INTRODUCTION

The diaphragm is the structure that separates the thoracic and abdominal cavities to maintain the pressure differentials of the respective compartments. Congenital diaphragmatic hernia refers to a developmental defect of the formation of the diaphragm that, in most cases, is evident at birth. This allows the herniation of the abdominal contents into the thoracic cavity **(Skari et al., 2002).**

prevalence rate for all types of congenital diaphragmatic hernia is approximately one in 3000 live births, although considerable variation has been reported with frequencies as low as one in 5000 **(Skari et al., 2002).**

Lower prevalence rates may be seen in studies that do not systematically detect congenital diaphragmatic hernia in pregnancy terminations, stillborn fetuses, or neonatal deaths, or in which cases diagnosed after infancy escape ascertainment. It has been reported that as many as 13% of Congenital diaphragmatic hernia cases are undiagnosed in early infancy. Higher prevalence rates may be seen in studies that have fuller ascertainment including a greater number of prenatally diagnosed cases or that examine a geographically defined population with a thorough review of all postmortem

cases, including those with unexplained respiratory distress. **(Skari et al., 2002).**

No significant variation in geographic region or ethnicity has been identified **(Robert et al., 1997).**

Some, but not all, studies have found more affected males than females with congenital diaphragmatic hernia. It is difficult to resolve these discrepancies, although they may be the result of differing study demographics, such as the distribution of isolated Congenital diaphragmatic hernia in which no other malformations are present versus complex Congenital diaphragmatic hernia in which other malformations are observed **(Robert et al., 1997).**

The true origin of congenital diaphragmatic hernia remains unknown, although exposure to teratogens, insecticides or certain pharmacological agents has been implicated. Specifically, phenmetrazine, thalidomide, quinine, nitrofen and vitamin A deficiency have been linked to congenital diaphragmatic hernia development **(Stolar & Dillon, 1998).**

It has generally been believed that congenital diaphragmatic hernia is the result of failure of the pleuroperitoneal canals to close at the end of the embryonic period (weeks 8 to 10), leading to a defect in the dorsolateral region of the diaphragm.

(Arensman & Bambini, 1999). During this early development of the diaphragm, the midgut is herniated into the yolk sac and returns to the abdomen during the 9th and 10th weeks of gestation. Failure of the pleuroperitoneal canals to close prior to this event allows the abdominal viscera to herniate through the hiatus into the ipsilateral thoracic cavity. According to this theory, the visceral herniation into the thorax creates a mass effect on the ipsilateral lung resulting in pulmonary hypoplasia **(Stolar & Dillon, 1998).**

Most cases of congenital diaphragmatic hernia are diagnosed prenatally. Other thoracic lesions that should also be considered when the diagnosis of Congenital diaphragmatic hernia is made prenatally by ultrasound include diaphragmatic eventration, congenital cystic adenomatous malformation, bronchopulmonary sequestration, bronchogenic cysts, bronchial atresia, enteric cysts and teratomas **(Cohen et al., 2002).**

The definitive sonographic diagnosis of fetal congenital diaphragmatic hernia relies on the visualization of abdominal organs in the fetal chest. A complete and accurate assessment of the fetal patient with congenital diaphragmatic hernia includes high resolution ultrasound, fetal MRI scan, echocardiography and amniocentesis for fetal karyotype assessment between 20 and 24 weeks of gestation. This allows for maximal information to be obtained from the imaging studies and allows

comprehensive non-directive counseling regarding congenital diaphragmatic hernia, including the option of elective termination. In order to provide optimal counseling, accurate prenatal prognostication is essential. Much effort has been directed toward identification of poor prognostic indicators in the fetus with congenital diaphragmatic hernia, often with conflicting results that are difficult to reconcile **(Graziano, 2005).**

Counseling is best performed by a multidisciplinary team that has extensive experience with the pre-, peri- and postnatal issues related to congenital diaphragmatic hernia, and includes obstetrics, pediatric surgery and neonatology. The family must understand the severity of this anomaly and the expected pre- and postnatal events that may transpire. They should be clearly informed of the potential for poor outcome for a severe congenital diaphragmatic hernia infant, including death, and severe neurologic, pulmonary and gastrointestinal morbidity and the potential impact on quality of life. Optimal prenatal counseling will result in anticipation and understanding of the events that follow and will allow the opportunity for informed decisionmaking with respect to options of termination or, as an experimental option prenatal therapy **(Hedrick et al., 2007)**.

Until recently, it was generally accepted that a fetus with liver-up Congenital diaphragmatic hernia and LHR <1.0 had a very little chance of survival, and prenatal interventions were aimed to improve survival in this subset of patients. **(Harrison et al., 1990).**

The initial prenatal intervention was in utero repair, first attempted in 1984. This was an open fetal operation requiring maternal laparotomy, hysterotomy, and fetal laparotomy/ thoracotomy. Successful repair was possible in fetuses with liver down congenital diaphragmatic hernia, but the mortality and morbidity with this procedure was not different from postnatal conventional management. **(Harrison et al., 1997)** In liver-up Congenital diaphragmatic hernia, the open procedure was not feasible because reduction of the liver obstructed the umbilical vein, the lifeline of the fetus) this procedure was therefore abandoned **(MacGillivray et al., 1994).**

Of all aspects of care of the congenital diaphragmatic hernia patient, postnatal management has undergone the most significant change in the last 10 years. Optimal postnatal management requires the efforts of a well-coordinated multidisciplinary team. Fetuses with known congenital diaphragmatic hernia should deliver at tertiary centers with extracorporeal membrane oxygenation capability preferably and immediate availability of neonatologists and pediatric surgeons.

Transport of Congenital diaphragmatic hernia infants is hazardous and can precipitate pulmonary vasospasm with resultant instability **(Okuyama et al., 2002)**

Extracorporeal membrane oxygenation is an invasive form of life support based on the principles of cardiopulmonary bypass which can be used to support patients with intractable cardio-respiratory failure. Its role in the setting of congenital diaphragmatic hernia is to treat potentially reversible pulmonary hypertension and to provide the 'ultimate' protective ventilation strategy. These potential benefits must be weighed against the inherent risks of extracorporeal membrane oxygenation, which include the need to instrument major neck vessels, exposure to blood products and the risk of bleeding from heparinization. It should be emphasized that extracorporeal membrane oxygenation is a form of life support and as such cannot cure fatal lung hypoplasia secondary to congenital diaphragmatic hernia **(Field et al., 1996).**

In recent years, survival to hospital discharge appears to have improved in newborns with severe congenital diaphragmatic hernia. There remains, however, significant late mortality and morbidity. There is a lack of criteria by which to definitively predict fatal lung hypoplasia in congenital diaphragmatic hernia and this makes the establishment of exclusion criteria for invasive therapies challenging. The precise

role of extracorporeal membrane oxygenation in these patients remains controversial, with practice varying widely between centers. The need remains for a multicenter randomized controlled trial **(Downard et al., 2003).**

The associated morbidity of congenital diaphragmatic hernia is now better appreciated. It is estimated that less than one-third of prenatally diagnosed foetuses will survive without significant morbidity. Some morbidity is anatomic and unavoidable. Other morbidity reflects potentially toxic effects of treatment and may be avoidable or eliminated in the future. Optimal care requires a multidisciplinary approach with co-ordinated input from a variety of specialties including surgery, neonatology, respiratory, dietetics, cardiology and audiology **(Metkus et al., 1996).**

Mortality from congenital diaphragmatic hernia continues to be high, ranging from 20% to 60%. Data from neonatal or referral centers operating on relatively selected cases, primarily those with isolated left-sided Bochdalek hernia, report 80%-90% survival. **(Downard et al., 2003)** However, population-based studies of outcome for all prenatally diagnosed congenital diaphragmatic hernia cases report mortality of at least 50%, if pregnancy terminations are included. In a meta-analysis, Stege et al 2003 observed that approximately one-quarter of all prenatally diagnosed cases were electively terminated, 3% spontaneously

miscarried, and 3% were stillborn; 31% of the live born died, the majority within the first 24 hours of life **(Colvin et al 2005).**

Minimal invasive surgery (MIS) has been first reported in infants with delayed hernias **(Van Der Zee & Bax, 1995).** However, this topic remains controversial as the benefits and risks have not been comparatively studied. Advances in minimally invasive surgery (MIS) have led to both thoracoscopic and laparoscopic repairs of congenital diaphragmatic hernia. Area and coworkers described the technical development of their minimally invasive approach to 15 children. **(Area et al., 2003)** They found laparoscopy to be a better approach to Morgagni defects and thoracoscopy a better approach to Bochdalek defects. They concluded that MIS was ideal for Morgagni defects, but that Bochdalek repair (via thoracoscopy) should be approached cautiously based on their high failure rate (14%), prohibitive increases in C02, and acidemia. Subsequently, formulated preoperative patient selection criteria to maximize successful thoracoscopic diaphragm repair. Preoperative requirements included an intraabdominal stomach, minimal ventilator support (PIP < 24), and no evidence of pulmonary hypertension. They found thoracoscopic primary repair to be safe, feasible, and comparable to open repair in their seven patients, although one patient developed a recurrence **(Yang et al., 2005).**

AIM OF THE WORK

The aim of this work is to highlight the incidence, clinical presentation, work up and prognosis of congenital diaphragmatic hernia and to evaluate the approved management as regard studies done and still going on.

EMBERYOLOGY OF THE DIAPHRAGM

The diaphragm (Greek: dia=in-between, phragma= fence) is a musculoaponeurotic structure that serves as the most important respiratory muscle and the separating structure between the abdominal and thoracic cavities **(Masaki Inraku, 2010).**

It has developed from the mesoderm in a complex process that had taken place between fourth and eighth weeks of fetal development through four embryonic components which are:

Septum transversum

This has formed from the inferior portion of the pericardial cavity and serves to separate the thoracic from the abdominal cavities as it forms the central tendinous area of the fully developed diaphragm. It defines the rudimentary pleuroperitoneal canals and allows for the establishment of mesenchymal tissue within these canals that ultimately results in pulmonary parenchymal development **(Stolar, 1998)**.

This part of the diaphragm grows dorsally from the ventral body wall and moves caudally with the other contributors of the diaphragm to reach the normal position of the diaphragm at about the eighth week of gestation **(Stolar, 1998)**.

Pleuroperitoneal membranes

They are two in number arising on the lateral body walls at the level where the cardinal veins swing around to enter the sinus venosus of the heart. These folds grow medially and ventrally to join with septum transversum and the dorsal mesentery during sixth week of gestation to complete the development of the diaphragm at about the eighth week of gestation. The right Pleuroperitoneal canal closes somewhat earlier than that on the left side **(Shields, 1996)**.

Short mesentery of the esophagus

It contributes to the development of the diaphragmatic Crura and the most dorsal portion of the diaphragm **(Masaki Inraku, 2010).**

Muscle fibres

They are a migrating myoblasts from the 3rd, 4th and 5th cervical myotomes carried along their innervations and grow between the two membranes to complete the muscular part of the diaphragm.

At the junction of the lumbar and costal muscle groups posterolaterally the fibrous lumbocostal trigon remains as a small remnant of the pleuroperitoneal membrane relaying for its

strength on the fusion of the two muscle groups in the final stage of development.

Delay or failure of muscular fusion leaves this area week perhaps predisposing to herniation **(Stolar, 1998)**.

The completed diaphragm therefore is the fusion of the following structures:

- The septum transversum forming the central tendon
- Bilateral pleuroperitoneal membranes
- Striated muscle components which reinforce the pleuroperitoneal membranes.
- The mesentery of the esophagus forming the crural and dorsal structures figure (1) **(Fauza, 2005)**.

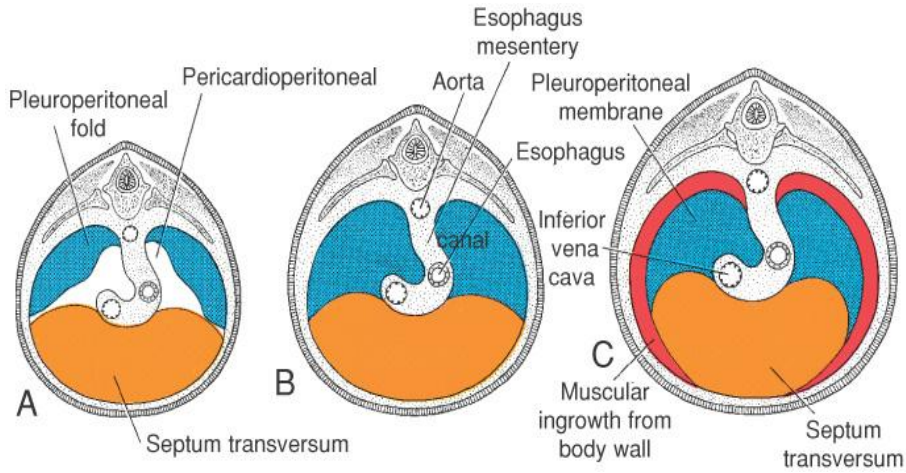

Fig. (1): Development of the Diaphragm **(Fauza, 2005)**.

Embryology of the lung

Lung development is a prenatal and postnatal process started from 3rd week of gestation up to age of eight years**.**

The prenatal process has four phases which are:

The embryonic phase:

This phase started from the 3rd week to the 6th week of gestation.

At the age of 9 days foregut started to develop from the embryonic endoderm and on the age of 3 weeks fetal lung started to develop as a ventral diverticulum 3mm length from the caudal end of the laryngeotracheal groove of the foregut which grows caudally to form the trachea.

This diverticulum is surrounded by mesenchyme which later on will form the visceral pleura.

On the 4th week

The end of the diverticulum divides to form the two primary lung buds which later on will form lobar buds.

On the 6th week

Lobar buds now are further subdivided to form the bronchopulmonary segments. By the end of this stage the

bronchial tree and the pulmonary arteries are fully developed and the common pulmonary vein drains into the sinoatrial region of the heart **(Reid, 1984)**.

Pseudoglandular phase:

This phase started from the seventh to 16th week of gestation. During this phase airways show repeated dichotomous branching to reach 16 to 25 generations of primitive airways and by the end of this phase all of the bronchial airways have been formed and the further growth occurs only by widening and elongation of the pre existing airways **(Richard et al., 2010).**

The canalicular phase:

This phase started from the 16th week to the 24th week of gestation. During this period the basic structure and gas exchanging portions of the lung are formed and vasscularized.

By the end of this phase the pulmonary venous drainage has completely developed. The lining epithelium is differentiated into type 1 pneumocyte with its cells are responsible for gas exchange and type 2 pneumocyte with its cells are responsible for surfactant production **(Snyder, 1981)**.

So by the end of this phase at the age of 24 weeks the lung is able to do gas exchange possibly.

Terminal saccular phase:

This phase started from the 24th week of gestation up to term. During this time there is continued remodeling of the air space dimensions and maturation of surfactant synthesis capabilities, so the air space walls are thin and capillaries are exposed to only one respiratory surface and the cells lining the saccules are recognizable type 1 and 2 pneumocytes concerned mainly with surfactant production.

Intrauterine surfactant is rich in phosphatidyl inositol while that of late gestation is rich in phosphatidyl glycerol **(Richard et al., 2010).**

Post natal phase (alveolar phase):

This phase started post natally and continues up to age of 8 years. At birth lung contains 20 millions of primitive terminal sacs instead of mature alveoli this number increases to reach 300 millions of alveoli at the age of 8 years with fastest rate of multiplications before 4 years. After 8 years increasing of lung volume is due to increase in size not in number of alveoli **figure (2) (Burri, 1984).**