



بسم الله الرحمن الرحيم

∞∞∞∞

تم رفع هذه الرسالة بواسطة / مني مغربي أحمد

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى

مسئولية عن محتوى هذه الرسالة.

ملاحظات: لا يوجد





Assessment of Thyroid Functions in Late Preterm Infants of Mothers on Antenatal Steroids

A Thesis

Submitted for partial fulfillment of Master degree
in Pediatrics

By

Basma Bassam Bassam Hassan
M.B., B.Ch (Ain Shams University 2012)

Under Supervision of

Prof. Dr. Rasha Tarif Hamza
Professor of Pediatrics
Faculty of Medicine, Ain Shams University

Prof. Dr. Amira Ibrahim Hamed
Professor of Clinical Pathology
Faculty of Medicine, Ain Shams University

Dr. Wafaa Osman Ahmed
Lecturer of Pediatrics
Faculty of Medicine, Ain Shams University

**Faculty of Medicine
Ain Shams University
2022**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢



Acknowledgments

*First and foremost, I feel always indebted to **Allah**, the **Most Beneficent** and **Merciful** who gave me the strength to accomplish this work,*

*My deepest gratitude to **Prof. Dr. Rasha Tarif Hamza**, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her valuable guidance and expert supervision, in addition to her great deal of support and encouragement. I really have the honor to complete this work under her supervision.*

*I would like to express my great and deep appreciation and thanks to **Prof. Dr. Amira Ibrahim Hamed**, Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her meticulous supervision, and her patience in reviewing and correcting this work,*

*I must express my deepest thanks to **Dr. Wafaa Osman Ahmed**, Lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, for guiding me throughout this work and for granting me much of her time. I greatly appreciate her efforts.*

*Special thanks to my **Parents**, my **Husband** and all my **Family** members for their continuous encouragement, enduring me and standing by me.*

 *Basma Bassam Bassam Hassan*

List of Contents

<i>Subject</i>	<i>Page No.</i>
List of Abbreviations.....	i
List of Tables.....	iii
List of Figures	iv
Introduction	1
Aim of the Work.....	3
Review of Literature	
Antenatal Corticosteroids.....	4
Prematurity and late preterm infants.....	15
Thyroid function in fetus and preterm infants	24
Patients and Methods.....	41
Results.....	47
Discussion	69
Summary	80
Conclusions and Recommendations	83
References	85
Arabic Summary	—

List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
ACOG	: American College of Obstetricians and Gynecologists
ACS	: Antenatal corticosteroids
ACTH	: Adrenocorticotrophic hormone
ANS	: Antenatal steroids
BMR	: Basal metabolic rate
CRH	: Corticotropin-releasing hormone
CS	: Caesarean section
D1	: Iodithyronine deiodinase
D2	: Type 2 deiodinase
DI3	: Monoamine deiodinase, type 3
DM	: Diabetes mellitus
DUE	: Dehydro-epiandrosterone
ELISA	: Enzyme linked immune sorbent assay
GR	: Glucocorticoid receptors
HTN	: Hypertension
IGF	: Insulin-like growth factors
IVH	: Intraventricular hemorrhage
LMP	: Last menstrual period
NIH	: National Institute of Health
NSAIDS	: Non-steroidal anti-inflammatory drugs
NTIS	: Non-thyroidal illness syndrome

NVD	: Normal vaginal delivery
PROM	: Premature rupture of membranes
RDS	: Respiratory distress syndrome
SD	: Standard deviation
SGA	: Small for gestational age
SMFM	: Society for Maternal Fetal Medicine
SPSS	: statistical analyses were performed using
TBG	: Thyroxine-binding globulin
TG	: Thyroglobulin
TRH	: TSH releasing hormone
TSH	: Thyroid stimulating hormone
WHO	: World Health Organization

List of Tables

Table No.	Title	Page No.
Table (1):	Clinical practice considerations for administration of antenatal corticosteroids for late-preterm and early term pregnancies.....	10
Table (2):	Late-preterm infants and the most frequent complications of prematurity during the birth hospitalization.....	18
Table (3):	Physiological and biochemical actions of thyroid hormone	33
Table (4):	Morphological and biochemical responses to thyroid hormone during amphibian metamorphosis.....	35
Table (5):	Maternal History.....	49
Table (6):	Neonatal Demographics	52
Table (7):	Neonatal clinical Outcomes.....	55
Table (8):	Thyroid profile.....	58
Table (9):	Complete Blood Count	60
Table (10):	Arterial Blood gases	62
Table (11):	Hematological findings	64
Table (12):	Binary logistic regression for prediction of serum TSH >6 MIU/L	67
Table (13):	Binary logistic regression for prediction of serum levothyroxine administration.....	68

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Figure (1):	Antenatal corticosteroids (ACS).....	5
Figure (2):	Approximate timeline of thyroid gland maturation in the human fetus.	25
Figure (3):	Changes in serum TSH, T4, and T3 following birth in term as compared to preterm newborn infants.....	27
Figure (4):	Normal ranges of thyroid function tests in premature infants	29
Figure (5):	Maternal-placental-fetal endocrine interaction.	31
Figure (6):	Rat thyroid total (A), protein-bound (B), and free (C) concentration of iodine during acute stress and post-stress periods.....	39
Figure (7):	Obstetric history.....	50
Figure (8):	Maternal history.....	50
Figure (9):	Distribution of neonatal sex and SGA among the study groups	53
Figure (10):	Mean birth weight distribution among the study groups.....	53
Figure (11):	Neonatal clinical outcomes.....	56
Figure (12):	Neonatal free T4 among the studied groups.....	58
Figure (13):	Neonatal free T3 among the studied groups.....	59

Figure (14): Neonatal serum TSH among the studied groups.....	59
Figure (15): Neonatal platelet count among the studied groups.....	61
Figure (16): Arterial PCO ₂ among the studied groups.....	62
Figure (17): Arterial HCO ₃ among the studied groups.....	63
Figure (18): Neonatal PTT among the studied groups.....	65
Figure (19): Neonatal PTT among the studied groups.....	65

ABSTRACT

Background: Antenatal steroids (ANS) are used widely for women at risk of preterm delivery. Evidence on the effects of ANS on thyroid hormone function in preterm infants is limited. There is no evidence on comparative effects of no ANS, one dose of ANS (partial), or two doses of ANS (complete) on thyroid hormone function among preterm infants.

Aim of the study: To study the effect of antenatal steroids on thyroid functions in late preterm infants on third to seventh day of life.

Patients and Methods: Comparative Cross-Sectional study was conducted on 90 neonates admitted in NICU in the first week of life. They were divided according to exposure to antenatal steroids to three groups. First group: exposed to complete course of ANS. Second group: exposed to partial course of ANS. Third group: not exposed to ANS.

Results: The study showed that there was significantly higher serum T4 levels in group A (who exposed to complete course) compared to group B (partial course) and C (Third group). While, there were no significant differences in serum TSH, T3 levels between groups.

Conclusion: Antenatal corticosteroids can influence thyroid function in late preterm infants as serum T4 was significantly higher in infants exposed to complete course compared to those who were exposed to partial course or did not receive antenatal corticosteroids.

Keywords: antenatal steroids, thyroid function, preterm

Introduction

Preterm infants have an increased incidence of complications and mortality roughly proportional to the degree of prematurity. Infants born >34 weeks and <37 weeks are considered late preterm, infants born >32 weeks and < 34 weeks are considered moderate preterm, infants born >28 weeks and < 32 weeks are considered very preterm. Infants born < 28 weeks are considered extremely preterm (**Shapiro-Mendoza and Lackritz, 2012**).

The use of antenatal steroids (ANS) has been associated with reductions in serious adverse outcomes of prematurity (**Roberts et al., 2017**).

The administration of ANS is very effective intervention in improving neonatal respiratory outcome after preterm birth (**Travers et al., 2017**). The beneficial effect of ANS is dose-dependent, with maximal benefit associated with a complete course of ANS (**Chawla et al., 2016**).

Thyroid hormone is essential for the regulation of intrauterine homeostasis, and for the timely differentiation and maturation of fetal organs. These hormones play complex roles during fetal life. They serve to modulate the functional adaptation for extra uterine life during the perinatal period. Abnormalities of thyroid gland function result not only in the metabolic consequences of thyroid dysfunction, but in unique effects on the growth and maturation of these thyroid hormone-dependent tissues (**Chung, 2014**).

Postnatal thyroid function of preterm infants differs from that of term Infants. Thyroid dysfunction is common among premature Infants (**Kaluarachchi et al., 2017**). The dramatic rise in serum TSH 30 to 60 minutes following delivery is reduced in preterm infants as compared to term infants, generally in proportion to their degree of prematurity (**Murphy et al., 2004**).

After birth, neonate must rapidly convert from the fetal state of predominant thyroid hormone inactivation to a state of relative hyperactivity; this is initiated by abrupt increase in hypothalamic TSH releasing hormones (TRH) and pituitary TSH secretion. The cold-stimulated TRH-TSH surge is short lived and peaks at 30 minutes, with peak concentration as high as 60-70 $\mu\text{U/L}$, after that serum TSH concentration progressively decrease to normal infant level by 3 to 5 days, while serum free **T4** levels remain elevated for several weeks (**Brown, 2012**).

Many factors affecting thyroid function as gestational age, gender, mode of delivery, birth weight, birth order, Apgar score at 5 minutes, the development of respiratory distress syndrome (RDS) requiring surfactant supplementation, history of surgical procedures which needed antiseptics containing iodine, antenatal administration of dexamethasone, cold exposure, use of morphine, dobutamine or dopamine on the day which thyroid function test was performed and nutritional status from the until tolerable feeding (**Chung et al., 2009**).

Aim of the Work

To study the effect of antenatal steroids on thyroid functions in late preterm infants on third to seventh day of life.

Antenatal Corticosteroids

Administration of maternal antenatal corticosteroids (ACS) is a well-adopted practice for preterm pregnancies death, neonatal death, RDS, and intra ventricular hemorrhage (IVH) (**Mc Goldrick et al., 2020**).

Type and dose of antenatal corticosteroids

Two types of corticosteroids are used antenatal to facilitate lung maturation: betamethasone and dexamethasone. The cellular mechanisms of corticosteroids in facilitating lung maturation involve the induction of pulmonary beta-adrenergic receptors, acceleration of the development of type 1 and 2 pneumocystis, and up regulation of gene expression for the epithelial Na⁺ channel. This leads to increased surfactant production and excretion which allows for improvement in gas exchange and lung mechanics, and increased absorption of alveolar fluid prior to delivery (**Htun et al., 2021**).