

**Assessment of glycemc control
In infant of diabetic mother**

Thesis

Submitted for partial fulfillment of Master Degree

In Pediatric

By

Eman Ahmed Mahmoud Abdel Rehim

M.B.B.CH

Under Supervision of

Prof.Nehal Mohamed EL-Raggal

Professor of Pediatric

Faculty of Medicine-Ain Shams University

Dr.Nancy Mohamed Abou-Shady

Lecturer of Pediatric

Faculty of Medicine-Ain Shams University

Dr.Noha Mohamed Refaat

Lecturer of Clinical Pathology

Faculty of Medicine-Ain Shams University

Faculty of Medicine

Ain Shams University

2013



Acknowledgment

- ✍ I would like to express my sincere gratitude and appreciation to **Prof. Dr. Nehal Mohamed EL-Raggal** professor of Pediatric Faculty of Medicine, Ain Shams University for her continuous guidance, valuable advice and support throughout the execution of this work, it was a great honor to work with her.
- ✍ I also express my deep thanks and gratitude to **Dr. Nancy Mohamed Abou shady** Lecturer of Pediatric, Faculty of Medicine, Ain Shams University, for her great support, encouragement, patience and help, without which this work would have never seen light.
- ✍ Also my deep thanks to **Dr. Noha Mohamed Refaat** Lecturer of Clinical Pathology, Faculty of Medicine Ain Shams University, for her great cooperation and generous help.
- ✍ **Lastly.** I would like to thank all members in my family specially, my father and my mother, for pushing me forward all the time.
- ✍ **My,** all thanks to all mothers of the newborns and all members in hospital who helped me in this work,

✍ **Eman Abdel Rehim**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسببناك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Contents

Subjects	Page
• List of abbreviations	I
• List of Tables.....	V
• List of Figures.....	VIII
• Introduction.....	1
• Aim of the study	3
• Review of literature	
- Chapter (I): Diabetes Mellitus.....	4
- Chapter (II): Infant of Diabetic Mother.....	14
- Chapter (III): Monogenic Forms of Diabetes.....	40
- Chapter (IV): Glycated Hemoglobin.....	46
- Chapter (V): Glycated albumin.....	58
• Subjects and Methods.....	77
• Results	89
• Discussion.....	115
• Summary and Conclusion	131
• Recommendations.....	134
• References.....	135
• Arabic summary.	

List of Abbreviations

1,5-AG	: 1,5-anhydroglucitol
67 KDa	: unified atomic mass unit
6q24	: q arm of 6 chromosome
HbAc	: Glycated hemoglobin.
ABCC8	: ATP-binding cassette, sub-family C (CFTR/MRP), member 8
AD	: Alzheimer's Disease.
ADA	: American Diabetes Association
AGEs	: Advanced glycation end products
AP-1	: Activator factor Protein-1
Ca	: Calcium
CAD	: Coronary artery disease
CSF	: Cerebrospinal fluid
DCCT	: Diabetes Control and Complications Trial
BMI	: Body mass index
DKA	: Diabetic ketoacidosis.
DM	: Diabetes Mellitus.
OGTT	: Oral glucose tolerance test
EPO	: Erythropoietin.
ER Kinase	: endoplasmic reticulum kinase
ESRD	: end-stage renal disease
FA	: Fructosamine

 *List of Abbreviations* 

FPG	: Fasting plasma glucose
G-Alb	: Glycated albumin
GCK	: Glucokinase
GDM	: Gestational diabetes mellitus.
HbA1c	: Glycosylated hemoglobin
HbA2	: Adult hemoglobin
HbF	: Fetal hemoglobin
PGDM	: Pregestational diabetes mellitus
PONDE	: Ponderal index
IDDM	: Insulin dependent diabetes mellitus.
IGT	: Intolerance glucose test
INS	: Insulin
IPEX Syndrome	: Immunodysregulation, polyendocrinopathy, and enteropathy, x-linked
IPF1(PDX1)	: pancreatic agenesis and insulin promoting factor 1
IUGR	: Intrauterine growth retardation
K ATP	: ATP-sensitive potassium channel
K-ATP	: Potassium mediated adenosine triphosphate
KCNJ11	: potassium inwardly-rectifying channel, subfamily J, member 11.
KIR.2,6	: Inwardly rectifying potassium channel .
LDL	: Low density lipo protein
MODY	: Maturity onset diabetes of young

 *List of Abbreviations* 

NDM	: Neonatal diabetes mellitus
NF	: Necrosis factor
NIDDM	: Non Insulin dependent diabetes mellitus.
NPH	: Neutral Protamine Hagedorn
OGTT	: Oral glucose tolerance test
GHB%	: Glycated hemoglobin
PDR	: proliferative diabetic retinopathy
MBG	: Maternal blood glucose
PNDM	: Permenant neonatal diabetes mellitus
PTF1A	: Pancreas Transcription Factor 1 Alpha
PVD	: Peripheral Vascular Disease.
RAGE	: Receptors for Advanced Glycation End Product.
NBG	: Neonatal blood glucose
RBCs	: Red blood cells
ROC	: Receiver Operator Characteristics curve
SDA	: small for gestational age
SMBG	: Self monitoring of blood glucose
SUR1	: sulfonylurea receptor 1
TGF	: Transforming growth factor
TNDM	: Transient neonatal diabetes mellitus
U.S	: United States
UKPDS	: United Kingdom Prospective Diabetes Study
UPD	: uniparentaldisomy

 *List of Abbreviations* 

VEGF	: Vascular Endothelial Growth Factor
WHO	: World health organisation
ZAC1	: Zinc finger
ZFP57	: (Zinc finger) protein regulating apoptosis and cell cycle arrest.
GA	: Gestational age
LGA	: Large gestational age
NICU	: Neonatal intensive unit
IGF-1	: Insulin-like growth factor-1
FGF-2	: Fibroblast-growth factor-2
RDS	: Respiratory distress syndrome
(NSLCS)	: Neonatal small left colon syndrome

List of Tables

Table No.	Table title	Page
Table (1)	Criteria for diagnosis of diabetes mellitus.	8
Table (2)	Whit's classification of diabetes during pregnancy.	12
Table (3)	Malformations associated with pre-existing diabetes	23
Table (4)	Etiologies of neonatal diabetes.	42
Table (5)	Hemoglobin structure.	48
Table (6)	Influential variable affecting GA/A1c ratio.	69
Table (7)	Comparison in between IDMs and INDMs as regard demographic data.	90
Table (8)	Comparison between IDMs and INDM in laboratory data.	91
Table (9)	Frequency of Co-morbidities in IDMs	93
Table (10)	Comparison in maternal data between GDM and PGDM.	94
Table (11)	Comparison between IDMs of GDM and PGDM as regard gestational age and anthropometric measures.	95
Table (12)	Comparison between GDM and PGDM in IDMs as regard laboratory investigations.	96
Table (13)	Comparison between IDMs of GDM and PGDM as regard frequency of morbidities.	98

 *List of Tables*

Table No.	Table title	Page
Table (14)	Comparison between macrosomic and non macrosomic newborn as regard gestational age and anthropometric measures.	99
Table (15)	Comparison between macrosomic and non macrosomic newborn as regard laboratory investigation.	100
Table (16)	Comparison between normoglycemic and hypoglycemic newborn as regard demographic data.	103
Table (17)	Comparison between normoglycemic and hypoglycemic newborn in laboratory investigation.	104
Table (18)	Correlations between GHB% and G-Alb with co-morbidities in infants of GDM group.	106
Table (19)	Correlations between GHB% and G-Alb with co-morbidities in infants of PGDM group.	106
Table (20)	Correlation between GHB% and G-Alb with GA and EBW and BMI in IDMs.	107
Table (21)	Correlation between MBG and NBG in IDMs.	109
Table (22)	Correlation between MBG with G-Alb in IDMs.	110

 *List of Tables*

Table No.	Table title	Page
Table (23)	Correlation between MBG with GHB% in IDMs.	111
Table (24)	Correlation between NBG with GHB% in IDMs.	112
Table (25)	Correlation between NBG with G-Alb in IDMs.	113
Table (26)	Correlation between GHB% with G-Alb in IDMs.	114

List of figures

Fig. No	Title figure	Page
Fig. (1)	Infant of diabetic mother.	17
Fig. (2)	Babygram	21
Fig. (3)	Erb's palsy. (a) Photo (b) x-ray	28
Fig. (4)	Gastrograffin enema showing abrupt transition at splenic flexure and narrow left colon	38
Fig. (5)	Each child of a parent with MODY has a 50 percent chance of inheriting the disease	44
Fig. (6)	The reaction of the non-enzymatic glycation of proteins	47
Fig. (7)	Glycation of albumin	65
Fig. (8)	Glycated albumin and diabetes complication	74
Fig. (9)	Comparison between IDMs and INDMs as regard GHB%	92
Fig. (10)	Comparison of the mean level of G-Alb between IDMs and INDMs.	93
Fig. (11)	The difference in mean of GHB% in PGDM and GDM.	97
Fig. (12)	Comparison of NBG in macrosomic newborn and non-macrosomic newborn.	101

Fig. No	Title figure	Page
Fig. (13)	The difference in level of GHB% in macrosomic and non-macrosomic newborn.	102
Fig. (14)	Comparison of the mean level of both MBG and G-Alb in macrosomic newborn and non-macrosomic newborn.	102
Fig. (15)	Comparison in level of GHB% between hypoglycemic newborn and normoglycemic newborn.	105
Fig. (16)	The difference in level of G-Alb between hypoglycemic newborn and normoglycemic newborn.	105
Fig. (17)	Correlation between EBW with GHB% within IDMs.	108
Fig. (18)	Correlation between EBW with G-Alb within IDMs.	109
Fig. (19)	Relationship between MBG and G-Alb in IDMs.	110
Fig. (20)	Correlation between MBG and GHB% in IDMs.	111
Fig. (21)	Relationship between GHB% and NBG in IDMs.	112
Fig. (22)	Correlation between G-Alb and NBG in IDMs.	113
Fig. (23)	Relationship between G-Alb and GHB% in IDMs.	114

Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in either insulin secretion or insulin action or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of different organs, especially the eyes, kidneys, nerves, heart and blood vessels(*ADA, 2010*).

Gestational Diabetes (diabetes that begins during pregnancy) can develop in overweight, hyperinsulinemic, insulin-resistant women or in thin relatively insulin-deficient women. Gestational diabetes occurs in 1 to 3% of all pregnancies but the rate may be much higher in certain groups (eg, Mexican, American, Indians, Asians, Pacific Islands) (*Thomas, 2005*).

Pregnancy aggravates preexisting type I (insulin-dependent) diabetes and type II (non insulin-dependent) diabetes but does not appear to exacerbate diabetic retinopathy, nephropathy, or neuropathy. Diabetes during pregnancy increases fetal and maternal morbidity and mortality(*Ogata, 2010*).

Neonates of diabetic mother are at risk of respiratory distress, hypoglycemia, hypocalcemia, polycythemia, hyperbilirubinemia and hyperviscosity. Poor control of

preexisting or gestational diabetes increases risk of major congenital malformations and spontaneous abortion (*Ogata, 2011*).

Hyperglycemia induces non-enzymatic glycation reactions in proteins which generates amadoric products and advanced glycation end-products; the latter are thought to participate in the vascular complications of diabetic patients (*Ahmed, 2005*).

Glycosylated hemoglobin is increased in the red blood cells of persons with poorly controlled diabetes mellitus, since the glucose stays attached to hemoglobin for the life of the red blood cells, so the level of the glycosylated hemoglobin reflects the average blood glucose level over the past 3 months (*Ruchi and William, 2010*).