AMNIOTIC FLUID ACID PROTEASE ACTIVITY AS AN INDICATOR FOR HYALINE MEMBRANE DISEASE

THESIS
Submitted for partial fulfilment

of

Master Degree in Pediatrics

By

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M.B.,B.Ch

Under Supervision Of

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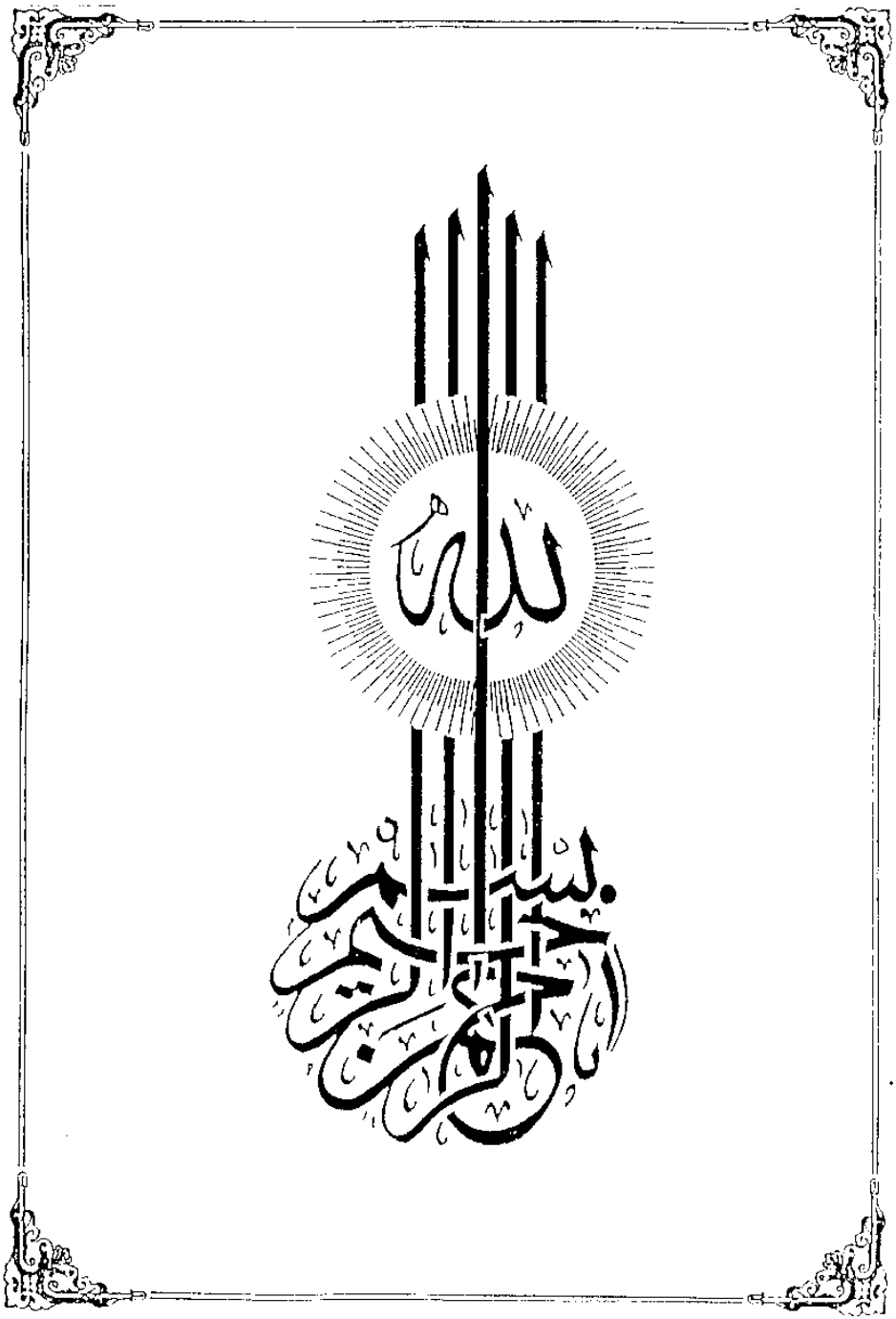

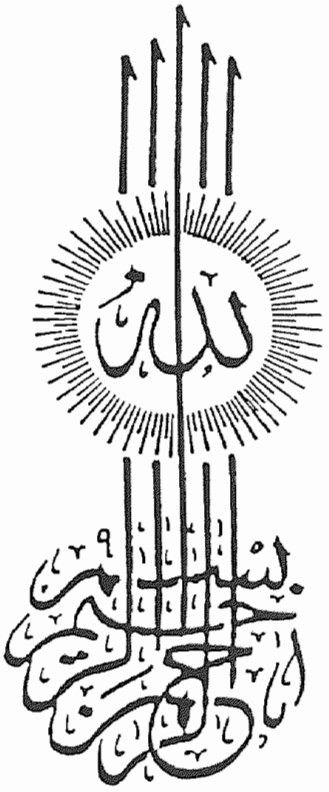

قالوا سبحانك لا علم لنا إلا ما
علمتنا إنك أنت العليم الحكيم.

صدق الله العظيم
البقرة - ٣٢ -

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LIST OF ABBREVIATION

AF : Artificial rupture of membrane.

CDP :Citidine diphosphate choline.

CS : Caesarean section .

CTP : Citidine triphosphate.

HMD : Hyaline membrane disease.

PAPase : Phosphatidic acid phosphohydrolase.

PC : Phosphatidylcholine.

PG : Phosphatidylglycerol.

RDS : Respiratory distress syndrome.

SP- A : Surfactant protein - A.

SP- B :Surfactant protein - B.

SP- C :Surfactant protein - C.

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Introduction

INTRODUCTION

Hyaline membrane disease is a major cause of death in the new born period. An estimated 50% of all neonatal deaths result from hyaline membrane disease or its complications.

It occurs primarily in premature infants and its incidence is inversly proportional to gestational age and birth weight (Green et al., 1983).

The search for new tests for predicting risk of hyaline membrane disease continues to be a main issue.

The determination of the amniotic fluid lecithin / sphingo myeline (L / S) ratio is a well established test but it is often unavailable and has the disadvantages of being time consuming and expensive . This has led to numerous efforts to find a reliable alternative test that is shorter and less cumbersome. (Milwidsky et al ., 1987) . However , most of the suggested alternatives proved to be either insensitive, non specific , or to give inconsistent results . (Golde et al., (1979)

Amniotic fluid contains several protease activities . Reybak et al., (1971) noted that acid protease activity in amniotic fluid increases with gestational age after 28 weeks of gestation .

Aim of the work

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The aim of this work is to assess acid protease activity in amniotic fluid in an attempt to test its predictive value for assessement of fetal maturation . Also a comparison between it and one of the other tests used for assessement of fetal lung maturity namely foam stability test for the prediction of the occurence of respiratory distress syndrome will be carried out .

Review of literature

Development And Maturation Of Fetal Lung

Lung development in the fetus passes through 4 stages (Hislop & Reed et al ., 1974) :

1- Embryonic period .

2- Pseudoglandular period .

3-Canalicular period .

4- Terminal sac period.

1- Embryonic period :

Starts from conception to the 5th week of gestation . During the fourth week of gestation the lung arises as a ventral diverticulum from the foregut and is lined by endodermally derived epithelium. (Inselman & Mellins et al ,. 1981)

2- Pseudoglandular period :

It starts from the 5th week to the 16 th week of gestation. During this period the lung starts to ramify from a gland - like structure into the primitive tracheobronchial tree in a centripedal way. The epithelium of the distal part of the tracheobronchial tree is tall columnar at first then low columnar later on with abundant cytoplasmic glycogen indicating their immaturity (Scarpelli ,1975). This glycogen may be used as an energy supply and as a substrate with other substances for phospholipid synthesis (Bleasdale et al ., 1979) .

3- Canalicular period :

It includes the appearance of respiratory bronchioles . Undifferetiated cells will proceed to be well differentiated into type I and II epithelial cells , the number of each type will increase with progression of gestation (Inselman et al., 1981)

4- Treminal sac period :

In 1974 , Hislop et al ., stated that, lung development stops at the terminal saccule stage at birth with alveoli starting to be formed from the saccules ofter birth. Yet in 1984 , Langston et al., had proved that alveoli do exist in the intrauterine life as early as 30 weeks gestation .They also estimated alveolar count at term to be about 50 million compared to the 300 million alveoli reported in the adult by Weibel in 1962 . There is a rapid alveolar multiplication during the first two years of life with little growth after that (Thurlbeck, 1982).

However, there is a wide variation in estimating alveolar count and the time at which alveolar multiplication ceases (Cooney et al., 1982). The size of the acinus increases from one millimeter at birth to one centimeter in the adult (Hislop et al., 1974). At the time of birth, the pattern of respiratory airway branching is complete, just as the pattern of conducting airway branching is complete at the 16 $\frac{th}{}$ week of gestation (Inselman etal., 1981) .

Maturation of type ll Epithelial cells :

These cells accounts for 16% of the total lung parenchymal cell count in human (Crapo et at .,1982) .

They are recognized as the stem cell of alveolar epithelium (Gail et al ., 1983) . These cells contain inclusion bodies which appear at the canaliculer stage (16 th week) and increase in number slowly till the 29 th week of gestation (Reynolds et al.,1965).

These inclusion bodies contain a lipid substance that was proved to be phospholipid in nature , most probably the lung surfactant (Chevalier , 1973) .

The air blood barrier consists of :

1- Alveoler lining layer which is an acellular lining layer formed over the alveolar epithelium and consists of non reabsorbed pulmonary fluid plus surfactant secreted by type II epithelial cells (Kaibara et al.,1971).

2- Type I epithelial cells , which cover 93% of the alveolar surface in human lung (Crapo et al. , 1982) .

These cells act as the drainage route of alveolar lipids , including surfactant (Kikkawa et al. , 1972) .

3- Interstitial layer .