Study of Metabolic Profile in Infants of Diabetic Mothers

Thesis
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List of Abbreviations

Abb.	Meaning
ADA	American Diabetes Association
AGE	Advanced glycosylation end products
AIB	Aminoisobutyrate
AMP	Adenosinemonophosphate nucleoside
AMPK	Adenosinemonophosphate nucleoside kinase
BALF	Bronchoalveolar lavage fluid
BMI	Body mass index
C0-Carnitine	Free carnitine
C10:1	Decenoylcarnitine
C10-Carnitine	Decanoylcarnitine
C12-Carnitine	Dedecanoylcarnitine
C14:1	Tetradeconylcarnitine
C14:2	Tetradecadienoylcarnitine
C14-Carnitine	Tetra decanoylcarnitine
C14-OH	3-Hydroxy-tetradecanoylcarnitine
C16:1	Hexadecanoylcarnitine
C16-Carnitine	Hexadecanoylcarinitine
C16-OH	3-Hydroxy-hexadecanoylcarnitine
C18-carnitine	Octadecanoylcarnitine
C2-carinitine	Acetyl carnitine
C3	Propionylcarnitile
C4 – Carnitine	Butyrylcarnitine
C5- Carnitine	Isovalerylcarnitine
C6- carnitine	Hexanoylcarnitine

Abb.	Meaning
C8-carnitine	Octanoylcarntine
CNS	Thecentral nervous system
CVS	Cardiovascular system
DM	Diabetes mellitus
EA	Experimental animals
ELBW	Extreme low birth weight
FC	Fold change
GA	Gestational age
GC–MS	Gas chromatography-mass spectrometry
GDM	Gestational diabetes mellitus
GSEA	Gene Set Enrichment Analysis
HA	Human adults
HbA1C	Glycated hemoglobin
HN	Human newborns
IDM	Infant of diabetic mother
IGF 1	Insulin like growth factor 1
IUGR	Intrauterine growth restriction
LC-MS	Liquid chromatography-mass spectrometry
LGA	Large for gestational age
LPS	Lipopolysaccharide
LSCS	Lower segment caesarian section
MESA	Metabolite Set Enrichment Analysis
MMA	Methylmalonicacidemia
MVM	Microvillous membrane
n	Number

Abb.	Meaning
NADPH	Nicotinamide adenine dinucleotide phosphate
NEC	Necrotizingenterocolitis
NMR	Nuclear magnetic resonance
NSCs	Neural stem cells
NTDS	Neural Tube Defect
NVD	Normal vaginal delivery
OFC	Occipitofrontal circumference
OHD	Oral hypoglycemic drugs
OS	Oxidative stress
PCA	Principal Component Analysis
PGDM	Pregestational diabetes mellitus
PLS-DA	Partial Least Squares - Discriminant Analysis
PTH	Parathyroid hormone
RDS	Respiratory distress syndrome
ROS	Reactive oxygen species
SD	Standard deviation
SFT	Skin fold thickness
SGA	Gestational age
SGA	Small for gestational age
TTN	Transient tachypnea of the newborn
UPLC/MS	The urine metabolomics
UPLC-Q-TOF-MS	Ultra-performance liquid chromatography–quadrupole time-of-flight mass spectrometry
VIP	Variable Importance in Projection

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Introduction

Women with diabetes mellitus or who develop diabetes mellitus during pregnancy can present some particular challenges for mothers and her infants. Gestational diabetes mellitus is a condition in which women without previous diagnosis as a case of diabetes exhibit high blood glucose levels during pregnancy especially during 3rd trimester ***(Donovan, 2010).***

Pregestational diabetes mellitus, gestational diabetes mellitus may be associated with a variety of fetal effects (diabetic fetopathy) including increased rate of spontaneous abortion, intra uterine fetal death, congenital anomalies, neurodevelopmental problems, and increase risk of perinatal complications. Additional problems include fetal growth disturbance causing increase or decrease birth weight, hyperglycemia and hyperinsulinemia. Optimal control of maternal blood glucose is known to reduce these changes ***(Epub, 2011).***

Fetal hypoxia and acidemia have been reported in pregestational diabetic pregnancies in relation to poor glycemic control, but it is still uncertain whether this is the cause in apparently well controlled gestational diabetes ***(Bjog, 2009).***

The infants of gestational diabetic mothers sometimes have increased umbilical blood glucose levels, reduction in oxygen saturation and oxygen content together with increased lactate concentration despite normal maternal glucose level reflecting altered fetal metabolism. These data suggest that good maternal metabolic control achieved by currently used methods of monitoring glucose control is not sufficient to ensure a normal oxygenation status and metabolic milieu for the fetus in gestational diabetes mellitus pregnancies ***(Sacco, 2009).***

The goal of infants of diabetic mothers' screening is to detect disorders that are threatening to life or long-term health problems before they become symptomatic. Early treatment of these disorders may significantly reduce mortality and morbidity in affected infants. An infant may present with a positive infant screen for one of the complication of infants of diabetic mothers before clinical manifestations are present or recognized ***(Pasquali and Longo, 2011).***

Extended metabolic screening of infants of diabetic mothers might disclose hidden metabolic disorders that can be related to early or late complications in those neonates. Metabolic profile of infants of diabetic mothers include different markers include amino acid profile and acylcarintine profile. Most amino acids (except argininosuccinic acid and alloisoleucine) are present in the plasma within a normal range

in healthy individuals. Mild elevations of 5 to 10 percent above normal usually are not significant elevations are reported only in groups of amino acids and specific disorders ***(Weiner, 2006).***

Analysis of acylcarnitine conjugates is performed by tandem mass spectrometry (MS/MS) as amino acids. It may show abnormal increase or decrease in their levels in specific disorders ***(Cleary and Green, 2005).***

Aim of the Study

The aim of this work is to study the metabolic profile (amino acid, and acylcarnitine profile) among infants of diabetic mothers to determine the infants outcome by correlation of this profile with profiles of other diseases.

Diabetes and Pregnancy

Diabetes is the most common metabolic disorder affecting pregnancy. Its prevalence seems to be growing in parallel with the epidemics of overweight and obesity. Recognizing and treating diabetes or any degree of glucose intolerance in pregnancy results in lowering maternal and fetal complications ***(Negrato and Gomes, 2013).***

Pre-gestational diabetes (ie, diabetes diagnosed before pregnancy, type 1 or type 2 diabetes mellitus) comprises approximately 13 percent of all diabetes in pregnancy, while gestational diabetes mellitus (GDM) (ie., diabetes with onset or first recognition in pregnancy) comprises the remaining 87 percent ***(Wier et al., 2010).***

The prevalence of pre-gestational diabetes has been increasing [due to the increasing prevalence of type 2 diabetes in women of reproductive age. The prevalence of GDM is also increasing, paralleling the increasing prevalence of obesity and undiagnosed type 2 diabetes in these women ***(Shaw et al., 2010).***

The mainstay of the medical management of pre-gestational diabetes involves frequent monitoring of blood glucose levels with adjustment of diet and insulin therapy to achieve normoglycemia. Normoglycemia is important because