PROLACTIN IN NEONATAL CORD BLOOD OF DIABETIC MOTHERS

Thesis

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OF THE MASTER DEGREE OF
(OBSTETRICS & GYNAECOLOGY)

رسالة

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سَنُرِيهِمْ آيَاتِنَا فِي الْآفَاقِ وَفِي أَنْفُسِهِمْ حَتَّىٰ يَتَبَيَّنَ لَهُمْ أَنَّهُ الْحَقُّ ۗ

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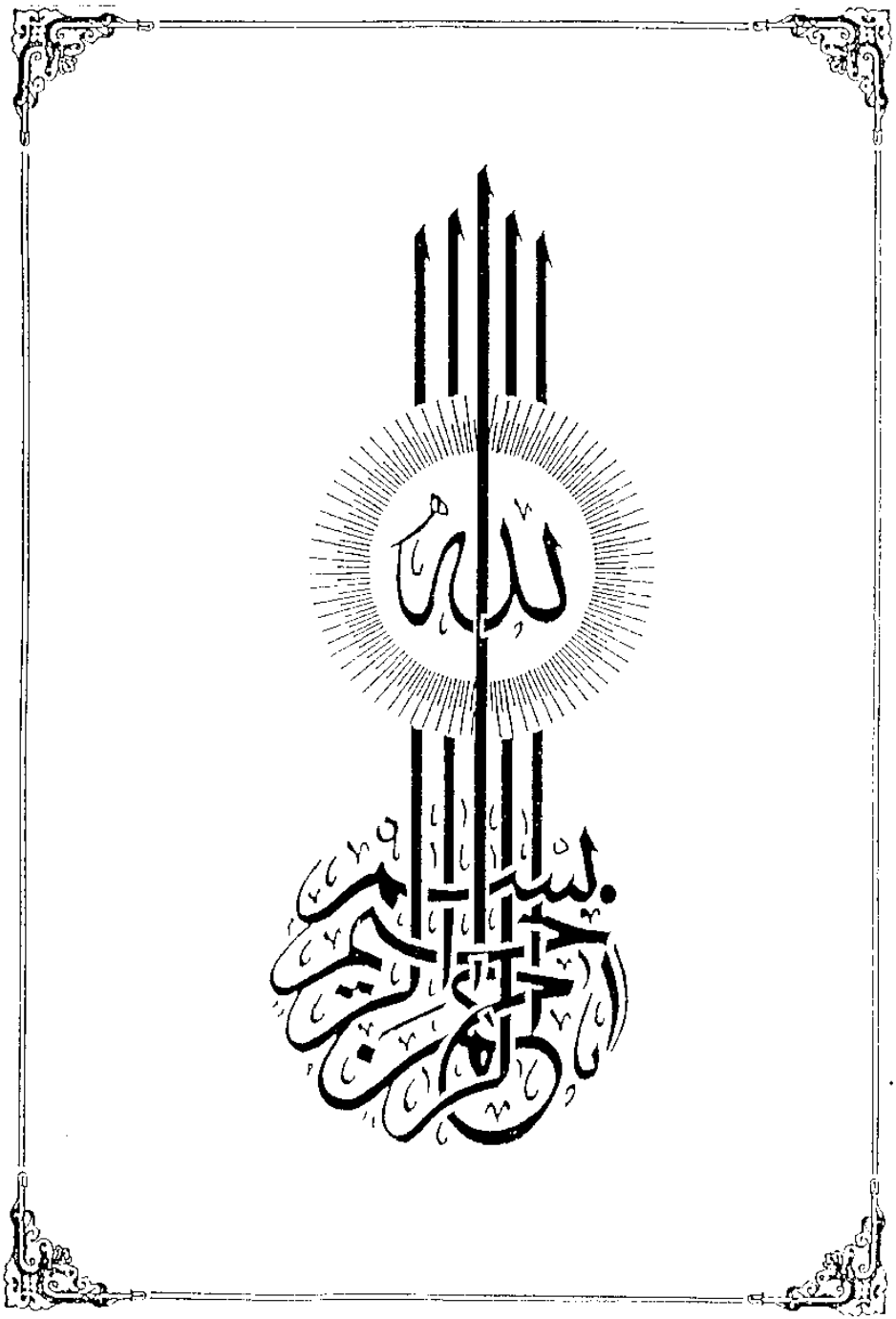

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INTRODUCTION

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AIM OF WORK

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INTRODUCTION

Respiratory distress syndrome is widely accepted as the major cause of morbidity and mortality in the newborn infants born to diabetic mothers **(Tsang et al, 1981)**.

Respiratory distress syndrome is believed to be the result of a deficiency of pulmonary surfactant **(Avery and Mead, 1959)**.

Surfactant is phospholipid rich material that lines the alveoli of the lungs and lowers surface tension at the air-alveolar interphase, thereby preventing alveolar collopse **(Clements et al, 1961)**.

Pregnancy in diabetic mothers is known to be associated with an increased incidence of respiratory distress syndrome of the newborn **(Usher et al, 1971)**.

The work of Ligginis in 1969 which first demonstrated that fetal lung maturation could be accelerated by corticosteroids focused an attention on the role of hormones in fetal lung development and the final rate of lung maturation depends on a balance between number of hormones.

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Of these hormones, prolactin was injected by Hamosh and Hamosh 1977 into fetal rabbits and resulted in increase of pulmonary lecithin, which is major surfactant.

In this thesis we try to spot light on the role of prolactin in fetal lung maturation and its relation to the incidence of respiratory distress syndrome in infants of diabetic mothers and normal infants.

AIM OF WORK

We try to explore the role of fetal prolactin in human lung maturation and if its level is affected in infants of diabetic mothers.

Another objective of this thesis is to determine that the incidence of neonatal respiratory distress syndrome is affected by diabetic pregnancy.

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REVIEW OF LITERATURE

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ASPECTS OF LUNG DEVELOPMENT

An out pouching of the foregut in the 26 day-old human embryo is the precursor of the future lung (Hallman and Gluck, 1977).

The morphologic development of the human fetal lung had been studied with the use of electron microscope by Campiche et al 1963 and reviewed by Alcorn et al, 1974 and Boyden 1977.

Three stages of development occur during fetal life:-

1. Glandular stage from conception to 16 weeks.
2. Canalicular stage from 16 weeks to 24 weeks.
3. Terminal sac stage from 24 weeks to term.

During the glandular stage, the lung is viewed as a loose mass of mesenchymal tissue surrounding the proliferating buds of endodermal cells which have the appearance of glandular structure. The mesenchymal tissue will give rise to cartilage, muscle, elastic and lymphatic tissues whereas the trachea and the entire epithelial lining of the respiratory system is derived from the endoderm.

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There is little vascularization of the mesenchymal tissue.

By the end of the glandular stage, the proliferating endodermal tissue has given rise to the bronchial airways. The respiratory portion of the lung becomes delinated and vascularized.

During the canalicular stage the terminal buds of the endodermal tissue branch and grow to form the respiratory bronchioles. Increasing vascularization of the mesenchyme occurs as capillaries push their way onto the epithelium of the primitive air ways.

During the terminal sac stage differentiation of the respiratory regions continues with further division of the respiratory bronchioles, from which clusters of thin walled terminal saccules arise. The epithelial lining of the airways continues to thin down as it is invaded by capillaries.

The terminal saccules are nearly tubular structures that often have irregular outlines in section but no actual alveoli. True alveoli usually begin to appear weeks prior to term.

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They develop into alveolar and terminal saccules through formation of secondary crests and subsequent growth and division.

An estimated 17 to 70million alveoli are present at birth, their number increases rapidly during the first neonatal months followed by gradual increase untill the age of 5 to 15 years.

The number of alveoli in the adult is 375 to 600 millions.

At term the capillary bed surrounding the terminal airways is well developed, however owing to the thick walled muscles of the pulmonary arteries only about 10% of fetal cardiac output courses through the lung.

At birth the rise in oxygenation in alveoli releases bradykinin and as a result pulmonary vessels dilate, vascular resistance falls and blood flow increases at least 5 folds.

After birth the thick walled muscular wall of the arterioles involutes gradually and reaches adult structure by about six months.

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The alveolar epithelium in the gas exchange areas of the fetal lung is formed by epithelial growth of the airways and the endothelial growth of the capillaries. In the first two months of development, the rapidly growing primitive airways are lined with a single layer of tall poorly differentiated columnar cells that contain large masses of glycogen deposits and few cytoplasmic organelles. Capillaries are very few in number and appear as round or ovoid group of overlapping endothelial cells with very small lumens. They are separated from the primitive airways by the loose network of intervening mesenchymal tissue.

By the third and fourth month, the epithelial lining of the distal airways becomes cuboidal, further differentiation of the epithelial cells is reflected by a decreasing nuclear/cytoplasmic ratio and increasing numbers of cytoplasmic organelles, well developed Golgi zones are present but the cytoplasm still contains abundant glycogen. Capillaries continue to invade the mesenchymal tissue as they approach the lumens of the primitive airways. The endothelial wall of the capillaries becomes thinner resulting in wider lumens.

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During the fifth month of development, the epithelial cells become pseudocolumnar and the amount of cytoplasmic glycogen begins to decrease. Concurrently, the capillaries progressively penetrate into the epithelium in a wedge like manner and begin to establish contact with the epithelial cells resulting in the thinning of the epithelium.

The potential blood-air barriers formed by this process are thicker but otherwise resemble those of the mature adult lung. The sixth month of gestation is characterized by the onset of epithelial differentiation into type I and type II cells.

Further proliferation of capillaries results in numerous potential blood-air barriers. Capillary lumen becomes wider and the basement membranes of the capillary endothelium and respiratory epithelium begin to fuse.

By the seventh month of gestation, differentiation into type I and type II cells has occured. Type I cells appear flat with long attenuated cytoplasmic extensions that form the major portion of the alveolar surface. Type I cells appear to have no secretory function and are regarded as

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structural cells of alveolar epithelium with significance in effective gas exchange.

Type II alveolar cells are relatively large and possess microvilli. Their cytoplasm reveals prominent endoplasmic reticulum membranes, Golgi apparatus and multivesicular bodies.

The most distinguishing intracellular structures are the characteristic rounded, osmiophilic structures called lamillar inculsion bodies or OIIBs within their limiting membranes. These contain osmiophilic material in concentric array.

OLIBs is the abbreviation of osmiophilic lamellar inculsion bodies.

At first, type II cells are few in number and occupy the junctional areas between adjacent alveoli.

As gestation progresses, the glycogen content of epithelial cells continue to decrease and the number of lamellar inculsion bodies in type II cells rapidly increase. Widespread vascularization of the epithelium has occured and by eight and half month of gestation the lung development is virtually complete.

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