

Esophagic atresia type and its association with heart malformations in a Northern Mexico hospital

Tipo de atresia esofágica y su asociación con malformaciones cardíacas en un hospital del norte de México

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Abstract

Objective: To know the cardiac malformations frequency associated with esophageal atresia and its type in patients of the Children's Specialties Hospital of Chihuahua as well as related sociodemographic characteristics. **Method:** The epidemiology, clinic and evolution of patients with esophageal atresia diagnosis who were admitted to this hospital for a period of two years were studied. Variables such as sex, gestational age, birth weight, Apgar score, atresia type, associated congenital malformations, hospital complications and parental related aspects were analyzed. **Results:** Twelve patients were studied, 50% of them were male, most of them were products of term pregnancies with adequate birth weight. There were mestizo ethnicity prevalence, young mothers children with a medium socio-economic level, without geographical predominance. 82% of the cases corresponded to type III esophageal atresia, the most frequent congenital malformations associated were cardiac in 83% of which 90% corresponded to atrial septum defects. **Conclusions:** Esophageal atresia is a relatively common congenital malformation of multifactorial etiology. A complete approach to patients with this pathology is necessary to identify a concomitant illness and provide adequate treatment.

Keywords: Esophageal atresia. Cardiac malformations. Mexico.

Resumen

Objetivo: Conocer la frecuencia de malformaciones cardíacas asociadas en pacientes con atresia de esófago y su tipo en el Hospital Infantil de Especialidades de Chihuahua, así como las características sociodemográficas relacionadas. **Método:** Se estudiaron la epidemiología, la clínica y la evolución de los pacientes con diagnóstico de atresia esofágica que ingresaron a dicho nosocomio durante un periodo de 2 años. Se analizaron variables como sexo, edad gestacional, peso al nacer, Apgar, tipo de atresia, malformaciones congénitas asociadas, complicaciones durante la estancia hospitalaria y aspectos relacionados con los padres. **Resultados:** Se estudiaron 12 pacientes, de los cuales el 50% eran de sexo masculino, y la mayoría de ellos fueron producto a término con peso adecuado al nacimiento. Predominio de etnia mestiza, hijos de madres jóvenes con nivel socioeconómico medio, sin predominio geográfico. El 82% de los casos correspondían a atresia esofágica tipo III, y las malformaciones congénitas más frecuentes asociadas fueron las cardíacas en el 83% de los casos, de las

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cuales el 90% correspondían a defectos del tabique auricular. **Conclusiones:** La atresia esofágica es una malformación congénita relativamente común y de etiología multifactorial. Es necesario realizar un abordaje completo de los pacientes con esta patología para poder identificar otra afección y brindar el tratamiento adecuado.

Palabras clave: Atresia esofágica. Malformaciones cardiacas. México.

Introduction

Definition

Esophageal atresia encompasses a group of congenital anomalies comprising an interruption of the continuity of the esophagus with or without a persistent communication with the trachea^{1,2}.

Epidemiology

The incidence of esophageal atresia, with or without tracheal fistula, is of one in every 3500 live births^{3,4}. However, there is a geographic variation. Approximately 2 million children are born in Mexico per year, and it is estimated that, every year, there are between 500 and 600 new cases of esophageal atresia in the country⁵. This data is not available for the State of Chihuahua. Most series show a slight predominance of males, with a 3:1 ratio and a higher incidence in pre-term infants^{6,7}. It has been observed that the incidence of esophageal atresia, and of other anatomical congenital malformations as well, is increased in patients that are the product of in vitro fertilization³.

Etiology

The etiology of esophageal atresia is likely to be multifactorial, encompassing genetic and environmental factors^{1,5,8}. In spite of the low concordance between twins and a low incidence of familial cases, genetic factors play an important role, as it is suggested by discreet genetic mutations in syndromic cases, such as the Feingold syndrome, the CHARGE syndrome (coloboma, heart defects, atresia choanae, retardation of growth or development, genital hypoplasia, ear abnormalities or deafness) and the anophthalmia-esophageal-genital syndrome⁹. Chromosomal abnormalities, such as trisomies (18 y 21) and deletions (22q11 and 17q22q23.3) are known to be associated with esophageal atresia, and they have been reported in up to 6% of patients with associated malformations in other systems^{1,10}.

Risk factors

A higher incidence of esophageal atresia has been observed in products of elderly parents, maternal diabetes, mother with phenylketonuria, alcohol intake during pregnancy, low maternal parity, obesity, and exposure to certain drugs during pregnancy (methimazole, carbimazole, caffeine, mycophenolate, doxorubicin, and diethylstilbestrol). Animal studies have been conducted and it has been shown that maternal exposure to cadmium, as well as vitamin A deprivation, alters the foregut development. In addition, the involvement of the neuropeptides present in this anatomical area is analyzed^{6-8,10,11}.

Presentation

In the obstetric surgery room, this anatomical anomaly should be suspected when there is difficulty in passing the tube to verify esophageal patency. The clinical signs the patients may show include excessive salivation, cough, cyanosis, respiratory distress and abdominal distension⁵.

Associated malformations

The abnormal organogenesis that causes deformities such as esophageal atresia affects other systems as well. Such related anomalies often significantly disrupt the treatment and have an impact on survival³. There are many studies which estimate that about 50-70% of pediatric patients with an esophageal atresia diagnosis have at least an additional associated congenital malformation. These malformations include the cardiovascular (24%), genitourinary (21%), digestive (21%), musculoskeletal (14%) and central nervous (7%) systems³ (Table 1).

Classification

Esophageal atresia can be classified in three different ways: 1) according to the presence and location of the atresia and the fistula; 2) based on the association with other anatomical abnormalities; and 3) according

Table 1. Congenital anomalies associated to esophageal atresia

Associated anomalies	%
Cardiovascular	24
Genitourinary	21
Gastrointestinal	21
Musculoskeletal	14
Central nervous system	7
VACTERL association	20
Overall incidence	50-70

VACTERL: vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb abnormalities.

to the presence of a known tracheoesophageal fistula in a specific syndrome^{6,11}. The original anatomical classification by Vogt in 1929 is still used today. Ladd and Gross modified that classification, which is the one more frequently used, dividing it into six types:

- Type I: Esophageal atresia with both esophageal ends blind without tracheoesophageal fistula, with a 5-8% incidence.
- Type II: Esophageal atresia with upper tracheoesophageal fistula and blind lower end, with a 0.5-1% incidence.
- Type III: Esophageal atresia with low tracheoesophageal fistula and blind upper esophageal end, with an 80-85% incidence.
- Type IV: Esophageal atresia with tracheoesophageal fistula in both esophagus ends, with a 0.5-1% incidence.
- Type V: “H” type tracheoesophageal fistula without esophageal atresia, with a 3-5% prevalence.
- Type VI: Isolated esophageal stenosis, with a 0.5-1% prevalence^{1,12,13}.

Diagnosis

In most cases, esophageal atresia diagnosis is established within the first 24 hours of life. However, it can be made prenatally or there may be a delay in reaching it^{2,14}.

PRENATAL DIAGNOSIS

The prenatal diagnosis can be suspected by performing an obstetric ultrasound after the 18th week. Polyhydramnios is the most frequent finding as a

consequence of the fetus inability to swallow and absorb the amniotic fluid through the intestine. It is observed in approximately 80% of patients with esophageal atresia without fistula and in 20% of those with distal fistula⁴⁻⁶. Prenatal ultrasound suggests the diagnosis with a 42% sensitivity when the stomach is not identified with fluid inside, while the combination of polyhydramnios and prenatal ultrasound suggesting esophageal atresia has a positive predictive value of 56%^{2,5}. The diagnostic criteria for esophageal atresia by means of magnetic resonance imaging is the non-visualization of the intrathoracic portion of the esophagus¹⁴. Currently, the prenatal diagnosis is addressed by means of ultrasound and the amniotic fluid index for esophageal atresia, a biochemical approach that measures alpha-fetoprotein and gamma-glutamyltransferase in the amniotic fluid^{6,11}. Even with the technological advances in imaging techniques, there is not any ideal prenatal diagnostic method for this pathology¹⁴.

POST-NATAL DIAGNOSIS

Esophageal atresia is observed in a high percentage of preterm births or newborns with low birth weight⁵. Patients affected by this pathology will remain asymptomatic during the first hours, but they will then show ptalism, respiratory distress, cough, and choking when eating. If the diagnosis is delayed, a severe pneumonic process hindering the prognosis may develop⁴⁻⁶. The diagnosis is confirmed by anteroposterior and lateral chest and neck radiographs, either placing a radiopaque tube or administering a water-soluble contrast medium (Fig. 1). If there is a distal tracheoesophageal fistula, the air in the stomach will appear in the radiographs and abdominal distension can be evident^{4,5,14}.

Treatment

The management of a newborn with esophageal atresia involves patient transfer-reception systems, diagnosis, medical treatment, prevention of complications, surgery, anesthesia, office and laboratory tests, and neonatal intensive care⁵. The management of these patients should involve a multidisciplinary team including neonatologists, pediatric surgeons, anesthesiologists, radiologists, cardiologists, pulmonologists and geneticists, while the assistance of nurses, psychologists and social workers is also vital for



Figure 1. Chest radiograph with contrast medium in the blind esophageal end.

supporting the parents⁵. The initial management should focus on the comprehensive assessment of the newborn, identifying the presence of associated malformations and evaluating a possible infectious involvement^{5,9,14}. Preoperative medical management of the patient should consist of minimal manipulation of the newborn because overstimulation can lead to respiratory complications, increased oxygen intake, cold stress, and regurgitation of gastric contents through the fistula^{2,5}. A double-lumen tube needs to be placed for continuous low-pressure aspiration and irrigation with normal saline⁵. Oxygen therapy, if required, should be administered for keeping an optimal saturation^{5,15}. Fasting needs to be prescribed, and intravenous solutions need to be administered for a proper supply of fluids, electrolytes and glucose⁵. These patients need to be admitted or transferred to a neonatal intensive care unit that has the above mentioned multidisciplinary medical team as soon as possible^{2,5,15}. Upon arrival, the preoperative laboratory tests will be done, as well as kidney, heart and transfontanelar ultrasounds in order to rule out other associated malformations. If pneumonia data are available, an

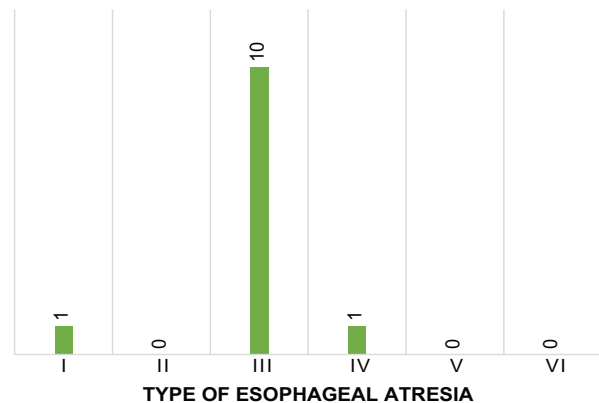


Figure 2. Type of esophageal atresia observed in patients admitted to the neonatal intensive care unit of the Children's Specialties Hospital of Chihuahua between January 2017 and December 2018.

antibiotics regime will be initiated. In addition, early parenteral nutrition will be initiated. The newborn will be taken to surgery once they are stable, the type and severity of the associated malformations are determined, and a surgical treatment plan is established. The latter generally consists of fistula closure and esophageal repair surgery⁵.

Complications

Surgical complications include dehiscence, anastomotic leakage, refistulization and stenosis^{8,9}. Respiratory, nutritional and gastrointestinal problems prevail not only during the first years of life, but also in adolescence and adulthood. Gastroesophageal reflux, peptic esophagitis, gastric metaplasia, Barrett's esophagus, eating disorders, dysphagia, tracheomalacia, recurrent lung infections, and esophageal dysmotility are the most common complications in the short and long term in patients with a history of this pathology. As regards adults, the presence of esophageal adenocarcinoma and of squamous cell carcinoma should be investigated, as they can be associated^{16,17}.

Problem statement

Esophageal atresia is an illness that occurs in newborn children around the world. In Mexico, it is relatively frequent and affects all the population groups. Its timely detection, preferably prenatally, is important for proper management. It is crucial to identify those individuals who present this anomaly to be able to

provide them with a satisfactory treatment, thus avoiding potential complications that may put the patients or their quality of life at risk. It is known that esophageal atresia can be associated with multiple congenital malformations; therefore, it is necessary to make a timely diagnosis of these and to adopt a complete multidisciplinary approach.

The purpose of this study is to observe the relationship between the esophageal atresia type and the cardiac malformations, and, in addition, to analyze the sociodemographics related to these patients. The foregoing has the aim of determining the current situation in the health facility where these cases are attended, in order to be able to provide these patients with the appropriate management they require.

Method

The objective of this work was to conduct a study of the epidemiology, clinics and progress of patients with an esophageal atresia diagnosis that were admitted to the Children's Specialties Hospital of Chihuahua from year 2017 to year 2018. Therefore, a prospective observational study of the patients affected by this pathology that were admitted to the neonatal intensive care unit was conducted. The main assessed values were sex, gestational age, birth weight, Apgar score, associated malformations, and complications during the hospital stay. Some characteristics related to the parents were also analyzed: maternal age, associated pathologies, educational status, prenatal control, ethnicity and place of residence.

Results

During the period between January 2017 and December 2018, a total of 12 patients diagnosed with esophageal atresia, referred by different hospitals in the State, were admitted to the neonatal intensive care area of the Children's Specialties Hospital of Chihuahua. Of those patients, 50% were male and 50% were female. Gestational ages ranged from 27 weeks to 41 weeks, with an average of 39 weeks. Half of the patients had an appropriate birth weight, with an average of 3.429 kg and 51.75 cm of height. The Apgar score at 5 minutes was mostly 9. When analyzing aspects related to prenatal care, it was observed that the average number of visits during pregnancy was 6.3. It should be noted that there were important differences both in the sociocultural level

and in the accessibility to health services among the different families studied, as it was found that some patients had good prenatal control, with up to 15 visits, compared to one patient who did not receive health care until the moment of delivery. The average of performed obstetric ultrasounds was 3.8, of which in seven patients they were reported as normal, in three, there was evidence of polyhydramnios, in one patient an umbilical cord variant was identified, and there was one case where no ultrasound screening was carried out.

As regards parent-related characteristics, the maternal average age was 23.4 years old, and the paternal one 25.1 years old. As for ethnicity, 82% of the families were mestizo, 9% Tarahumara, and 9% Menonites. Most of the analyzed patients' mothers had complete secondary education (50%), 17% had finished high school, 17% had complete primary education, one mother had finished her professional education and another one was illiterate. Regarding the analyzed risk factors, none of the mothers had been diagnosed with diabetes mellitus or any other disease. They denied having taken alcoholic drinks or any type of teratogen during pregnancy, which are risk factors that have been associated with the increase of esophageal atresia incidence. The place of residence of most of the families (four) was the city of Chihuahua, two were from Guachochi, and as for the rest, one was from Saucillo, one from Delicias, one from Cuauhtémoc, one from La Junta and another one from Carichi. The esophageal atresia diagnosis was established postnatally in 100% of the cases.

When analyzing the malformations in the studied patients, it was observed that 82% corresponded to type III atresia (with distal tracheoesophageal fistula), one to type I (without fistula) and one to type IV (with proximal and distal fistula) (Fig. 2). Congenital malformations most frequently associated with esophageal atresia were cardiac in 83% of the cases. Vertebral malformations were observed in one patient with incomplete sacrum. One was diagnosed with low anorectal malformation. Cerebral malformations were observed in a case with hydrocephalus (Fig. 3).

The cardiac malformation analysis of the affected patients revealed that 90% of those with cardiac anomalies had atrial septal defect. Five out of the 10 patients had patent ductus arteriosus and one had ventricular septal defect. Other reported malformations

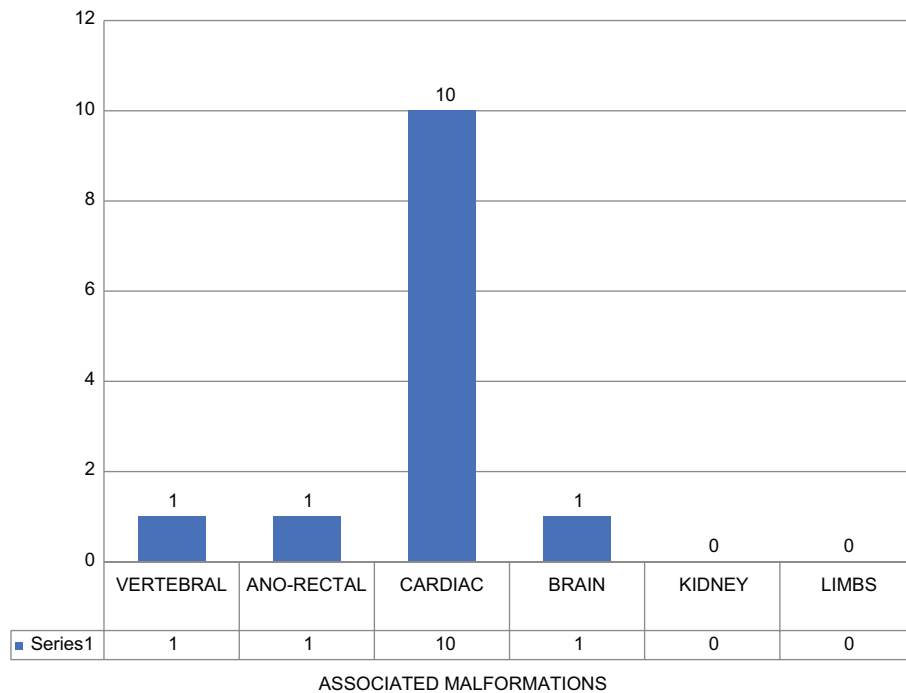


Figure 3. Congenital malformations found in patients with esophageal atresia admitted to the neonatal intensive care unit of the Children's Specialties Hospital of Chihuahua between January 2017 and December 2018.

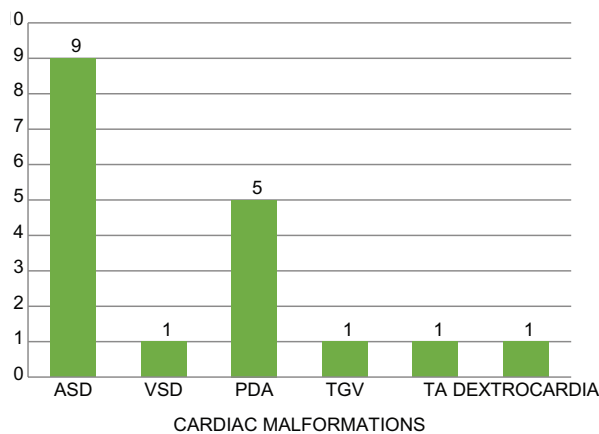


Figure 4. Cardiac malformations reported in patients with esophageal atresia admitted to the neonatal intensive care unit of the Children's Specialties Hospital of Chihuahua between January 2017 and December 2018. ASD: atrial septal defect; VSD: ventricular septal defect; PDA: patent ductus arteriosus; TA: truncus arteriosus; TGV: transposition of the great vessels.

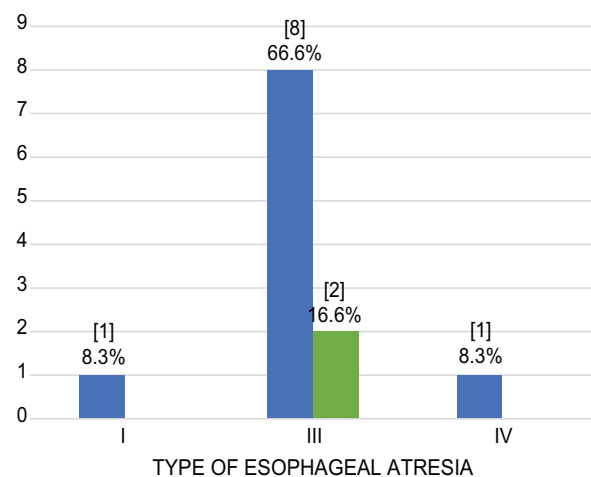


Figure 5. Cardiac malformations and their relationship with the esophageal atresia type in patients admitted to the neonatal intensive care unit of the Children's Specialties Hospital of Chihuahua between January 2017 and December 2018.

were dextrocardia, transposition of the great vessels, and truncus arteriosus (Fig. 4).

According to the observations in this group of patients, it is reported that 80% of the patients with type III esophageal atresia have some cardiac malformation, of which atrial septal defect is the most common ($p = 0.78$). This is not statistically significant, since the minimum

sample size is not reached. However, it has clinical significance for the studied population (Fig. 5) (Table 2).

The complications found in the patients included dehiscence of the esophageal repair in 40% of the cases, esophageal stenosis in 25%, and the development of some type of infection in 90% of them. Mortality represented the 42% (Table 3) (Fig. 6).

Table 2. Type of esophageal atresia and its relationship with cardiac malformations in patients admitted to the neonatal intensive care unit of the Children's Specialties Hospital of Chihuahua between January 2017 and December 2018

	Cardiac malformations, n (%)		Total
	Yes	No	
Atresia type			
I	1 (100.0)	0 (0)	1 (100.0)
III	8 (80.0)	2 (20.0)	10 (100.0)
IV	1 (100.0)	0 (0.0)	1 (100.0)
Total	10 (83.3%)	2 (16.7%)	12 (100.0)

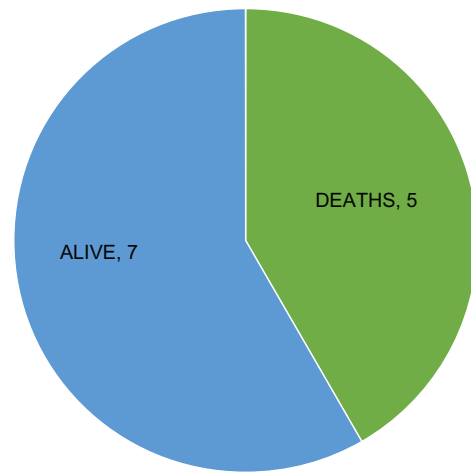
Table 3. Complications in patients with esophageal atresia admitted to the neonatal intensive care unit of the Children's Specialties Hospital of Chihuahua between January 2017 and December 2018

Complications	
Nosocomial infection	11
Dehiscence	5
Stenosis	3

Discussion

Esophageal atresia requires a timely detection and appropriate multidisciplinary management for the accomplishment of its complete resolution. These patients require collaborative work from the time of pregnancy by the obstetrics and gynecology services, as well as radiology, for timely detection. After childbirth, the neonatologist's medical treatment and the pediatric surgeon's surgical treatment are crucial. The assessment of these patients involves pediatric cardiologists, anesthesiologists, radiologists, pulmonologists and geneticists, as well as nursing, psychology and social work personnel. There are potential complications during the hospital stay: immediate post-operative ones, high risk of infection, and those related to other congenital malformations. The environmental characteristics of the patients with this pathology should be known in order to try to identify the cause. In addition, the family characteristics should be known for the recommendations at discharge, genetic counseling and appropriate follow-up.

This study was able to prove that the diagnosis of esophageal atresia is established late due to low prenatal detection, increasing the time of arrival at the

**Figure 6.** Reported mortality in patients with esophageal atresia admitted to the neonatal intensive care unit of the Children's Specialties Hospital of Chihuahua between January 2017 and December 2018, corresponding to 42%.

hospital to which the patient is referred. Since there is no obstetric surgery department at the hospital where this work was conducted, patients referred from hospitals around the State of Chihuahua are received, and surgical management is provided after the patient's stabilization and assessment at the neonatal intensive care unit.

In this study, where sociodemographic features related to patients diagnosed with esophageal atresia were analyzed, no risk factors associated with such pathology were found. Most mothers were healthy, had not been exposed to toxins during pregnancy, and geographic prevalence was not observed. As regards the types of esophageal atresia, type III predominates, with blind proximal end and distal tracheoesophageal fistula, as reported in the literature. Concerning associated malformations, cardiac anomalies are the main ones, with atrial septal defects being the most frequent, as reported in other case series. In contrast to what has been presented in the literature, this study shows a higher mortality rate, over 40%, in patients with esophageal atresia. It is believed that this is due to the factors previously described, especially those related to infectious process. Also, the low syndromic association found in this study should be noted, where only two patients have some set of specific signs and symptoms, such as one with Down syndrome and another one with Goldenhar syndrome. Although the total number of patients that were admitted with an esophageal atresia diagnosis during the study period were analyzed, it is insufficient to establish statistically

significant results. Nonetheless, the presented results are clinically significant for the population with esophageal atresia.

Conclusions

Esophageal atresia is a relatively common congenital malformation, with an unknown etiology, but believed to be multifactorial. Most cases are sporadic, non-syndromic, associated to familial cases in less than 1%. Currently, studies are underway to try to analyze the pathogenesis of this anomaly. These are mainly focused on the ontogeny of neuropeptides related to the esophagus, studies with different drugs, such as doxorubicin or antithyroid agents, and studies in animal models. The diagnosis should be made prenatally, by means of imaging techniques, where a small stomach or the lack of it plus polyhydramnios has a positive predictive value of 56%⁸. Nonetheless, in this study, the diagnosis was established postnatally in all cases, by means of X-rays and radiopaque instruments. Esophageal atresia is known to be related to other congenital anomalies, including cardiovascular, anorectal, genitourinary, gastrointestinal, skeletal, and neurological, among others. It is necessary to initiate a complete approach to patients presenting esophageal atresia in order to identify any other condition and provide appropriate treatment. Conducting an echocardiogram is crucial to be able to identify both associated heart defects, and the position of the aortic arch and the descending aorta for the surgical plan. In this study, it was possible to observe that cardiac malformations are the most frequent, as they were present in 83% of the analyzed patients, with the main of these being atrial septal defects and patent ductus arteriosus.

There are different risk classifications for this pathology, which take factors such as weight, cardiac malformations, and the need for mechanical ventilation into account. In general, the survival rate has increased, and a survival higher than 90% is reported. However, in this study a high mortality rate of 42% was observed, which, in most cases, was related to some infectious process. As regards treatment, surgical repair of the esophagus is urgent, but it does not represent an emergency and will not be performed until the patient has been stabilized. The most frequent complications include anastomotic leakage, postoperative esophageal stenosis, recurrent tracheoesophageal fistula, tracheomalacia, infections and gastroesophageal reflux⁸.

In this research, it was found that this is a relatively frequent malformation in our area. It was reported that the mothers of the patients with this pathology had a regular prenatal control, and they were young women without any relevant disease during pregnancy. The average gestational age at birth was term (39 weeks of gestation), most of the patients had adequate weight and height at birth, and the Apgar score at 5 minutes was, for most of them, 9. It should be noted that the average number of ultrasounds performed during pregnancy was 3.8, about 60% were reported as normal, and only 25% showed polyhydramnios. However, the esophageal atresia diagnosis was not established prenatally in any of the cases. Neither ethnic nor geographic prevalence in the State was observed regarding this pathology. Both in analyzed patients and in the literature, type III esophageal atresia was the most frequent one, and as for the associated congenital malformations, cardiac malformations were the most frequently found, with atrial septal defects standing out. The high mortality rate found in this work, compared to what has been reported in other analyses, is worth noting. The foregoing is of utmost importance in order to take measures in the future and thus enhance the survival of patients with this diagnosis.

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Conflicts of interest

The authors declare that they do not have conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments have been made on human beings or animals for this research.

Data confidentiality. The authors declare that they have followed the protocols of their work center regarding the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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