The Libyan International Medical University

Faculty of Basic Medical Science

The Effect of Congenital Diaphragmatic Hernia on The Development of Left-Sided Heart Structures

Heba Mohamed Albreiki

2090

Supervised by: Eman layas

Assisted by: Heba Alshalmani

Report Submitted to fulfill the requirements for Scientific Research Activity

Date of Submission: 11/3/ 2020

Abstract

The hernia involves an abnormal exit of tissue or an organ, through the wall of the cavity in which it normally resides, it has different forms and causes. This report discussed the congenital hernia specifically the diaphragmatic type. In general, the diagnosis of congenital diaphragmatic hernia (CDH) can be made prenatally or after birth by imaging such as: ultra-sonographic, echocardiography, magnetic resonance imaging (MRI). In consequence to the herniation it leads to many complications in digestive and respiratory systems, the majority of the cases presenting with pulmonary hypoplasia and persistent pulmonary hypertension (PPHN). In addition to its effect on the development of the heart structures which is the aim of the report by focused on the left sided structures because left-sided CDH is more common due to the protective effect of the liver on the right preventing herniation.

Introduction

Hernias occur in several forms most often affecting the abdomen other hernias include hiatus, incisional, and hernias. In addition the CDH can be associated with cardiac, gastrointestinal, genitourinary anomalies or with chromosomal aneuploidy such as trisomies. Multiple genetic factors along with environmental exposures and nutritional deficiencies have been proposed to be the possible etiologies for CDH. (1)

Congenital diaphragmatic hernia (CDH) is a congenital anomaly that occur in approximately 1 in 2,000 to 4,000 live births. (1) Babies with CDH have a hole in their diaphragm, the wide, flat muscle that separate the chest from the abdominal cavity. (2) Normally, the diaphragm forms during the 6^{th} through the 12^{th} week of pregnancy, is formed by the fusion of several embryonic components which include the septum transversum, pleuroperitoneal membranes, esophageal mesentery, and body wall mesoderm. The development of the diaphragm is divided into two phases at firstly the development of the diaphragmatic pericardium secondly the development of the pleural cavity and the closure of the pleuroperitoneal canal (PPC). In the normal embryogenesis, the septum tranversum separates the pericardial and the peritoneal cavities as it fuses dorsally with the mesodermal tissue surrounding the foregut. As this occur, the PPC remains patent, connecting the pleural spaces and peritoneal cavity. (2)

The pathogenesis of CDH is still not fully understood, and until recently, the general hypothesis is that the defect in CDH results from failure of complete closure of the PPC at the embryonic period 8^{th} -10^{th} gestational week, which is an essential embryological step that completes the formation of the primitive fetal diaphragm. (2) The hole in the diaphragm allows the contents of the abdomen which may include the stomach, intestine, liver, spleen or kidney to herniate up into the chest. (3)

Figure 1 illustrate the CDH based on location, the postero-lateral hernias known as Bochdalek hernias are the most common type (70–75%) with the majority occurring on the left side (85%) and less frequently on the right side (13%) or bilateral (2%). Anterior defects or Morgagni hernias (23–28%) and central hernia (2–7%) and other types. (1)

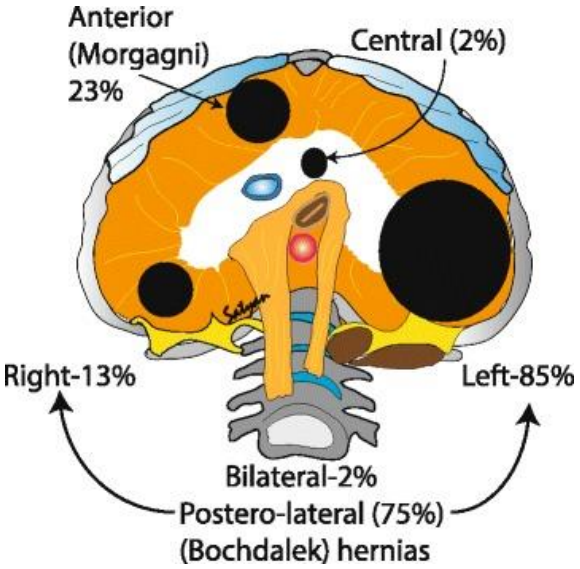


Figure 1: The classification of CDH based on location

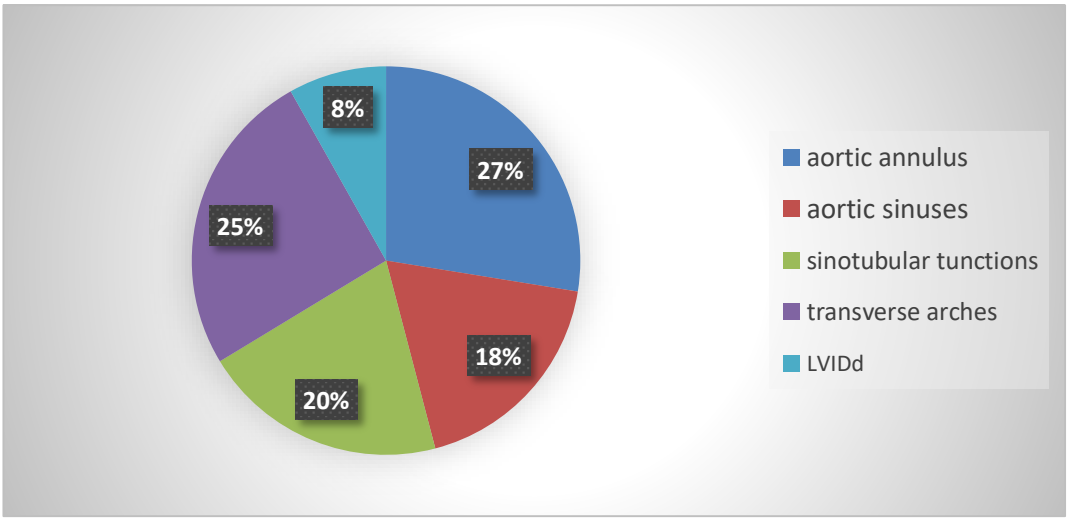
The aim of this report is to evaluate which left-sided heart structures are affected in neonates with congenital diaphragmatic hernias. (4)

Materials and Methods

Retrospective review of neonates between May 2007 and April 2015 with a diagnosis of a congenital diaphragmatic hernia was performed. Clinical and echocardiographic data were extracted from the electronic medical record and indexed to body surface and compared to normative values. Univariable regression models assessed for association between different variables and length of stay. (4)

Results

Data of 52 patients showed decreased mean z scores for the left ventricular internal diameter in diastole (LVIDd) (-3.16), left ventricular internal diameter in systole (LVIDs) (-3.05), aortic annulus (-1.68), aortic sinuses (-2.11), transverse arch (-3.11), and sinotubular junction (-1.47). Regression analysis showed a percent reduction in length of stay per 1 mm size increase for LVIDd (8%), aortic annulus (27%), aortic sinuses (18%), sinotubular junctions (20%), and transverse arches (25%). (4)



Discussion

Prenatal diagnosis by ultrasound detects more than 50% of CDH cases at a mean gestational age of 24 weeks. Three dimensional ultrasound imaging, fetal echocardiography and Fetal Magnetic Resonance imaging (MRI) are other prenatal diagnostic modalities used in assessing the severity and outcome of CDH. (5) Left sided CDH may be characterized by the presence of heterogeneous mass which may be stomach filled with fluid or intestines. In contrast, isolated right-sided CDH is extremely difficult to diagnose by ultrasound if the liver is the only organ that has herniated. (2) Indirect signs such as a shift of cardiac axis, identifying the gall bladder and vasculature in the liver using Doppler may aid in the diagnosis. MRI has been found to be useful in detecting fetal anomalies and can be valuable adjunct to evaluate the position of the liver and estimating lung volume. Associated cardiac and neural tube defects may affect the outcome of infants with CDH. (5)

Postnatal presentation of Bochdalek hernia may be symptomatic or asymptomatic and may be discovered as an incidental finding. However, they may be diagnosed later in

adulthood with nonspecific respiratory and gastrointestinal symptoms and signs. Acute presentation of CDH include sever immediate cardiorespiratory distress with cyanosis, tachypnea, tachycardia with findings of a prominent hemithorax with minimal air entry, a displaced apex beat indicating mediastinal shift, and often a scaphoid abdomen (Fig. 2). (1)

For those that present later in life, the most frequent features include respiratory symptoms (43%), gastrointestinal symptoms (33%), both respiratory and gastrointestinal symptoms (13%) , and asymptomatic (11%). (4) The majority of right-sided lesions present with respiratory symptoms, while for left sided lesions, equal incidence of respiratory and GI symptoms have been observed. Clinical symptoms may include upper abdominal pain, bloating, discomfort after meal, vomiting, cough, dyspnea, and palpitation. (4) Bochdalek hernia may present late or may present with complications such as gastric volvulus (Fig.3), splenic rupture, gastric or other intestinal obstruction, and/ or perforation. (5)

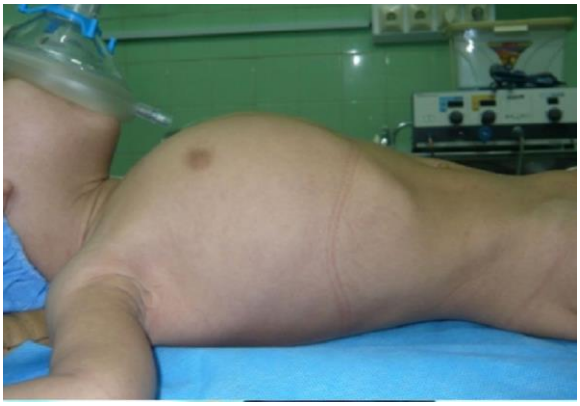


Figure 2: Scaphoid Abdomen

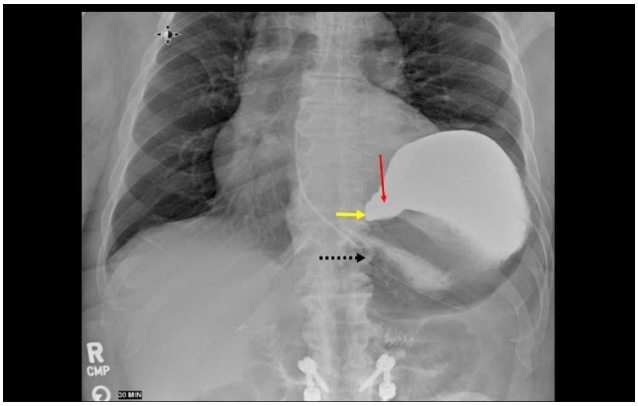


Figure 3: Gastric Volvulus

The major underlying pathophysiology of CDH appears to be a combination of lung of immaturity and hypoplasia that leads to Persist Pulmonary Hypertension (PPHN). This may be further aggravated by left ventricular underdevelopment and right ventricular hypertrophy resulting in ventricular dysfunction. (1)

Lung hypoplasia/immaturity occurs on the ipsilateral side of herniation, with the contralateral side being affected to a variable extent. Hypoplasia was initially thought to be secondary to physical compression of the lung by abdominal contents arresting lung development. Recently, a Two-hit hypothesis has been proposed based on rat model explaining the lung injury in CDH. according to this hypothesis, the initial insult occurs during the stages of organogenesis resulting in bilateral hypoplasia, followed by compression of the ipsilateral lung secondary to the herniation of the abdominal viscera at later stages. This theory explains the variability of lung hypoplasia on the contralateral side. The interference results in decreased branching of bronchioles and pulmonary vessels leading to acinar hypoplasia (Fig.4). The terminal bronchioles are decreased with thickening of the alveolar septa. The lung is relatively immature and hypoplasia of pulmonary vasculature leads to PPHN. (1)

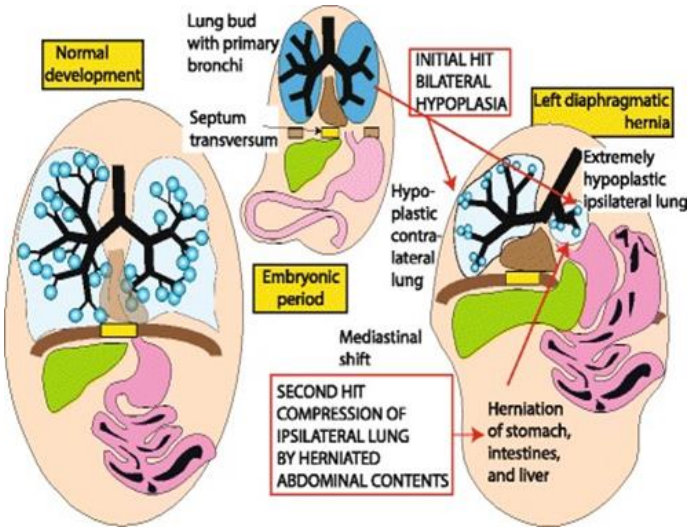


Figure 4: Two-hit hypothesis for CDH

The total pulmonary vascular bed is reduced with decreased number of vessels per unit of lung. In addition, pulmonary vascular remodeling with medial hyperplasia and peripheral extension of the muscle layer into small arteries is evident. The paucity of pulmonary vasculature and remodeling of the vessels contribute to the 'fixed' or irreversible component of PPHN in CDH .Altered vasoreactivity possibly due to an imbalance of autonomic innervation (increased sympathetic and decreased parasympathetic) ,and/or impaired endothelium-dependent relaxation of pulmonary arteries or an imbalance between vasoconstrictor and vasodilator mediators may

contribute to the reversible component of PPHN .Following birth, a combination of pulmonary arterial hypertension, right ventricular hypertrophy and/or failure, and left ventricular hypoplasia with pulmonary venous hypertension results in severe PPHN unresponsive to conventional management. (1)

Finally, ventricular dysfunction which is observed in some patients with severe PPHN due to CDH. During fetal life, the ductus arteriosus serves as a pop-off value and limits right ventricular strain. After birth, remodeled pulmonary vasculature in CDH results in pulmonary hypertension and leads to right ventricle (RV) dysfunction. This is more pronounced after birth when there is excessive strain on the right ventricle. Abnormalities of the left ventricle (LV) have been reported in infants with CDH. When compared to neonates with other causes of PPHN, infants with left sided CDH had significantly lower left ventricular mass assessed by echocardiography. Reduced left ventricular output has been documented in left sided and right sided CDH. The reduced left ventricular mass contributes to functional LV hypoplasia and may result in increased left atrial pressure and pulmonary venous hypertension. (1) Patients with congenital diaphragmatic hernias often have concomitant congenital heart disease (CHD), with small left-sided cardiac structures as a frequent finding. (4)

Conclusion

Patients with congenital diaphragmatic hernias have significantly smaller left-sided heart structures compared to age-matched normative data. Additionally, length of stay appears to be prolonged with decreasing size of several of these structures.

References

1. Leeuwen, L. and Fitzgerald, D. (2014). Congenital diaphragmatic hernia. *Journal of Paediatrics and Child Health*, 50(9), pp.667-673.

2. HASHIMOTO, R. (2008). Congenital Diaphragmatic Hernia: Experimental Approach. *Congenital Anomalies*, 39(2), pp.75-87.

3. Defect Size Determines Survival in Infants With Congenital Diaphragmatic Hernia. (2007). PEDIATRICS, 120(3), pp.e651-e657.

4. Coffman, Z., McGahren, E., Vergales, B., Saunders, C. and Vergales, J. (2019). The effect of congenital diaphragmatic hernia on the development of left-sided heart structures. Cardiology in the Young, 29(06), pp.813-818.

5. Kiss, J., Mader, K., Katona, M., Turi, S. and Talosi, G. (2010). PP-104. Congenital diaphragmatic hernia: Prognostic factors and outcomes. Early Human Development, 86, p.S59.