The Role of Umbilical Cord Thickness and Hba1c Levels for Prediction of Fetal Macrosomia in Pregnant Diabetic Patients

Thesis

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Glossary of Terms

3DUS	Three-Dimensional Ultrasound
ACBDUK	The Association For Clinical Biochemistry And Diabetes United Kingdom
ADA	American Diabetes Association
AHSCT	Autologous non-Myeloablative Hematopoietic Stem Cells Transplantation
BMI	Body Mass Index
CAP	College Of American Pathologists
CB-SC	Cord Blood-Derived Multipotent Stem Cells
CS	Cesarean Section
DCCT	Diabetes Control And Complications Trial
DHA	Docosahexaenoic Acid
DKA	Diabetic Ketoacidosis
DPP	Dipeptidyl Peptidase
eAG	Estimated Average Glucose
EASD	European Association For The Study Of Diabetes
EPC	Endothelial Progenitor Cells
EPOCH	Exploring Perinatal Outcomes Among Children
FPG	Fasting Plasma Glucose
GCK	Glucokinase
GCT	Glucose Challenge Test
GDM	Gestational Diabetes Mellitus
GHB	Glycated Hemoglobin
GVHD	graft-versus-host disease
HLA	Human Leukocyte Antigen
hPL	Human Placental Lactogen

HPLC	High-Performance Liquid Chromatography
HSCs	Hematopoietic Stem Cells
HSCT	Hematopoietic Stem Cells Transplantation
IADPSGCP	International Association Of Diabetes And Pregnancy Study Groups Consensus Panel
IDF	International Diabetes Federation
IFCC	International Federation Of Clinical Chemistry
IL6	Interleukin 6
MDRTC	Michigan Diabetes Research And Training Center
MHC	Major Histocompatibility Complex
MiG	Metformin In Gestational Diabetes
MSCs	Mesenchymal Stem Cells
NGSP	National Glycohemoglobin Standardization Program
NGT	Normal Glucose Tolerance
NOD	Non-Obese Diabetic
OCT4	Octamer-Binding Transcription Factor 4
PHA	Phytohemagglutinin
STZ	Streptozotocin
T1D	Type 1 Diabetes
T2D	Type 2 Diabetes
TNFα	Tumor Necrosis Factor Alpha
TUI	Tomography Ultrasound Imaging
UCB	Umbilical Cord Blood
UKPDS	United Kingdom Prospective Diabetes Study
WHO	World Health Organization
WJ	Wharton's Jelly

Alphabetically ordered

Introduction

The umbilical cord is responsible for maternal-fetal blood flow. Normally, it is composed of two arteries permeated with venous blood and a vein that transports arterial blood, cushioned by a special type of mucous connective tissue known as Wharton's jelly (WJ) and by remnants of the allantoids **(Wang et al., 2004).**

There is a significant differences in mean gestational age, mode of delivery, birth weight, and adverse perinatal outcome between fetuses with umbilical cord thickness below the 5th percentile (lean umbilical cord) vs. those with umbilical cord thickness above the 5th percentile (non-lean cord) in the first and early second trimesters of gestation **(Goynumer et al., 2008).**

Others have shown that umbilical cord diameter and area measurements are associated with increased fetal macrosomia **(Weissman and Jakobi, 1997; Ghezzi et al., 2007).**

Macrosomia defined as weight of a full-term infant greater than 90th percentile for gestational age or higher than 4000 gm occurs in 6%-10% of all deliveries **(Martin et al., 2008; Mondestin et al., 2002).**

Reported risk factors of macrosomia are Body mass index (BMI) before pregnancy, gestational weight gain, gestational diabetes mellitus (GDM), mother's age and gender **(Yu DM et al., 2008).**

GDM is associated with many adverse pregnancy outcomes such as macrosomia and CS delivery **(Crowther et al ., 2005; Barakat et al., 2010)** and at the same time Macrosomia is a well-known indicator of maternal diabetes in fetus which is strongly associated with prematurity, respiratory distress syndrome, birth trauma, fetal death and adverse maternal outcome **(Koklu et al., 2007; Yessoufou & Moutairou, 2011; Lepercq et al., 2001; Cox, 1994; Stotland et al., 2004).**

Socioeconomic advances and the improvement in women's living standards can predispose to the development of fetal macrosomia, which may result in childhood obesity, it is a vicious cycle **(Van Eerden, 2011; Satpathy et al., 2008).**

Obesity in pregnancy is also recognized as a risk factor for many maternal and neonatal adverse outcomes including macrosomia, increased rate of cesarean section (CS), preeclampsia and gestational diabetes (GDM) **(Callaway et al., 2006; Athukorala et al., 2010 and Di et al., 2012).**

Also, The placenta, as the interface between mother and fetus, is central to prenatal growth control. The fetus is dependent upon the placenta for its supply of nutrients and oxygen from the mother. Previous research found that the placental weights in the macrosomic fetuses were significantly higher than those with normal weight and placental weight was positively correlated with birth weight **(Hua Jiang et al., 2009).**

Fetal macrosomia is associated with a higher frequency of operative deliveries, post-partum hemorrhages, birth injury during vaginal delivery, and neonatal hypoglycemia. Known maternal risk factors are only identified in 40% of women who deliver macrosomic babies **(Auger et al., 2013).**

Macrosomia has been suggested as one of the possible risk factors for obesity in many studies **(Van Eerden, 2011; Satpathy et al., 2008).**

Children with macrosomia tend to gain weight faster than those born at normal weight. Abnormal weight gain in the uterus and during infancy may have an adverse influence on health in childhood and adult life. Studies show that macrosomic infants have a higher risk of developing obesity and metabolic disorders **(Boney et al., 2005; Dyer et al., 2007).**

Macrosomia is also associated with higher risk of certain cancers **(Sprehe et al., 2010; Harder et al., 2010; Ognjanovic et al., 2010; Ahlgren et al., 2007).**

The morbidity of macrosomia reaches 7-10% **(Stotland et al., 2004).**

Therefore, tracking of abnormal birth weight and related risk factors have significant public health implications **(Shan et al., 2014).**

Diabetes represents a major public health concern and efforts to control hyperglycemia are an important element of the management of patients with type 2 diabetes **(American Diabetes Association, 2011).**

Hyperglycaemia is measured using hemoglobin A1c (HbA1c) test which assesses the average level of blood glucose in the preceding 60-120 days. For diabetes patients an HbA1c target of 6.5% (48 mmol/mol) is recommended **(National Institute for Health and Clinical Excellence, 2008 and International Diabetes Federation, 2013).**

Gestational diabetes mellitus (GDM) affects 2-6% of pregnant women and is associated with increased risk of important adverse perinatal outcomes, including macrosomia and birth injury **(Hong et al., 2009; Stotland et al., 2004).**

The birth of a macrosomic fetus has been associated with adverse outcomes for both mother and fetus. Shoulder dystocia during delivery and related permanent brachial plexus injury may be seen. Both neonatal mortality and morbidity are higher in macrosomic fetuses compared with normal weight fetuses **(Ghezzi et al., 2007).**

Maternal complications such as postpartum hemorrhage, infections, as well as third- or fourth-degree vaginal lacerations may occur as a result of operative delivery **(Ferber, 2000).**