#### CORRELATION BETWEEN MATERNAL AND CORD SERUM LIPID PROFILES OF PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME

#### **Thesis**

Submitted for partial fulfillment of Master Degree in **Pediatrics** 

#### By

Nesrine Mohsen Kamel M.B.B.CH (2005)

#### **Under Supervision of**

#### Prof. Mohamed Ashraf Abd El-Wahed

Professor of Pediatrics Faculty of Medicine Ain Shams University

#### **Dr. Tarek Mohey Abdel Meged El-Gammasy**

Assistant Professor of Pediatrics
Faculty of Medicine
Ain Shams University

#### **Dr. Hala Abdel Al Ahmed**

Lecturer of Clinical and Chemical Pathology
Faculty of Medicine
Ain Shams University

Faculty of Medicine Ain Shams University

2011

#### Acknowledgement

Words do fail me when I come to express my sincere indebtedness and profound gratitude to my Prof. Dr. Mohamed Ashraf Abd El-Wahed, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, who guided this work and helped whenever I was in need. His great patience, close supervision, and constant encouragement throughout this work are beyond my words of thanks.

Special thanks are due to Dr. Tarek Mohey Abdel Meged El-Gammasy, Assistant Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for dedicating so much of his precious time and effort to complete this work.

All thanks are due to Dr. Hala Abdel Al Ahmed, Lecturer of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for helping and supporting me all the time.

Lastly but not least, I would like to thank all members in my family specially, my father and my mother for pushing me forward all the time

**Nesrine Mohsen Kamel** 

العلاقة بين نسبة الدهون في مصل الأمهات ومصل الحبل السرى في الأطفال المبتسرين المصابين المصابين بمتلازمة الكرب التنفسي

رسالة توطئة للحصول على درجة الماجستير في طب الأطفال

مقدمة من

الطبيبة/ نسرين محسن كامل بكالوريوس الطب والجراحة العامة (٢٠٠٥)

تحت إشراف الأستاذ الدكتور / محمد أشرف عبد الواحد

> أستاذ طب الأطفال كلية الطب – جامعة عين شمس

الأستاذ الدكتور / طارق محى عبد المجيد الجمسى

أستاذ مساعد طب الأطفال كلية الطب – جامعة عين شمس

الدكتورة / هالة عبد العال أحمد

مدرس الباثولوجيا الإكلينيكية والكيميائية كلية الطب – جامعة عين شمس

كلية الطب

# جامعة عين شمس ۲۰۱۱ **LIST OF CONTENTS**

Title	Page No.
Introduction	1
Aim of the work	3
Review of Literature	
Respiratory distress syndrome (RDS)	4
Lipid metabolism	29
Placental lipid transfer	40
Maternal lipid metabolism and placental lipid tran	sfer51
Pulmonary surfactant	58
Patients and methods	71
Results	81
Discussion	112
Summary	126
Conclusion and recommendations	129
References	130
Arabic Summary	

# **LIST OF TABLES**

Tab. No.	Title	Page No.
Tables in	the Review of Literature	
<b>Table</b> (1):	Classification of lipids:	30
<b>Table (2):</b>	Composition of lipoproteins	35
<b>Table (3):</b>	General roles of lipoproteins	36
<b>Table (4):</b>	Maternal Prenatal Status and Short- and Long-Term Outcomes.	44
<b>Table (5):</b>	Increased Maternal Nutritional Requirements During Pregnancy	45
<b>Table (6):</b>	Micronutrients that Play a Role in the Normal Development of Function of Fetal and Neonatal Organs.	46
<b>Table (7):</b>	Plasma triglyceride, cholesterol, lipoproteins in 553 selected women at 36 gestation	52
<b>Table (8):</b>	Surfactant therapy	68
Tables in	the Results	
<b>Table</b> (1):	Comparison between group A and group B preterm infants regarding clinical data	81
<b>Table (2):</b>	Comparison of some clinical data of mothers of group A and group B preterm infants	82
<b>Table (3):</b>	Comparison between group A and group B regarding cord serum lipid profile (mg/dl)	83
<b>Table (4):</b>	Comparison between group A and B regarding mother's lipid profile (mg/dl)	84
<b>Table (5):</b>	Correlations between maternal and cord serum lipid profile of preterm infants in group A	87
<b>Table (6):</b>	Correlation between maternal and cord serum lipid profile of preterm infants in group B	90

# LIST OF TABLES (Cont...)

Tab. No.	Title	Page No.
<b>Table (7):</b>	Correlation between maternal weight gain during pregnancy and cord serum lipid profile of preterm infants in group A	91
<b>Table (8):</b>	Correlation between maternal weight gain during pregnancy and cord serum lipid profile of preterm infant in group B	94
<b>Table (9):</b>	Correlations between gestational age and cored serum lipid profile of preterm infant in group A	97
<b>Table (10):</b>	Correlation between gestational age and cord serum lipid profile of preterm infant in group B	100
<b>Table (11):</b>	Correlation between preterm infant birth weight and cord serum lipid profile in group A	103
<b>Table (12):</b>	Correlation between preterm infant birth weight and cords serum lipid profile in group B	104
<b>Table (13):</b>	Correlations between body mass index of mothers and cord serum lipid profile of preterm infant in group A	105
<b>Table (14):</b>	Correlations between body mass index of mothers and cord serum lipid profile of preterm infant in group B	106

# LIST OF ABBREVIATIONS (Cont...)

Abbrev.	Full term
NVD	: Normal vaginal delivery
PC	: Phosphotidylcholine
PDA	: Patent ductus arteriosus
PDGF	: Platelet-derived growth factor
PEEP	: Peak end expiratory pressure
PG	: Phosphatidylglycerol
PIP	: peak inspiratory pressure
PMT	: Pulmonary mechanics testing
PN	: Parentral nutrition
RDS	: Respiratory distress syndrome
ROP	: Retinopathy of prematurity
SIMV	: Synchronized intermittent mandatory ventilation
SP	: Surfactant protein
TG	: Triglyceride
TI	: Transcutaneous
<b>VLDLs</b>	: Very low density lipoproteins

# **LIST OF FIGURES**

Fig. No.	Title	Page No.
Figures in the Review of Literature		
Figure (1):	Neonatal Respiratory Distress Syndrome	5
Figure (2):	Silver man retraction score for assessing the magnitude of respiratory distress. $0-3 = no$ or mild RD. $4-6 = moderate$ RD, $7-10$ severe RD	13
Figure (3):	RDS grade 1: fine reticuloglanular mottling	16
Figure (4):	RDS grade 2: mottling with air bronchograms	16
<b>Figure (5):</b>	RDS Grade 3: Diffuse mottling, heart borders are just discriminable with prominent air bronchograms.	16
Figure (6):	RDS Grade 4: Bilatral confluent opacification of lungs (White lung).	16
<b>Figure (7):</b>	Phospholipids: phsophatidylethanolamine, phosphatidylserine, sphingomyelin phosphatidylcholine,	33
Figure (8):	Schematic model of lipoprotein	34
Figure (9):	Composition of triglyceride-rich lipoproteins	35
<b>Figure (10):</b>	Lipoproteins transport lipids in three separate but interacting pathways through the body	37
Figure (11):	Schematic representation of the relationship of adipose tissue lipolytic activity with lipoprotein metabolism during late pregnancy and its role as a source of essential fatty acids (EFA) and long chain polyunsaturated fatty acids (L-PUFA) for the fetus.	54
<b>Figure (12):</b>	Composition of surfactant	58
<b>Figure (13):</b>	Bar chart demonstrates the composition of lung surfactant.	61

# LIST OF FIGURES (Cont...)

Fig. No.	Title	Page No.
Figures in th	e Results	
Figure (1):	Comparison between group B and group A regards mean values of cholesterol of mothers a preterm infants	and
Figure (2):	Comparison between group B and group A regards mean values of triglycerides of mother and preterm infant	ers
Figure (3):	Comparison between group B and group A regards mean values of HDL of mothers a preterm infant	and
Figure (4):	Comparison between group B and group A regards mean values of LDL of mothers a preterm infant.	and
Figure (5):	Regression analysis showing the correlative between preterm – cholesterol and moth cholesterol in group A.	ers
Figure (6):	Regression analysis showing the correlative between preterm-HDL and mothers HDL in ground A	oup
Figure (7):	Regression analysis showing the correlative between preterm LDL and mothers LDL in group A	oup
Figure (8):	Correlation between maternal weight gain and conserum cholesterol in preterms with RDS (Groad).	oup
Figure (9):	Correlation between maternal weight gain and co serum HDL-cholesterol in preterms with RI (Group A)	DS
<b>Figure (10):</b>	Correlation between maternal weight gain and co serum LDL-cholesterol in preterms with RI (Group A).	

# LIST OF FIGURES (Cont...)

Fig. No.	Title	Page No.
Figure (11):	Correlation between maternal weight gain and coserum triglycerides in preterms with RDS (Groad).	
<b>Figure (12):</b>	Correlation between maternal weight gain and conserum cholesterol in preterms without RDS (Grown)	
<b>Figure</b> (13):	Correlation between maternal weight gain a cord serum HDL in preterms without RDS (Groß)	oup
<b>Figure (14):</b>	Correlation between maternal weight gain and co serum LDL in preterms without RDS (Group B).	
<b>Figure (15):</b>	Correlation between maternal weight gain and coserum triglycerides in preterms without R (Group B).	DS
<b>Figure (16):</b>	Correlation between gestational age and conserum cholesterol of preterms with RDS (Grown).	oup
<b>Figure (17):</b>	Correlation between gestational age and coserum HDL-cholesterol of preterms with R (Group A)	DS
<b>Figure (18):</b>	Correlation between gestational age and conserum LDL-cholesterol of preterms with R (Group A)	DS
<b>Figure (19):</b>	Correlation between gestational age and conserum triglycerides of preterms with RDS (Groad).	oup
<b>Figure (20):</b>	Correlation between gestational age and conserum cholesterol in preterms without RDS (Grown)	oup
<b>Figure (21):</b>	Correlation between gestational age and conserum HDL in preterms without RDS (Group B)	

# LIST OF FIGURES (Cont...)

Fig. No.	Title	Page No.
<b>Figure (22):</b>	Correlation between gestational age and serum LDL in preterms without RDS (Group	
<b>Figure (23):</b>	Correlation between gestational age and serum triglycerides in preterms without (Group B).	RDS
<b>Figure (24):</b>	Sensitivity and specificity of mat triglycerides	
<b>Figure (25):</b>	Sensitivity and specificity of maternal total s cholesterol.	
<b>Figure (26):</b>	Sensitivity and specificity of maternal LDL	109
<b>Figure (27):</b>	Sensitivity and specificity of maternal serum H	HDL110

# **LIST OF ABBREVIATIONS**

Abbrev.	Full term
%	: Percent
A/CV	: Assisted/control ventilation
ANS	: Antenatal steroid
<b>APACHE</b>	: Acute physiology and chronic health evaluation
Apo	: Apolipoprotein
BMI	: Body mass index
BPD	: Bronchoalveolar lavage
cGMP	: Cyclic guanosine monophosphate
CHD	: Coronary heart disease
CLD	: Chronic lung disease
CPAP	: Continuous positive airway pressure
CS	: Caesarian section
DPPC	: Dipalmitoylphosphatidyl choline
EFA	: Essential fatty acid
ETT	: Endotracheal tubes
FGF	: Fibroblast growth factor
gm	: gram
HDLs	: High density lipoproteins
HFOV	: High frequency oscillatory ventilation
HMD	: Hyaline membrane disease
IMV	: Intermittent mandatory ventilation
iNO	: Inhaled nitric oxide
IVH	: Intraventricular hemorrhage
LCAT	: Lecithin cholesterol acyl transferase
LCL	: Long chain lipoprotein
LDL	: Low density lipoprotein
LDLs	: Low density lipoproteins
LP	: Lipoprotein
LPL	: Lipoprotein-lipase
NEC	: Necrotizing entercolitis
NO	: Nitric oxide
NRDS	: Neonatal respiratory distress syndrome

#### **INTRODUCTION**

Previously called hyaline membrane disease, is a syndrome caused in premature infants by developmental insufficiency of surfactant production and structural immaturity in the lungs (*Rodriguez*, 2002).

RDS affects about 1% of newborn infants and is leading cause of death in preterm infants. The incidence decreases with advancing gestational age, from about 50% in babies born at 26-28 weeks, to about 25% at 30-31 weeks (*Horbar*, 2002).

RDS begins shortly after birth, manifested by tachypnea, tachycardia, chest wall retraction (recession), expiratory grunting, flaring of the nostrils and cyanosis during breathing efforts. Radiological findings including (diffuse reticulogranular pattern with air bronchograms) can be confirmed by chest x-ray (*Soll*, *2001*).

Cholesterol was found to represent over 50% of neutral lipid of both the total surfactant and lamellar body fractions and de novo synthesis of cholesterol accounted for only 1% of the surfactant cholesterol, the remainder being derived from exogenous cholesterol supplied as serum lipoproteins (*Gunes et al.*, 2007).

The main lipids in plasma are cholesterol and triglyceride, they required to be transported in plasma encapsulated in shell of phospholipids forming lipoproteins.

Lipid metabolism has important role in fetal development during late stage of gestation including growth and fat accretion in utero, increasing amniotic fluid lecithin levels with maturation of pulmonary function and changes in levels of minor phospholipids in amniotic fluid. A deficiency or reduced transport of essential or long chain polyunsaturated fatty acids, resulted in alterations of lipid in the fetus which could inhibit normal fetal growth maturation, which may lead to delayed development of fetal lungs (*Lane*, 2002).

# **AIM OF THE WORK**

The aim of this study is to explore the role of lipid profile in mothers and cord blood of babies in pathogenesis of RDS by evaluating lipid profile in babies with RDS and their mothers compared to babies with no RDS and their mothers.