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# Congenital Diaphragmatic Hernia and Associated Anomalies

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## 1. Introduction

Congenital diaphragmatic hernia (CDH) is associated with multiple reported associated anomalies. Knowledge of these anomalies and their management if required should be part of overall treatment. Many of these are fatal and have known association with chromosomal abnormalities and can result in still born babies. Another aspect of the knowledge of these anomalies is in predicting the recurrence in the subsequent pregnancies.

The key determinants of mortality are whether the CDH is isolated or complex, co existence of major anomalies, size of the diaphragm defect, degree of pulmonary hypoplasia, severity of pulmonary hypertension in the perinatal period, side of the hernial defect. The major morbidity associated with CDH are pulmonary, gastro intestinal, neurological, musculoskeletal, hearing loss (1).

It has been well established that disruption of the retinoic acid signaling pathway is associated with development of CDH <sup>(1)</sup>. There is evidence that retinoic acid and vitamin A play an important role in the development of diaphragm and other aspects of organogenesis. However, it is difficult to explain the role of vitamin A in cases of isolated CDH. One small study showed decreased levels of retinol in the newborns with CDH compared to controls (2).

The reported incidence of CDH is between 1 in 2000 to 5000 births (3). The incidence of still births is not well documented but about one third of these babies are still born. The deaths are due to associated fatal congenital anomalies. Bilateral CDH are associated with high incidence of associated anomalies than the unilateral one (4). Infants with isolated CDH are more likely to be premature and macrosomic and male.

About one third of the patients have major congenital malformation (5). Although CDH is thought to be a sporadic developmental anomaly familial cases have been reported and recurrence risk in a first degree relative has been estimated to be about 2%. Chromosomal anomalies have been reported to occur in 9 to 34% patients common being trisomies, deletion and translocation. The combination of CDH and associated abnormal karyotype has been associated with a poor outcome. The incidence of associated malformations in CDH patients is about 10-50%.

## 2. Chromosomal abnormalities

About 10% of all individuals with CDH have a chromosome abnormality. The most common abnormalities are trisomy 18 and isochromosome 12p (6).

### **2.1 Chromosome 12p (Pallister Killian syndrome)**

The presence of supernumerary isochromosome, with double copy of short arm of chromosome 12 is confirmatory. Isochromosomal mosaicism is the cardinal finding in this syndrome. This is commonly found in the infants born to the mothers of advanced age. The spectrum of the clinical problems in this syndrome ranges from multiple malformations incompatible with life to milder phenotypes.

The documented abnormalities include CDH, relatively shortened limb, CNS anomalies and ventricular dilatation, craniofacial dysmorphism, presence of nuchal skin edema, hydrops or polyhydramnios (7).

The typical facial dysmorphism include brachycephaly, high broad forehead, ocular hypertelorism, low set ears, broad nasal bridge, anteverted nostrils, long philtrum. Patients have normal growth and most patients have at least moderate intellectual disability. The distinguishing features from Fryns syndrome are the non hereditary nature, rare occurrence of nail hypoplasia which is one of the hallmark for Fryns syndrome (8).

Patients with Fryns syndrome have CDH, cleft palate, distal phalangeal and or nail hypoplasia, cardiovascular and renal malformations.

### **2.2 Trisomy 21**

Infants with trisomy 21 can have Bochdalek or Morgagni hernia. It can be seen in association with presence of right sided diaphragmatic hernia or diaphragmatic eventration. (9).

### **2.3 Wolf Hirschhorn syndrome**

This is characterized by deletion of distal portion of short arm of chromosome 4. It is possible that gene responsible for development of the diaphragm is deleted because there is very common association of this syndrome with CDH (10). The various other reported genetic syndromes are trisomy 18 and trisomy 22 (11).

### **2.4 Single gene disorders**

Some of the more common single gene disorders in which CDH occurs are Cornelia de Lange syndrome, Denys Drash syndrome, Donnai Barrow syndrome, Fryns syndrome, spondylocoastal dysostosis, Meachan syndrome (8,12,13,14).

## **3. Malformations seen in non syndromic CDH**

At least 33% of the CDH patients have associated major congenital malformations, commonly cardiovascular and pulmonary, central nervous, musculoskeletal.

### **3.1 Cardiovascular malformations**

About one fourth of the patients with CDH have cardiovascular malformations. The most common malformations are ventricular septal defects and atrial septal defects.

The less commonly documented are Fallot's Tetralogy, hypoplastic left heart syndrome and dextrocardia, transposition of great vessels, double outlet of right ventricle and aortic

coarctation. Anatomic anomalies of the tracheobronchial tree have been found in 18% of the patients. Congenital tracheal stenosis, tracheal bronchus and trifurcated trachea are reported (15).

### **3.2 Central nervous system abnormalities**

This is the most common associated abnormality in fetuses stillborn with CDH. The most commonly diagnosed are neural tube defects, hydrocephalus (16,17) and rarely corpus callosum agenesis. The presence of sensorineural hearing loss also forms the part of the associated anomalies.

### **3.3 Musculoskeletal abnormalities**

The incidence is about 10% non syndromic CDH. The common occurrence limb reduction defects, polydactyly, syndactyly, hypoplastic thumb and Poland syndrome. This syndrome is associated with hypoplastic ribs on one side along with absence of ipsilateral pectoralis minor muscles (18,19,20,21,22).

### **3.4 Genitourinary abnormalities**

Undescended or ectopic testis, thoracic ectopic kidney (23,24), ectopic kidney, horse shoe kidney are reported in the literature. Gonadal aplasia and hypoplasia, ambiguity have also been reported with CDH.

### **3.5 Gastro intestinal malformations**

The common associations are malrotation, atresia, omphalocele and rarely situs ambiguous. Presence of abnormal gastroesophageal reflux and esophageal dysmotility is very common. Improper fixation of the ligaments of the stomach and subsequent volvulus of the stomach are also known in patients of CDH(25). Presence of Cantrell's Pentalogy is one of the classical associations. This association is presence of anterior diaphragmatic hernia with, omphalocele, bifid sternum, ectopia cordis and congenital heart defects as ventricular septal defects and ventricular dilatation( 25).

## **4. References**

- Brennan P, Croaker GD, Heath M: Congenital diaphragmatic hernia and interstitial deletion of chromosome 3. *J Med Genet* 2001;38:556-557.
- Clugston RD, Zhang W, Alvarez S, de Lera AR et al. Understanding abnormal retinoid signaling as a causative mechanism in congenital diaphragmatic hernia. *Am J Respir Cell Mol Biol* 2010; 42: 272-285.
- Cohen MS, Rychik J, Bush DM, Tian ZY et al. Influence of congenital heart disease on survival in children with congenital diaphragmatic hernia. *J Pediatr* 2002; 141:25- 30.
- Dott MM, Wong LY, Rasmussen SA. Population based study of congenital diaphragmatic hernia : risk factors and survival in metropolitan Atlanta, 1968-1999. *Birth defects Res A Clin Mol Teratol.* 2003; 67:267-269.
- Day R, Fryer A. Diaphragmatic hernia and preaxial polydactyly in spondylothoracic dysplasia. *Clin Dysmorphol.* 2003;12: 277-278.

- Friedman S, Chen C, Chapman J et al. Neurodevelopmental outcomes of congenital diaphragmatic hernia survivors in a multidisciplinary clinic at ages 1 and 3. *J Pediatr Surg.* 2008; 43: 1035-1046.
- Joshi M, Parelkar S, Shah H et al. Acute gastric volvulus in children: 6 years experience at a single centre. *Afr Jour Pediatr Surg.* 2010; 22: 22-24.
- Losty PD, Vanamo K, Rintala RJ et al. Congenital diaphragmatic hernia – does the side of the defect influence the incidence of associated malformations? *J Pediatr Surg* 1998; 33: 507-512.
- Lurie IW. Where to look for genes related to diaphragmatic hernia? *Genet Couns* 2003; 14:75-78.
- Kantarci S, Casavant D, Prada C et al. Findings from ACGH in patients with congenital diaphragmatic hernia: a possible locus for Fryns syndrome. *Am J Med Genet A.* 2006; 140:17-23.
- Kantarci S, Al-Gazali L, Hill R et al. Mutations in LRP2, which encodes the multiligand receptor megalin, cause Donnai Barrow and facio-oculo-acoustico-renal syndromes. *Nat Genet.* 2007; 39: 957-959.
- Klaassens M, Scott D, van Dooren M et al. congenital diaphragmatic hernia associated with duplication of 11q 23 qter. *Am J Med Genet A.* 2006; 140: 1580-1586.
13. Masturzo B, Kalache KD, Cockell A. Prenatal diagnosis of ectopic intrathoracic kidney in right sided congenital diaphragmatic hernia using color Doppler ultrasonography. *Ultrasound Obstet Gynecol.* 2001; 18: 173-174.
- Major D, Cadenas M, Fournier L et al. Retinol status of new born infants with congenital diaphragmatic hernia. *Pediatr Surg Int.* 1998; 13: 547-549.
- Miagliazza L, Otten C, Xia H et al. cardiovascular malformations associated with congenital diaphragmatic hernia: experimental and human studies. *J Pediatr Surg.* 1999; 34: 1352-1357.
- Miagliazza L, Xia H, Diez-Pardo JA et al. Skeletal malformations associated with congenital diaphragmatic hernia : experimental and human studies. *J Pediatr Surg.* 1999; 34: 1624-1629.
- Neville HL, Jaksic T, Wilson JM et al. Congenital diaphragmatic hernia study group: bilateral congenital diaphragmatic hernia. *J Pediatr Surg.* 2003; 38: 522- 524.
- Nose K, Kamata S, Sawai T et al. Airway anomalies in patients with congenital diaphragmatic hernia. *J Pediatr Surg.* 2000; 35: 1562-1565.
- Panda B, Rosenberg V, Cornfeld D. Prenatal diagnosis of ectopic intrathoracic kidney in a fetus with left sided diaphragmatic hernia. *J Clin Ultrasound.* 2009; 37: 47-49.
- Sergi C, Schulze BR, Hager HD et al. Wolfe Hirsch Horn syndrome: case report and review of the chromosomal aberrations associated with congenital diaphragmatic defects. *Pathologica.* 1998; 90: 285-293.
- Slavotinek AM. Fryns syndrome: a review of the phenotype and the diagnostic guidelines. *Am J Med Genet A.* 2004; 124A: 427-433.
- Skari H, Bjornland K, Frencker B et al. Congenital diaphragmatic hernia: a meta analysis of mortality factors. *J Pediatr Surg.* 2000; 35: 1187-1197.
- Van Dooren MF, Brooks AS, Tibboel D et al. Association of congenital diaphragmatic hernia with limb reduction defects. *Birth defects Res A Clin Mol Teratol.* 2003; 67: 578- 584.
- Witters I, Leguis E, Moerman P et al. Associated malformations and chromosomal anomalies in 42 cases of prenatally diagnosed diaphragmatic hernia. *Am J Med Genet* 2001 ; 103: 278- 280.
- Yamataka T, Puri P. Pulmonary artery structural changes in pulmonary hypertension complicating congenital diaphragmatic hernia. *J Pediatr Surg.* 1997; 32: 387- 390.

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