# Introduction

Respiratory distress is a common reason for a neonate seeking medical attention. The clinical features are tachypnea, intercostals retractions, grunting or cyanosis; could be the manifestations of a variety of etiological causes. Both pulmonary and extra pulmonary causes could present as tachypnea and respiratory distress ***(Diwakar et al., 2003)***

The birth of a child is preceded by several changes to prepare for the transition from intrauterine to extra uterine life. The five major events that establish the lungs as the organ of gas exchange at birth include: clearance of fetal lung fluid, establishment of spontaneous breathing, decrease in pulmonary vascular resistance, release of surfactant, and cessation of the right-to-left shunting of venous blood returning to the heart. ***(Lokesh. et al., 2008).***

Several methods of evaluation have been used by anesthesiologists in an attempt to separate out the fetal/neonatal effects of their interventions from concomitant medical and nursing management, and from the influence of pre-existing maternal conditions. The Apgar score rates of five physical signs traditionally used by anesthesiologists to monitor a patient's condition: heart rate, respiratory effort, muscle tone, reflex irritability, and colour, at one, five minutes after birth. ***(Judith Littleford, 2004).***

All anesthetic interventions in the pregnant woman can profoundly affect the fetus and neonate. Three areas where anesthesiologists are involved in the care of the parturient include (1) providing analgesia for labor and vaginal delivery (2) providing anesthesia for cesarean delivery, and (3) participating in the critical care of the pregnant patient with concurrent medical or obstetrical problems ***(John and Jaya, 1998).***

Most anesthetic and analgesic agents in current use traverse the placental barrier in varying degrees, but are well tolerated by the fetus if judiciously administered. For labor analgesia, many options are available. Systemic administration of opioids and sedatives is one such option. Repeated maternal administration of opioids such as pethidine (meperidine) results in significant fetal exposure and neonatal respiratory depression. Patient-controlled analgesia with synthetic opioids such as fentanyl, alfentanil, and the new ultra-short-acting remifentanil may be used for labor analgesia in selected patients. Other options for labor analgesia include epidural and combined spinal-epidural techniques. With such techniques, neonatal exposure to opioids and sedatives can be minimized or totally avoided. While limiting the fetal exposure to the harmful effects of depressant drugs, epidural anesthesia and/or analgesia improves placental perfusion and oxygenation of the fetus,

which is beneficial, especially in conditions such as pregnancy-induced hypertension ***(Mattingly et al., 2003).***

Regional blocks are also administered for the majority of cesarean deliveries because of the overwhelming and unequivocal evidence of maternal and fetal safety compared with general anesthesia for this indication. However, in some instances, administration of general anesthesia is unavoidable. Neonatal respiratory depression with low Apgar scores, and umbilical arterial and venous pH associated with general anesthesia, is often transient (***Mattingly et al., 2003).***

When a neonatologist or pediatrician has been summoned to the operating room or labor suite just prior to, or immediately after the delivery of an infant, he or she is focused on the neonate's immediate status. The condition of the neonate at birth is affected by many factors, such as concurrent maternal obstetric and medical problems, therapeutic interventions, and maternal drug use. In terms of maternal analgesia and anesthesia, factors such as the effects of intravenous opioids and sedatives, adequacy of maternal oxygenation, hemodynamic stability, as well as the direct and indirect effects of regional and general anesthesia are significant. If systemic opioids have been used, it is important to know the type of drug, route of administration, dose, and timing in relation to the time of delivery ***(Mattingly et al., 2003).***

Following induction of general anesthesia and tracheal intubation, anesthesia is maintained by oxygen, low concentrations of one of the volatile anesthetic agents such as halothane, enflurane or isoflurane, and possibly nitrous oxide. General anesthesia is often administered for cesarean section when there is fetal distress ***(Mattingly et al., 2003).***

Spinal (intrathecal) anesthesia involves the injection of local anesthetic through a small gauge needle directly into the cerebrospinal fluid of the subarachnoid space, which lies just anterior to the epidural space. The procedure is typically performed by an anesthesiologist. Much smaller volumes of local anesthetic are required in comparison to epidural anesthesia, because the drug is deposited in close proximity to the spinal nerves ***(Riley and Ross, 2004).***

# Aim of the work

The aim is to find the relation between development of respiratory depression in neonates and general & spinal anesthesia during caesarean section.

# Fetal and postnatal anatomical development of the lung

## The Anatomy of the Lung

Each lung is divided into lobes. The right lung, which has three lobes, is slightly larger than the left, which has two. The lungs are housed in the chest cavity, or thoracic cavity, and covered by a protective membrane called the pleura. The diaphragm, the primary muscle involved in respiration, separates the lungs from the abdominal cavity. The pulmonary arteries carry de-oxygenated blood from the right ventricle of the heart to the lungs. The pulmonary veins, on the other hand, carry oxygenated blood from the lungs to the heart, so it can be pumped to the rest of the body ***(Pallav, 2008).***

## Anatomical development of the lung

The structural design of the lung and its developmental history are governed by task of gas exchange. The lung can be subdivided into 3 functional zones, a zone of conduction for the mass transport of air and blood, respiratory zone where gas exchange takes place between the 2 media and an intermediate zone where the airway structures still contain purely conductive sections, but also allows gas exchange ***(Burri, 1995)***.

The respiratory region contains the gas exchanging generations of alveolar ducts terminating in the blind ending alveolar sacs. The epithelial covering comprises 3 cells types; type 1 pneumocyte: squamous cells that cover about 93% of the alveolar surface, forming the air blood barrier, type 2 pneumocytes: cuboidal cells that are located within niches between two capillaries covering the remaining 7% of the alveolar surface and containing lamellar bodies which are the storage form of the surfactant material, and type 3 pneumocytes: they are rare cells and their function is not yet determined ***(Burri, 1995).***

## ❖ Stages of Lung Development

Growth and development of the lung starts soon after conception, and continues until somatic growth ceases. The division into pre- and postnatal phases is arbitrary but nevertheless does allow one to consider the important differences in extent of development and functional demands between intra-uterine and extra-uterine existence ***(Phelan, 1994)***.

They include four major stages. They are based on the microscopic appearance of the lung; pseudo glandular, canalicular and saccular. One stage gradually merges into the next with considerable individual variation ***(Hislop, 1999).***

Glucocorticoids have profound maturational effects on developing fetal lung. These effect enhanced alveolar differentiation, thinning of alveolar septae and capillary walls and upregulation of surfactant production ***(Vyas,1997)***.

## ❖ Stages of lung development:

### ☒ Prenatal phase:

Four stages of human fetal lung development are recognized:

1- Embryonic stage.

2- Pseudoglandular stage.

3- Canalicular stage.

4- Terminal sac stage.

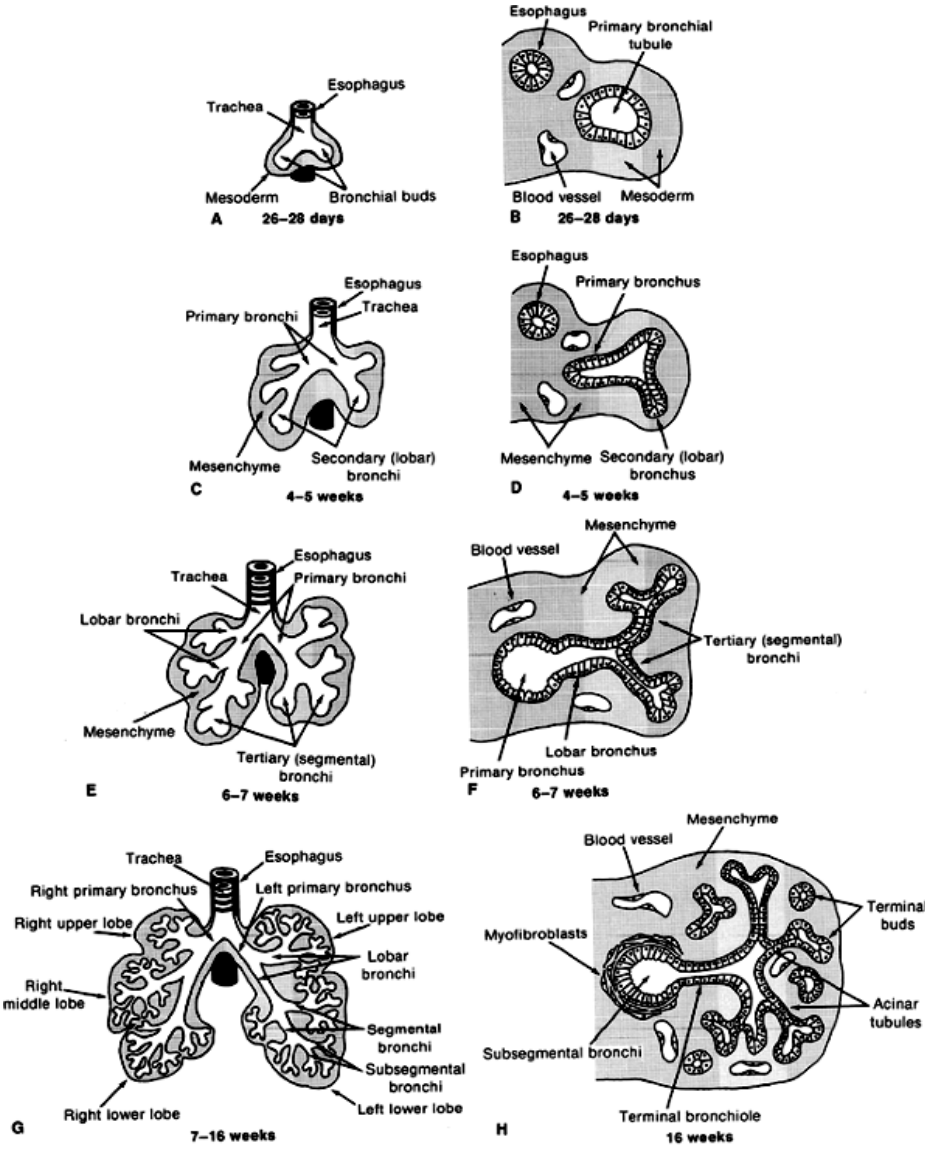


**Fig. (1):** Lung development during the embryonic (A-F) and pseudoglandular (G, H) stages of organogenesis. The overall branching pattern of the primitive lung (left panels) results in the development of the bronchial tree. The histological organization of the fetal lung becomes more complex as branching morphogenesis progresses through these stages (right panels).

During the embryonic period the lung primordium is formed, while the pattern of bronchial branching occurs in the pseudo glandular stage, in the canalicular stage the stage the branches elongate and the lining epithelium becomes flattened , while during the terminal sac stage thin-walled air passages are formed.

The peripheral structures, the alveoli do not develop to any extent until after birth. When considered remolding and growth of the acinus takes place ***(Phelan, 1994)***.

- **Embryonic stage (first 5 weeks after fertilization)**

Single ventral out pocketing quickly divides into two lung buds; mesenchyme surrounds endodermal lung buds, which continue to divide and extend into mesenchyme. Branching of the airways begins. Pulmonary arteries invade lung, following the airways, and divide as the airways divide. Pulmonary veins arise independently from the lung parenchyma and return to the left atrium, thus completing the pulmonary circuit ***(Merenstein, 2000).***

- **Pseudoglandular stage (5-16 weeks of gestation)**

The major airways develop during this period, bronchi and terminal bronchioles form. Muscle fibers, elastic tissue, and early cartilage formation can be seen along the tracheobronchial tree. Mucous glands are found at 12 weeks and increase in

number until 25-26 weeks, when cilia begin to develop. Diaphragm develops ***(Mernstein, 2000)***.

- **Canalicular stage (16-24 weeks of gestation)**

This stage is characterized by proliferation of mesenchyme and the development of a rich blood supply within it. The laminas of the epithelial tubes widen and flatting of the lining epithelium occurs, giving the lung the appearance of a group of canals ***(Phelan, 1994)***.

The proliferation of the vascular supply together with the relative decrease in the mesenchyme brings the capillaries closer to the airway epithelium. Capillaries protrude into the epithelium and at this stage occasional areas of blood airway interaction may be seen. Progressive thinning of the epithelium and protrusion of the capillaries give rise to more areas of close approximation of the capillary lumen to the airway surface. At the end of the canalicular period respiration is possible ***(Kitaokal, et al, 1996).***

- **Terminal sac stage (6-9 months gestation)**

During this stage further differentiation of the respiratory portion of the lung occurs, with transformation of some terminal bronchioles into respiratory bronchioles and the appearance distally of terminal clusters of airways called

saccules. They are not true alveoli because they are longer and lack the smooth outline, but can function for gas exchange since the thickness of the blood-gas is similar to that of adult alveoli ***(Phelan, 1994).***

There are some data to suggest that a placental derived factor inhibits fetal breathing and removal of this factor at birth then permits initiation of a regular respiratory pattern. This placental inhibitor theory intriguing, but it does not explain the totality of response needed to initiate and maintain a normal respiratory pattern at birth; also, no candidate inhibitor has been suggested. Development and maintenance of respiration in the newborn is more likely due to a complex interaction of sensory stimuli and both central and peripheral chemoreceptor inputs. The degree of maturation in the central respiratory centers also appears to be important since the responses to these stimuli in the term infant are more developed than in the preterm infant ***(Kitaoka, et al, 1996).***

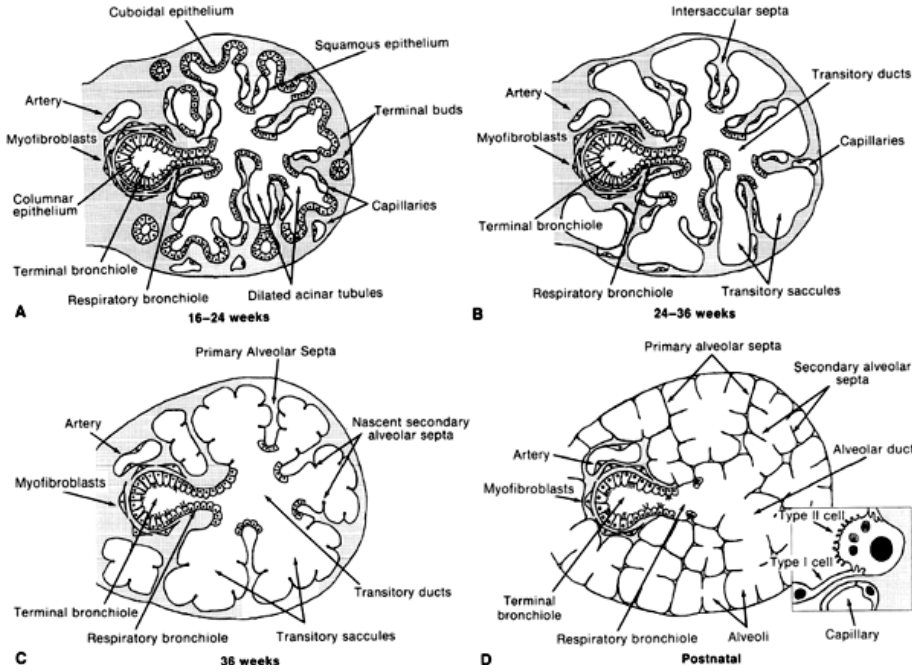


**Fig. (2):** Lung development during the canalicular (A), saccular (B), and alveolar stages of organogenesis (C, D). Dramatic histological changes in tissue organization occur during these periods. The adult alveolar epithelium is composed of squamous type I cells and cuboidal type II cells (inset).

- **Prenatal lung function:**

Three items are to be considered:

1- Fetal lung liquid.

2- Surfactant.

3- Intra uterine breathing movements.

- **Fetal lung liquid (FLL):**

The lungs of the fetus are filled with fluid. The volume is similar to that of the functional residual capacity of a newborn

infant. About 20 - 30 ml / kg body weight. The fluid is formed by the transfer of solutes and water across the capillary endothelium and epithelium of the developing lung and is not as earlier thought, aspirated amniotic fluid. The fluid moves up the tracheobronchial tree to the mouth where it is swallowed or added to the amniotic fluid. FLL is important in the development of the lung and it appears to play a major role in determine the shape and volume of the peripheral lung units ***(Phelan, 1994).***

The rate of liquid formation and the volume of the fluid in the lung decreases just before birth. The cause of this reduction is not known but it is thought that hormones such as catecholamine, arginine, vasopressin and prostaglandin E2 probably play a role ***(Sadler et al., 2003).***

The rapid removal of liquid from the potential air spaces during and after birth is a critical event in the switch from placental to pulmonary gas exchange ***(Phelan, 1994)***.

It is removed via the pulmonary lymphatics, the circulation, the pleural spaces, the mediastinium and the upper airway. Air inflation shifts residual fluid from the lumen into the perivascular spaces around the blood vessels and airways ***(Phelan, 1994)***.

- **Surfactant:**

The unique physical-chemical boundary between the alveolar gases and the highly solvated molecules at the apical surface of the respiratory epithelium generates a region of high surface tension produced by the unequal distribution of molecular forces among water molecules at an air-liquid interface. Surface-active material at this interface in the alveoli provides surface-tension-lowering activity that contributes to the remarkable pressure-volume association's characteristic of the lung. This surface-active material, called surfactant (***Nogee, et al., 2001).***

Deficiency or dysfunction of pulmonary surfactant plays a critical role in the pathogenesis of respiratory diseases in the newborn period. Pulmonary surfactant exists in a variety of physical forms when isolated from the alveolar wash of the lung ***(Shulenin, 2004).***

o **Composition of Surfactant:**

Pulmonary surfactant is composed primarily of the phospholipids phosphatidylcholine and phosphatidylglycerol. These lipid molecules are enriched in dipalmitoyl acyl groups attached to a glycerol backbone that pack tightly and generate low surface pressures. Rapid spreading and stability of pulmonary surfactant are achieved by the interactions of