# COMPARATIVE STUDY OF THE VALUE OF LECITHIN TO SPHINGOMYELIN RATIO, PHOSPHATIDYLGLYCEROL, FOAM STABILITY TEST, CREATININE, AND OPTICAL DENSITY OF AMNIOTIC FLUID IN THE PREDICTION OF RESPIRATORY DISTRESS SYNDROME

*THESIS*

Submitted in Partial Fulfillment of the Requirements
of the M.D. Degree
In Clinical and Chemical Pathology

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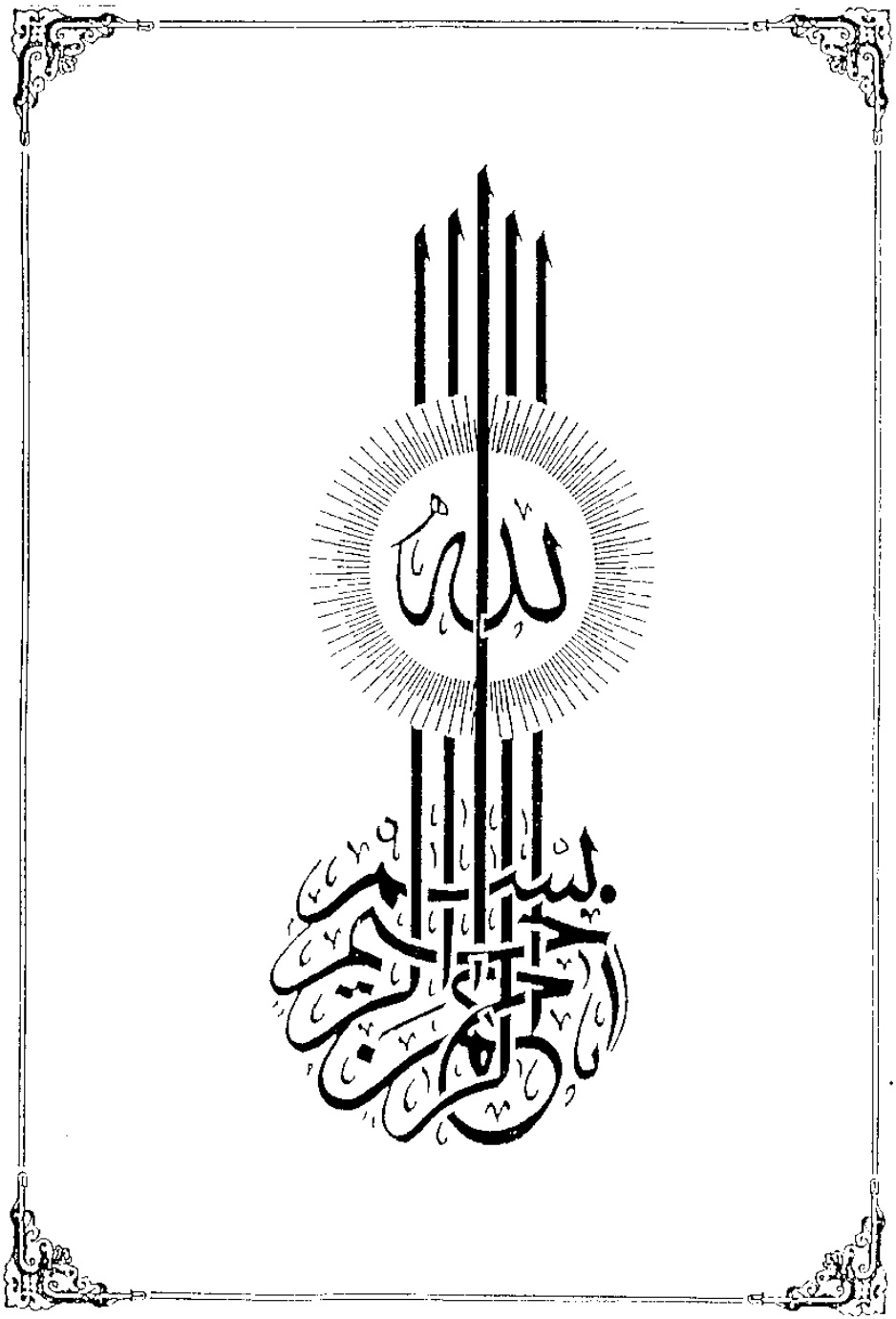
1989

*To my Parents, Husband and Children,*
*for their everlasting patience, understanding and support*
*throughout this work*



# ACKNOWLEDGEMENT

*I would like to acknowledge with my sincere thanks and gratefulness Prof. Sawsan Hosny Hamza,Professor of Clinical Pathology, Ain Shams University, for her helpful guidance, constant encouragement and supervision.*

*I wish to express my deepest appreciation and gratitude to Prof. Mahmoud Sabry Sallam, Professor of Clinical pathology, Ain Shams University, for suggesting this research problem, for his valuable instructions and endless support, both in his personal and official capacities throughout the course of this study. It is really wonderful to work under his supervision.*

*I am particularly indebted to Professor Mohamed Abdallah El-Maraghy, Professor of Obstetrics and Gynaecology, Ain Shams University for his valuable supervision and fruitful suggestions in initiating and completing this work.*

*I wish to express my thanks and appreciation to Dr. Hanzada Ibrahim, Lecturer of Clinical Pathology, for her valuable time and interest during preparation of this manuscript.*

*The words fail to express my gratefulness to Dr. Nadia Mohamed Abd El-Monem Nagui, Lecturer of Clinical Pathology, Ain Shams University, for her friendly assistance, honest advice and faithful enthusiastic encouragement during the course of this study.*

*I wish to express my grateful acknowledgement which is due to my husband Dr. Sherif El-Ghetany, Lecturer of Obstetrics and Gynaecology, Ain Shams University for his continuous support and encouragement.*

*I am greatly indebted to all workers in the Clinical Pathology Department, Ain Shams University Hospitals for their continuous support and help throughout this work which markedly contributed to its final accomplishment.*

*Nashwa El-Badawi*
*1989*

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## INTRODUCTION

It is often desirable in obstetric practice to assess the risk of respiratory distress syndrome (RDS) of the newborn in high risk pregnancies. In these situations, the infant may be delivered before his lungs are sufficiently well developed to support respiration. Since 1959, Avery and Mead stated that the pulmonary function, that apparently supports survival, is the formation and maintenance of a phospholipid rich surface active alveolar lining, without which atelectasis occurs and respiratory distress develops. Because fluid drifts from the fetal lung to the amniotic cavity carrying with it suspended surface active material (surfactant) from the alveoli, the concentration of this material in amniotic fluid would reflect its availability at the alveolar surface and thus the potential stability of the alveolar structure *(Clements et al., 1972).* Fetal tissue maturation in utero is a preparatory stage for the postnatal period, and is reflected in various constituents of the amniotic fluid. Amniotic fluid (AF) analysis may therefore offer appropriate means by which functional maturity can be assessed *(Tyden et al., 1981).*

Phospholipid analysis of amniotic fluid for estimation of fetal lung maturity and prediction of (RDS) in the newborn had been performed with increasing frequency, since the introduction of the lecithin/sphingomyelin (L/S) ratio by *Gluck et al.* in *1971.* Phosphatidylglycerol (PG) is the second most abundant phospholipid in mature surfactant, and most investigators agree that its presence in amniotic fluid is indicative of lung maturity *(Kulovich and Gluck, 1979; Tsai and Marshall, 1979 and Moodly et al., 1983).* Many authors advocate the use of PG measurement in combination with L/S ratio to enhance the reliability of L/S ratio

*(Kulovich et al., 1979, Skjaeraasen and Stray-Pedersen, 1979, and Hallman and Teramo, 1981).*

As the ideal prenatal test for fetal maturity should be simple, sensitive, accurate and inexpensive, *Clements et al. in 1972* tried to develop a method for the estimation of pulmonary surfactant, which might be applicable at the bed side. The semiquantitative and qualitative foam stability test is a practicable test that seems sufficiently sensitive and reliable for clinical use.

The absorbance of light at a wavelength of 650 nm ($A_{650}$) by amniotic fluid had also been advocated as a means of assessing fetal maturity. An absorbance greater than 0.15 is associated with a low probability of respiratory distress *(Sbarra et al., 1976).*

Amniotic fluid creatinine levels of 2 mg% or more appear to be a reliable index of fetal maturity. Its value may be further enhanced by the fact that medical complications of pregnancy do not seem to affect the creatinine level *(Pitkin and Zwirck, 1967).*

## AIM OF WORK

The aim of this study is to compare the diagnostic reliability of the amniotic fluid L/S ratio, PG measurement, foam stability test or shake test, absorbance at 650 nm and creatinine concentration. The sensitivity, specificity, predictive value both positive and negative and efficiency of each test will be evaluated together with the effect of combination testing on such parameters. The key to this study is the assessment of fetal lung status, which has become a highly dependable monitor in the management of pregnancies, in which preterm delivery is indicated. This occurs in cases of diabetes, Rh sensitization, hypertensive disorders and poor obstetrical history.

# REVIEW OF LITERATURE

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## AMNIOTIC FLUID

The amniotic sac arises during the first week of gestation. It consists of an inner layer of mesoderm and an outer layer of ectoderm. It starts as a minute vesicle then develops into a small sac that covers the dorsal surface of the embryo. As the amnion enlarges, it gradually engulfs the growing embryo. The amniotic cavity thus forms a definite fluid filled compartment which is well developed by the 9$^{th}$ week of gestation *(Seeds, 1965).*

The amniotic fluid functions to equalize the pressure and thus protects the fetus from external trauma, and assures fetal mobility. It helps in maintaining a constant temperature. It is active in the disposal of fetal secretions and excretions, may provide nutrients by fetal swallowing and, in addition, it probably has innumerable immunological and biochemical functions. Even during labor, the hydrostatic action of amniotic fluid may be of importance in dilating the cervical canal *(Pritchard and MacDonald, 1976).*

The origin of the amniotic fluid is a matter of speculations. *Ostergard (1970)* reported that it may arise as a transudate of maternal serum across the placental and fetal membranes, or as a transudate across the umbilical cord. A portion of the amniotic fluid also arises from fetal skin. Active secretion by amniotic epithelium is a third potential source. Each of these sources may contribute to the formation of amniotic fluid to varying degrees at specific times during gestation.

According to *Lind et al. (1971),* the composition of amniotic fluid early in pregnancy resembles more closely fetal plasma than maternal plasma. This suggests that the amniotic fluid found early in gestation is probably an extension of fetal

extracellular fluid. At the early stage of gestation, the outer limit of the extracellular fluid is probably the amnion rather than the fetal skin. Later in gestation, as the skin becomes more stratified, the movement of fluid by this route is restricted.

As gestation proceeds, there is an increased participation by the fetal renal and respiratory systems in amniotic fluid formation. Fetal urine is formed as early as 14 weeks, however, its contribution to amniotic fluid is probably not significant until approximately the 20th week of gestation. The contributions of the secretions from the tracheobronchial tract, salivary glands, and buccal mucosa to the content of amniotic fluid have not been fully clarified. The increase in concentration of certain amniotic fluid lipids late in pregnancy, when at the same time the developing lung tissue shows a similar lipid change, suggests that respiratory tissue secretions also contribute to the amniotic fluid composition *(Biezenski et al., 1968).* Whatever the source of amniotic fluid, it is not a static pool as its water is turned over once every 2.9 hours and its sodium once every 20.5 hours *(Vosburgh et al., 1948).*

The volume of amniotic fluid increases rapidly as pregnancy progresses from an average of 50 ml at 12 weeks to about 400 ml at midpregnancy to reach a maximum of about one liter at 36-38 weeks. However, there is a marked individual variation in amniotic fluid volume *(Gillibrand, 1969).*

The fate of amniotic fluid, like its formation is not clearly understood. Amniotic fluid is most likely exchanged across the placental and umbilical membranes. Fetal swallowing is thought to play a major role in removal of the fluid. This is substantiated by the excessive accumulation of amniotic fluid when there is a mechanical or neurological disturbance of swallowing. It has been estimated that near term, approximately 500-1500 ml of fluid per hour are

swallowed. The total water exchange between the fetus and the mother at term is approximately 3500 ml per hour *(Fiereck, 1982).*

The composition of the amniotic fluid varies considerably with the duration of gestation. In the early stages of pregnancy the composition of electrolytes is similar to that of plasma. The amniotic fluid becomes progressively hypotonic with drop of osmolality owing mainly to a decrease in sodium and chloride. This is accompanied by a marked increase in urea, creatinine, and uric acid levels approximately 2 to 3 times those found in maternal serum. These changes result from admixture of fetal urine, which dilutes amniotic fluid and adds nonprotein nitrogenous constituents *(Abdul-Karim and Beydoun, 1972).* Potassium levels remain relatively stable throughout gestation (approximately 4.4 mmol/L).

No significant changes in the values for calcium, phosphorus, or glucose occur between the second and third trimesters. Amniotic fluid glucose values near term have been reported as 10 to 61 mg% for normal nondiabetic mothers and from 23 to 139 mg% for diabetic mothers *(Brosnes, 1966).* Total protein and albumin decrease with gestational age (1/10 of normal serum level during second trimester and 1/20 near term). Globulins may increase slightly throughout gestation, and fibrinogen is absent *(Ostergard, 1970).*

Some changes in enzyme activities have been reported during gestation. Aspartate amino transferase activity increases approximately two folds from the second to the third trimester. Lactate dehydrogenase activity is normally lower in amniotic fluid than in maternal serum. Alkaline phosphatase activity increases with the length of gestation *(Fiereck, 1982).*

A number of hormones have been detected in the amniotic fluid e.g. the serotonin metabolite 5 hydroxy-indole acetic acid and estriol. Prostaglandins, both

of the E and F series, have been detected in amniotic fluid and they may be related to initiation of labor *(Abdul-Karim and Beydoun, 1972)*.

As gestation advances, phospholipids, primarily from the lungs, accumulate in the fluid together with variable amounts of particulate matter in the form of desquamated fetal cells, lanugo, scalp hair and vernix caseosa. These contribute to the turbidity of the amniotic fluid *(Biezenski, 1970)*.

## LUNG SURFACTANT

The ability of the fetus to survive extrauterine adaptation is greatly dependent on the proper functioning of the pulmonary system. This vital function depends on both adequate anatomical and physiological maturation. The lungs should have developed alveoli with adequate surface area to sustain ventilatory movements for gas exchange. Also a surfactant system must be in place for the physicochemical requirements of pulmonary function.

Surfactant facilitates pulmonary function. It has three main actions. The first one is to reduce surface tension, so less pressure is required to hold the alveoli open. The second is to maintain alveolar stability by varying surface tension with the alveolar size. The third function is to inhibit the exudation of liquid from the pulmonary circulation into the airways *(Russell, 1987)*.

In the fetus, surfactant is thought not to be produced before the 24th week of gestation. At this time, the alveolar epithelial cells differentiate into two types of cells (Fig. 1). Type I cells become specialized for gaseous exchange. The large alveolar epithelial cells known as Type II pneumonocytes are concerned with surfactant production and storage. These cells contain lamellar bodies, which are the storage granules for surfactant phospholipids. Their amount increases directly

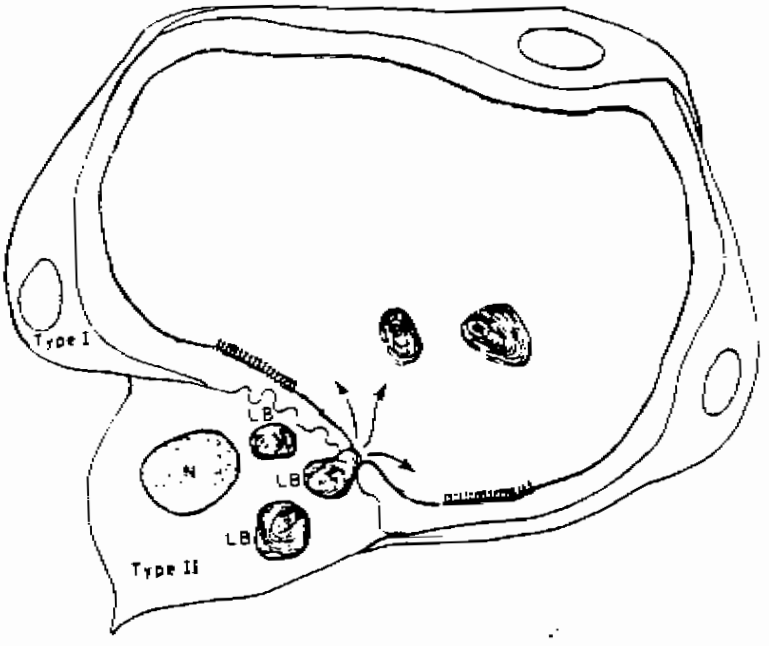


Figure 1 : A diagram of an alveolus with a type II cell, the site of formation of lamellar bodies (LB) that are excreted into the lumen of the alveolus *(Pritchard and MacDonald, 1976).*