



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



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شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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Impact of Carbamoyl-Phosphate Synthetase Gene Polymorphism on Increased Susceptibility to Persistent Pulmonary Hypertension in Neonates

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا
إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

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Dedication

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List of Abbreviations

Abb.	Full Term
SNPs.....	Single Nucleotide Polymorphisms .
CPS1.....	Carbamoyl-Phosphate Synthetase 1.
PPHN.....	Persistent pulmonary hypertension of Newborn .
Thr.....	Threonine .
Asn.....	Asparagine .
PVR.....	Pulmonary Vascular Resistance .
NO.....	Nitric Oxide .
GMP.....	Guanosine Monophosphate .
CAMP.....	Cyclic Adenosine Monophosphate .
DA.....	Ductus Arteriosus .
PBF.....	Pulmonary Blood Flow.
FO.....	Foramen Ovale .
PaO ₂	Arterial Partial Pressure of Oxygen .
PG.....	Prostaglandin .
CDH.....	Congenital Diaphragmatic Hernia .
RDS.....	Respiratory Distress Syndrome .
MAS.....	Meconium Aspiration Syndrome .
TTN.....	Transient Tachypnea of the Newborn .
ABCA3.....	ATP Binding Cassette protein member A3.
SP-B.....	Surfactant Protein B .
CRHR1.....	Corticotropin-Releasing Hormone Receptor 1.

List of Abbreviations cont ...

Abb.	Full Term
CRHBP.....	CRh-binding protein .
NSAIDs.....	Non steroidal Anti-Inflammatory Drugs .
TTE.....	Transthoracic echocardiogram .
PaCO ₂	Partial Pressure of Carbon Dioxide .
ABGs.....	Arterial Blood Gases .
ECMO.....	Extracorporeal Membrane Oxygenation .
OI.....	Oxygenation index.
CBC.....	Complete blood count .
RDW.....	Red cell distribution width .
NICU.....	Neonatal intensive care unit .
PT.....	Prothrombin time .
PTT.....	Partial Thromboplastin Time .
INR.....	International Normalized Ratio .
RVSP.....	Right Ventricle Systolic Pressure .
RAP.....	Right Atrial Pressure .
PDP.....	Pulmonary Diastolic Pressure .
TAPSE.....	Tricuspid Annular Plane Systolic Excursion .
TR.....	Tricuspid Regurgitation .
GLPS.....	Global Longitudinal Peak Strain .
CT.....	Computed Tomography .
MRI.....	Magnetic Resonance Imaging .
ATS.....	American Thoracic Society .

List of Abbreviations cont ...

Abb.	Full Term
AHA.....	American Heart Association .
PAH.....	Pulmonary artery hypertension .
HFV.....	High-frequency ventilation .
CNS.....	Central nervous system .
NG.....	Nasogastric .
NAGS.....	N-acetylglutamate Synthase .
OTC.....	Ornithine transcarbamylase .
ASS1.....	Argininosuccinate synthetase 1 .
ASL.....	Argininosuccinate lyase .
NOS.....	Nitric oxide synthase .
TBX4.....	T-box transcription gene 4 .
PSAP.....	Pulmonary systolic artery pressure .
FRET.....	Fluorescence Resonance Energy Transfer.
NVD.....	Normal Vaginal Delivery.
CS.....	Cesarean section .
BEAE.....	Bilateral equal air entry.
BDAE.....	Bilateral diminished air entry.
CRP.....	C-reactive protein .

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Introduction

INTRODUCTION

Persistent pulmonary hypertension of Newborn (**PPHN**) is a life threatening condition , it is characterized by sustained elevation of pulmonary vascular resistance , and this leads to extra pulmonary right to left shunting across the patent ductus arteriosus and foramen oval [**Dagle J.M. 2018**] .

Consequence threatening hypoxemia , right ventricular failure occurs , and the story ends in death . PPHN is a serious neonatal disease . PPHN results from failure of pulmonary vascular transition to extra uterine life [**Dong X 2019**] .

It occurs mostly in term or near term infants and occurs in 2/1000 newborn infants . PPHN can be idiopathic or can result secondary to neonatal pulmonary diseases such as congenital diaphragmatic hernia , pulmonary hypoplasia , respiratory distress syndrome , pneumonia and meconium aspiration syndrome [**Alec W. A. 2004**] .

Vascular endothelial cells can synthesize endogenous L- arginine by recycling L-citrulline , the byproduct of nitric oxide synthesis, using components of the urea cycle ; argininosuccinic acid synthase and lyase, respectively [**Kaluarachchi D.C 2018**] .

In addition , endothelial cells may utilize circulating L-citrulline, formed by the mitochondrial enzymes of the urea cycle in the liver and proximal intestines [**Klein J.M 2018**] .

Thus , a potential link exists between nitric oxide production and the urea cycle . Gene analysis that studied 48 **SNPs (single nucleotide polymorphisms)** in 6 urea cycle enzyme genes (**CPS1, NAGS, ASS, ASL, ARG1, OTC**) studied the association with **PPHN** [**Chen X 2019**] .