exams, electronic cross-checking of information between discharge diagnoses and fetal medicine evaluation databases. Likewise, the information corresponds to an institution specialized in maternal and perinatal care.

Prenatal diagnosis of esophageal atresia offers numerous advantages for patients and the medical team. It allows for adequate planning of delivery and neonatal care, with the availability of specialists and adequate resources at the time of birth. In addition, early diagnosis facilitates discussion and counseling for parents about treatment options, as well as psychological and emotional preparation for coping with the challenges associated with this condition.

In conclusion, in the present study the recorded frequency of 3.9 cases per 10,000 live newborns underlines the relative rarity of this congenital malformation. Based on ultrasonographic findings there was a high rate of suspected prenatal diagnosis (55%). Intrauterine growth restriction was present in 66.6% of the fetuses affected by esophageal atresia, which should be considered for the suspicion of this pathology. The incidence of associated malformations occurred in more than half (66.7%) of the cases and the incidence of chromosomopathies was 27.7%. The crude infant mortality reached 50% while that corrected for malformations decreased to only 20%. This study represents the first approach in our environment to prenatal diagnosis and perinatal results of this pathology.

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