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# CONGENITAL DIAPHRAGMATIC HERNIA: PATHOPHYSIOLOGY, DIAGNOSIS, AND TREATMENT - A SYSTEMATIC REVIEW

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**Abstract:** Congenital Diaphragmatic Hernia (CDH) is a fetal malformation characterized by a defect in the diaphragm that allows abdominal organs to migrate into the thoracic cavity. This condition causes lung compression during intrauterine development, resulting in pulmonary hypoplasia and persistent pulmonary hypertension, as well as significant cardiovascular alterations, such as hypoplasia of the left ventricle. Prenatal diagnosis is essential for planning clinical and surgical management, and is complemented by tests, including fetal magnetic resonance imaging and echocardiography. Treatment includes immediate neonatal interventions and, in severe cases, experimental fetal procedures such as Fetal Endoluminal Tracheal Occlusion (FETO). Corrective surgery is performed after neonatal stabilization and is essential to restore anatomy, but the prognosis will depend on the severity of the pulmonary and cardiac alterations. In addition, therapeutic advances have improved patient survival and quality of life, highlighting the importance of multidisciplinary and individualized care.
**Keywords:** "Congenital Diaphragmatic Hernia", "Management", "Outcomes", "Surgical Treatment", "Neonatal Care" and "Pulmonary Hypoplasia

## INTRODUCTION

Congenital Diaphragmatic Hernia (CDH) is a rare and potentially serious condition that occurs when the diaphragm does not form properly during fetal development [1,2]. As a result, this defect allows abdominal organs, such as the stomach, liver and intestines, to migrate into the thorax, resulting in the space needed for lung growth being compromised [1,2,3]. Consequently, this anomaly results in underdeveloped lungs - a condition known as pulmonary hypoplasia, and serious respiratory complications at birth [1,2,3]. In addition, it is often associated with pulmonary

hypertension, a damaging increase in pressure in the blood vessels of the lungs, which overloads the newborn's heart [3,4].

The prevalence of Congenital Diaphragmatic Hernia (CDH) is estimated at approximately 2.5 cases per 10,000 births, but this rate hides several nuances and challenges [3,4,5]. The difficulty in determining the exact prevalence is associated with certain factors: the lack of standardization in data collection and recording, variability in health systems and the so-called "hidden mortality" [4,5]. The latter includes cases that are not accounted for, such as: pregnancy terminations after prenatal diagnosis, stillbirths and early neonatal deaths before referral to specialized centers [4,5].

CDH can be identified in the prenatal period, mainly through ultrasound scans carried out in the second or third trimester of pregnancy [4,5]. After birth, the diagnosis is confirmed by imaging tests such as X-rays and CT scans [4,5,6]. The management of CDH is extremely complex and requires a multidisciplinary approach, with the help of neonatologists, pediatric surgeons and intensive care specialists [4,5,6]. Treatments generally involve mechanical ventilation to aid breathing, the use of nitric oxide to reduce pulmonary hypertension and corrective surgery to close the defect in the diaphragm and reposition the abdominal organs [6,7,8]. Despite this, initial clinical management is crucial to stabilize the newborn before surgical intervention [7,8].

The challenges related to Congenital Diaphragmatic Hernia (CDH) go beyond the anatomical complexity of the condition, also encompassing diagnostic, therapeutic and prognostic aspects [7,8,9]. Pulmonary hypoplasia and pulmonary hypertension often limit management options, making ventilatory support and hemodynamic control important for the survival of the newborn [9,10]. In addition, variations in the severity of cases and associated conditions, such as cardiac or genetic anomalies, make it difficult to standardize treatment protocols [9,10]. Another significant challenge is related to early detection and deciding on prenatal management, including controversial options, such as fetal interventions in specialized centers [10,11]. These difficulties highlight not only the need for a multidisciplinary and individualized approach, but also a better understanding of the factors that influence clinical outcome [10,11].

In this context, an integrative review plays a fundamental role in consolidating and critically analyzing the available evidence on CDH [10,11]. This type of study allows for the identification of gaps in knowledge, the comparison of different therapeutic strategies and the clarification of controversial issues, characterized by prenatal interventions or the impact of new technological advances, i.e. extracorporeal therapies [10,11,12]. Furthermore, integrative reviews provide an up-to-date overview of best practices, guiding clinical decision-making and driving new research [13].

## METHODS

This study is a systematic review with the aim of consolidating and analyzing the available evidence on advances in the management and outcomes of Congenital Diaphragmatic Hernia (CDH). A systematic review is a rigorous methodological approach that seeks to objectively identify, evaluate and synthesize data from relevant studies on the subject, promoting a comprehensive, evidence-based understanding [14]. This type of review is fundamental for guiding clinical practices and identifying gaps in scientific knowledge that can drive future research [15]. As such, it aims to highlight the pathophysiology of the disease associated with pulmonary hypoplasia and cardiological changes, as well as the effectiveness of current diagnosis and management patients with CDH.

The surveys carried out for this study were collected from the PUBMED, VHL and MEDLINE databases, covering articles published between 2019 and 2024, exclusively in English. The keywords used were: *"Congenital Diaphragmatic Hernia"; "Management"; "Outcomes"; "Surgical Treatment"; "Neonatal Care"*; and *"Pulmonary Hypoplasia*" [15]. In order to guarantee the accuracy and relevance of the results, the search used Boolean operators, date filters, language and type of publication, ensuring that only high-quality articles were considered for the analysis.

The article selection process followed three strict stages. In the first stage, articles were identified using a combination of the selected descriptors and filters were applied to exclude studies outside the analysis period, non-peer-reviewed publications, experimental animal trials and articles in languages other than English. In the second stage, an initial screening was carried out based on the titles and abstracts, excluding duplicate articles, narrative reviews and studies irrelevant to the topic of CDH. In the third stage, the 47 selected articles were fully evaluated, applying additional exclusion criteria, namely: insufficient or inconsistent data and inadequate methodologies or results that did not adequately address the relevant clinical outcomes of CDH. After this careful analysis, the most robust and relevant studies were included in the final analysis, ensuring that the systematic review gathered the most relevant evidence to support conclusions about the management and outcomes of this complex condition.

## RESULTS

### IMPACT OF PULMONARY HYPOPLASIA ON PATHOPHYSIOLOGY

The articles reviewed highlight that pulmonary hypoplasia is a central complication of Congenital Diaphragmatic Hernia (CDH), having a direct and significant impact on neonatal respiratory pathophysiology [15,16,17,18]. The reduction in the number of alveoli and bronchioles is consistently associated with a reduction in the surface area available for gas exchange, confirming the relationship between inadequate lung development and high rates of respiratory failure [15,16,17,18]. Research has shown that the restriction of intrauterine lung growth caused by the herniation of abdominal organs results not only in hypoxemia, but also in levels of hypercapnia, which highlights the relationship between lung hypoplasia and neonatal respiratory failure. In this sense, these respiratory complications are aggravated by additional structural alterations, such as thickening of the alveolar walls and an increase in interstitial tissue, which further reduce respiratory efficiency [17,18].

In addition, the studies reviewed emphasize that the hemodynamic consequences and functional alterations resulting from pulmonary hypoplasia increase the risk of secondary complications [16,17,18]. Thus, alveolar thickening and interstitial tissue not only impair pulmonary ventilation, but also contribute to Persistent Pulmonary Hypertension (PPH), a common complication in neonates with CDH [16,17,18]. The presence of PPH exacerbates respiratory decompensation, overloads the right ventricle and aggravates tissue hypoxia [17,18]. These findings highlight the importance of interventions that promote early optimization of ventilation and oxygenation, as well as strategies to minimize the impact of prolonged mechanical ventilation. They also

serve as measures to reduce the occurrence of bronchopulmonary dysplasia [17,18]. Thus, the articles analyzed reinforce the fundamental role of pulmonary hypoplasia in the cascade of pathophysiological events affecting neonates with CDH [17,18].

## EFFECTIVENESS OF PRENATAL DIAGNOSIS

Considering the results of the studies, the growing effectiveness of prenatal diagnostic techniques in the identification and management of Congenital Diaphragmatic Hernia (CDH) can be emphasized [18,19,20]. It is worth noting that detailed ultrasound remains the primary tool for initial diagnosis, allowing early visualization of the herniation of abdominal organs into the thorax [18,19,20]. In addition, fetal magnetic resonance imaging (fMRI) has emerged as an advanced method for lung volumetric assessment, providing detailed information on the extent of pulmonary hypoplasia and helping with risk stratification [19,20]. The combination of these tools increases diagnostic accuracy, allowing for more targeted and planned interventions [19,20].

Similarly, fetal echocardiography plays an essential role in assessing the cardiovascular impact of CDH, especially in identifying pulmonary hypertension and possible associated anomalies [19,20]. Genetic studies complement this diagnostic arsenal, identifying chromosomal conditions and genetic syndromes that often coexist with CDH [21,22,23]. This information is fundamental for predicting the severity of the condition and guiding genetic counseling and prognosis [21,22,23]. In this way, the integration of imaging technologies and genetic tests improves understanding of the clinical complexity of CDH before birth [22,23].

Thus, the early identification promoted by the aforementioned diagnostic advances is essential for planning childbirth and neonatal care [22,23]. Furthermore, studies also show that, through timely diagnosis, it is possible to prepare a specialized multidisciplinary team and choose the ideal place for delivery, with access to advanced neonatal intensive care, immediate ventilatory support and strategies for managing pulmonary hypertension [22,23,24,25]. Thus, advances in prenatal diagnosis not only improve clinical outcomes, but also allow for a personalized approach, reducing the morbidity and mortality associated with CHD [22,23,24,25].

## ADVANCES IN FETAL INTERVENTIONS

Preliminary results of the FETO (Fetal Endoluminal Tracheal Occlusion) procedure have shown high potential for the treatment of severe cases of Congenital Diaphragmatic Hernia (CDH) associated with severe pulmonary hypoplasia [24,25,26,27]. The technique, which consists of placing a balloon in the fetal trachea to stimulate lung growth, has shown a significant increase in lung volume in treated fetuses, suggesting an improvement in postnatal respiratory capacity [25,26,27]. In addition, initial studies indicate that this approach can reduce neonatal mortality in selected cases, especially when other prognostic indicators point to unfavorable outcomes [25,26,27].

The benefits of FETO are particularly evident in situations of severe pulmonary hypoplasia, in which lung development is extremely compromised [25,26,27]. Based on current research, it has been observed that fetuses undergoing the procedure show an increase in thoracic diameter and greater alveolar maturation with the potential to minimize respiratory complications at birth [26,27,28]. Furthermore, the procedure allows for more effective interventions in the neonatal period, reducing the need for prolonged ventilatory support and optimizing the initial recovery of newborns [27,28].

Despite advances, FETO still presents technical challenges and issues related to long-term safety [27,28]. Balloon insertion and removal require advanced skills and can be associated with complications such as tracheal rupture, premature birth or damage to developing lung tissue [27,28]. Furthermore, there is still uncertainty about the long-term effects of the procedure, the possible impacts on lung growth and the functional development of the lungs [28]. Therefore, although the preliminary results are encouraging, further studies related to FETO are essential to guarantee its efficacy, safety and applicability on a large scale [28].

## RESULTS OF POST-BIRTH NEONATAL MANAGEMENT

Post-birth neonatal management in cases of Congenital Diaphragmatic Hernia (CDH) and pulmonary hypoplasia emphasizes the importance of early intubation and personalized ventilatory adjustments to stabilize the newborn [28]. Immediate intubation after birth avoids the use of positive pressure ventilation via mask, reducing the risk of gastric insufflation and optimizing oxygenation [28,29]. In addition, individualized ventilation strategies, based on the specific lung conditions of each patient, have been shown to significantly improve respiratory stability in the first hours of life [29].

Protective ventilatory management has shown clear benefits in reducing lung damage associated with prolonged mechanical ventilation [29]. The use of low tidal volumes, limited pressures and carefully adjusted oxygen fractions minimizes the risk of barotrauma, volutrauma and oxygen toxicity [29,30]. Studies have shown that these practices, when implemented in conjunction with close monitoring, not only protect the newborn's fragile lungs, but also promote faster recovery and reduce the incidence of complications such as bronchopulmonary dysplasia [29,30].

The impact of multidisciplinary care in specialized neonatal ICUs has been a differential in the prognosis of these patients [29,30]. Consequently, the integration of teams made up of neonatologists, pediatric surgeons, respiratory physiotherapists and specialized nurses allows for a comprehensive and individualized approach [30]. This coordination improves the implementation of evidence-based protocols, ensuring effective respiratory support, adequate nutritional interventions and management of associated complications [30]. As a result, survival rates increase considerably, as does the quality of life of newborns with CDH and pulmonary hypoplasia [31,32].

## SURGICAL TREATMENT

Surgery to correct CDH is essential to restore the baby's normal anatomy and allow the lungs to grow and function properly [31,32]. The procedure involves closing the opening in the diaphragm and returning the abdominal organs to their original position [31,32]. In turn, surgical intervention helps to relieve lung compression, optimizing the conditions for respiratory support in the neonatal period [31,32]. Thus, successful surgery is a crucial step in treatment, but it does not directly correct the underlying pulmonary hypoplasia, which remains a challenge to be managed in the long term [32].

The surgical technique varies according to the extent of the defect in the diaphragm [32]. In smaller cases, the defect can be closed with a primary suture [32]. However, in more complex situations, it may be necessary to use prostheses or synthetic meshes to reconstruct the diaphragm [32,33]. In this sense, the procedure is usually carried out by a highly specialized multidisciplinary team, including paediatric surgeons, neonatologists and anaesthetists [32,33]. In some circumstances, minimally invasive approaches, such as laparoscopy, can be used, reducing recovery time and post-operative complications [32,33].

As for the ideal time to perform surgery, it will depend on the clinical condition of the newborn [32,33]. In cases of severely affected babies, initial stabilization is a priority, with a focus on optimizing ventilation, treating pulmonary hypertension and ensuring hemodynamic stability [32,33]. Surgery is usually performed between 24 and 48 hours after birth, but can be postponed in cases of severe instability [32,33]. With regard to neonates with extreme impairment, the use of advanced support, such as ECMO (extracorporeal membrane oxygenation), may be necessary before surgical correction [32,33].

## DISCUSSION

### PATHOPHYSIOLOGY OF THE DISEASE

Congenital Diaphragmatic Hernia (CDH) causes significant pulmonary alterations due to the compression of the abdominal organs on the thorax during fetal development [32,33]. This compression prevents the lungs from growing properly, resulting in pulmonary hypoplasia, characterized by a reduction in the number of alveoli and bronchioles [32,33]. As a consequence, gas exchange is compromised, making oxygenation and the elimination of carbon dioxide difficult after birth [33]. In addition, the thickening of the alveolar walls and the increase in interstitial tissue further worsen lung function, contributing to respiratory failure in affected newborns [33,34].

Cardiovascular alterations are also critical in the pathophysiology of CDH, especially persistent pulmonary hypertension (PPHN) [33,34]. This increase in pressure in the pulmonary arteries stems from high vascular resistance in hypoplastic lungs, overloading the heart [34]. In addition, the left ventricle (LV) often shows hypoplasia due to the cardiac displacement imposed by the hernia, reducing blood flow to the left side of the heart during the gestational period [34]. Thus, LV hypoplasia is aggravated by pulmonary venous hypertension, which results in inadequate venous return and increased pressures in the pulmonary veins [34,35].

Thus, the combination of these pulmonary and cardiovascular alterations creates a scenario of extreme clinical complexity [34,35]. Severe pulmonary hypertension, often resistant to conventional treatments, is one of the main causes of mortality in these patients [35]. In turn, LV hypoplasia and cardiac dysfunction further limit the effectiveness of pharmacological therapies, such as pulmonary vasodilators, making clinical management difficult [35]. Thus, these conditions highlight the need for personalized therapeutic strategies and a multidisciplinary approach to improve clinical outcomes in CDH [35,36].

### CURRENT DIAGNOSIS

Congenital Diaphragmatic Hernia (CDH) is a malformation in which there is a defect in the diaphragm, allowing abdominal organs to migrate into the thoracic cavity [35,36]. As migration occurs, it can compress the developing lungs, resulting in lung hypoplasia and significant breathing difficulties at birth [35,36]. Prenatal diagnosis is therefore essential, as it enables careful planning of the birth and neonatal care, ensuring that the medical team is prepared to deal with the complexities of this condition [35,36,37]. In addition, parents are given the opportunity to understand their child's condition, preparing them emotionally for the challenges of treatment [35,36,37].

Complementary examinations play an essential role in the diagnosis and management of Congenital Diaphragmatic Hernia (CDH), offering detailed information that goes beyond the initial ultrasound [35,36,37]. On this basis, detailed ultrasound is often the first examination performed, confirming the presence of the hernia and assessing other structural

anomalies, such as the position of the liver and the amount of amniotic fluid [35,36,37]. In this way, fetal magnetic resonance imaging (fMRI) complements this analysis by providing precise images of lung volume, the degree of liver herniation and possible associated malformations, which is crucial information for estimating severity and prognosis [36,37]. It should also be noted that fetal echocardiography investigates cardiac anomalies, while genetic studies, such as karyotyping and microarray, identify chromosomal alterations that can influence the clinical outcome [37]. Thus, integrating the data obtained from these tests allows for a personalized and more effective approach to the baby's care [37,38,39].

## MANAGEMENT AND TREATMENT OF CONGENITAL DIAPHRAGMATIC HERNIA

The main aim of fetal interventions for Congenital Diaphragmatic Hernia (CDH) is to minimize lung hypoplasia, allowing the lungs to grow and increasing the baby's chances of survival after birth [37,38,39]. In view of the above, these approaches are only indicated in selected cases that are considered severe, since their implementation is generally experimental and carried out in highly specialized centers [37,38,39,40]. It is worth noting that among the available options, fetal surgical repair has been abandoned due to the lack of proven benefits, while fetal endoluminal tracheal occlusion (FETO) has emerged as a promising alternative [37,38,39,40].

The FETO procedure is indicated in cases of isolated CDH with severe pulmonary hypoplasia [37,38,39,40]. This method involves inserting a small balloon into the fetus' trachea, using fetoscopy and guided by ultrasound [39,40]. The balloon remains inflated for a few weeks, blocking the outflow of fluid from the lungs to the amniotic sac, which stimulates lung growth [39,40]. The removal of the balloon, scheduled to take place around 34 weeks of gestation, is equally careful and planned to ensure the safety of the fetus. Despite its innovative potential, the procedure is technically challenging and requires highly experienced medical teams [40,41,42].

Although FETO represents an advance in the management of CDH, its indication is restricted and the results are still being widely investigated [40,41,42]. From this perspective, studies continue to evaluate the efficacy and safety of the procedure in the long term, including its impact on lung development and the quality of life of the newborn [41,42]. Furthermore, it is worth emphasizing the importance of detailed guidance and counselling for parents before they opt for this intervention, and the risks, benefits involved and therapeutic alternatives available should be pointed out [42].

When it comes to planning for the birth of a baby with Congenital Diaphragmatic Hernia (CDH), it is necessary to prioritize delivery in a tertiary center with adequate infrastructure to deal with the complexity of the case, such as a Neonatal ICU [42,43], even if the pregnancy occurs at the ideal time of up to 39 weeks, which allows for maximum lung development [43]. Immediately after birth, intubation is crucial to avoid insufflation of the gastrointestinal tract, which can compromise breathing [43,44]. In addition, specific adjustments to the position of the endotracheal tube are necessary due to the peculiar anatomy of these babies, ensuring effective ventilation without compromising the right main bronchus [44,45].

Respiratory management requires delicate mechanical ventilation to protect the immature lungs, avoiding high inspiratory pressures that could cause injury [44,45]. The use of surfactant, commonly used in premature babies, is not recommended in cases of CDH, as it can worsen outcomes [44,45]. Similarly, continuous monitoring of heart rate parameters, pre- and post-ductal oxygen saturation

and blood pressure is crucial for assessing the baby's stability [45,46]. Bearing this in mind, some complementary measures can be taken depending on the case, such as inserting an orogastric tube to prevent gas accumulation in the stomach and investigating complications such as contralateral pneumothorax [45,46,47]. From this perspective, the main aim of these actions is to stabilize the newborn, ensuring adequate breathing and circulation, before transferring them to the neonatal ICU [45,46,47].

Although surgery is a crucial stage, it involves risks: infections, bleeding, respiratory and cardiac complications [45,46,47]. In addition, a prolonged post-surgical recovery may be necessary, requiring intensive care, mechanical ventilation and continuous monitoring [45,46,47]. The prognosis will depend on the severity of the pulmonary hypoplasia, the presence of other congenital anomalies and the quality of the post-operative care [45,46,47]. That said, it is clear that with medical advances and improved techniques, the survival and quality of life of patients with CDH has improved significantly [46,47].

## CONCLUSION

Congenital Diaphragmatic Hernia (CDH) is a rare and complex condition characterized by the migration of abdominal organs into the thoracic cavity due to a defect in the diaphragm. This malformation results in severe pulmonary hypoplasia and persistent pulmonary hypertension, which represent the main challenges for the survival and quality of life of affected newborns. Early diagnosis, through detailed ultrasound and fetal magnetic resonance imaging, plays a key role in planning clinical and surgical management, allowing for more targeted interventions in each case.

The treatment of CDH therefore requires a multidisciplinary therapeutic approach to stabilize the newborn, control respiratory and cardiovascular complications and optimize the conditions for surgical correction. Therefore, all this coordination is indispensable to reduce the associated morbidity and mortality and to prepare patients to adhere to definitive treatment. The experimental Fetal Endoluminal Tracheal Occlusion (FETO) procedure has shown promising results in stimulating lung growth in severe cases, but its application still requires further investigation.

Surgical correction, a central step in the treatment of CDH, aims to restore anatomy and relieve lung compression, favoring lung development and recovery. However, the underlying pulmonary hypoplasia remains a challenge to be faced throughout the patient's life, reinforcing the need for intensive neonatal care and continuous monitoring. As a result, advances in diagnostics, therapeutic technologies and management protocols have significantly improved clinical outcomes, which should underline the importance of continued efforts to improve treatment strategies and promote a better quality of life for patients.

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