Use of Hemoglobin A1c as An Early Predictor of Gestational Diabetes Mellitus

Thesis

Submitted for partial fulfillment of the Master Degree
in Obstetrics and Gynecology

By

Sayed Elsamman Elsayed
M.B.B.Ch, (2009) - Cairo University
Resident at El-Monira General Hospital

Under the Supervision of

Prof. Hesham Mahmoud Mohammed Harb
Professor of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Dr. Mohammed Hussein Mostafa
Assistant professor of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
Cairo – 2016

سورة البقرة الآية: ٣٢

Acknowledgments

First and forever, thanks to ***Allah****, Almighty for giving me the strength and faith to complete my thesis and for everything else.*

I would like to express my sincere gratitude to ***Prof. Hesham Mahmoud Mohammed Harb,*** *Professor of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University, under his supervision, I had the honor to complete this work, I am deeply grateful to him for his professional advice, guidance and support.*

My deep gratitude goes to ***Dr. Mohammed Hussein Mostafa,*** *Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University, for his invaluable efforts and tireless guidance and meticulous supervision throughout this work.*

Last but not least, I like to thank all my ***Family****, especially my beloved* ***Parents*** *for their kind care, help and encouragement.*

Sayed ElSamman

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List of Abbreviations

Abbr.	Title

ACOG ..... American College of Obstetricians and Gynecologists

ACSM ..... American College of Sports Medicine

ACTH……. Adrenocorticotropic hormone

ADA ..... American Diabetes Association

AHA ..... American Heart Association

ATP ..... Adenosine triphosphate

BMI ..... Body mass index

CNS ..... Central nervous system

CSII ..... Continuous subcutaneous insulin infusion pump

CVD ..... Cardiovascular disease

DM ..... Diabetes Mellitus

FDA..... Food and Drug Administration

FFA ..... Free fatty acids

GCT ..... Glucose challenge test

GDM ..... Gestational diabetes mellitus

GINF ..... Glucose infusion

GLUT 4..... Glucose transporter 4

HCS..... Human chorionic somatomammotropin

HDL-C ..... High-density lipoprotein cholesterol

HOMA ..... Homeostatic Model Assessment

IDF ..... International Diabetes Federation

IGT.....Impaired glucose tolerance

IL.....Interleukins

IR.....Insulin resistance

Kcal .....Kilo calories

LD .....Lipodystrophy

LDL-C.....Low-density lipoprotein cholesterol

MCP-1.....Monocyte chemoattractant protein-1

MDI.....Multiple daily injections

MS .....Metabolic syndrome

NAFLD .....Nonalcoholic fatty liver disease

NASH .....Nonalcoholic steatohepatitis

NDDG .....National Diabetes Data Group

NPH.....Isophane insulin

OGTT .....Oral glucose tolerance test

PCOS .....Polycystic ovarian syndrome

QUICKI ....Quantitative insulin sensitivity check index

T2DM.....Type 2 diabetes mellitus

TG .....Triglycerides

TNF-α .....Tumor necrosis factor-α

TZDs .....Thiazolidinediones

UK.....United Kingdom

US.....Ultrasound

VLDL-C.....Very-low-density lipoprotein cholesterol

WHO.....World Health Organization

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Abstract

Background: The prevalence of GDM is rising worldwide with 1% to 14% of pregnancies being affected. In low-risk populations, the estimated GDM prevalence is 1.4% to 2.8%; in higher risk populations, the estimated prevalence is 3.3% to 6.1% and in some high-risk populations, the prevalence may be higher than 10%. **Aim of the Work:** The purpose of this study is to assess an early hemoglobinA1c (HgbA1c) value as an early predictor of progression to gestational diabetes (GDM). **Materials and Methods:** Subjects: This study was conducted at Ain Shams University Maternity Hospital from March 2016 to July 2016. It is a prospective cohort study which included 220 pregnant women in their first trimester who regularly attended the outpatient clinic for routine antenatal care were 200 women. The remaining 20 were dropped out from the study, 10 women developed abortion and the others discontinued there antenatal care. **Results:** The study showed a statistically significant difference between women with a hemoglobin A1c value [<5.7% vs. 5.7-6.4%] according gestational age at hemoglobin A1c testing. **Conclusion:** An HgbA1c level of 5.7-6.4% is an effective means of identifying patients at the highest risk of the development of GDM. It may be most prognostic in an obese population. Its efficacy has been demonstrated when the sample is drawn during the first trimester and may be effective up to 20 weeks of gestation. This information may help providers target the patients who will benefit the most from GDM screening and treatment. **Recommendations:** HbA1c test does not need fasting and would be more comfortable for pregnant women than the OGTT and fasting glucose insulin ratio. Nevertheless, its use for the diagnosis of GDM has not yet been recommended by any current guidelines.

Key words: GDM, HgbA1c, OGTT, pregnancy

Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance that has onset during pregnancy. The incidence of GDM is rising, parallel to the increase in maternal age, type II diabetes and obesity prevalence **(El-Chaar et al., 2013).**

The prevalence of GDM is rising worldwide with 1% to 14% of pregnancies being affected **(Han et al., 2012).** In low-risk populations, the estimated GDM prevalence is 1.4% to 2.8% **(Noctor et al., 2013);** in higher risk populations, the estimated prevalence is 3.3% to 6.1% and in some high-risk populations, the prevalence may be higher than 10% **(Noctor et al., 2013).**

There is a range of known health risks associated with pregnancy hyperglycaemia without meeting GDM diagnostic criteria. A large multicentre and multiethnic cohort study (HAPO study) of 25,505 women assessed the effect of maternal hyperglycaemia on pregnancy outcomes. This study found a significant, continuous association between maternal glucose concentrations below those for a diagnosis of GDM and caesarean section and pre-eclampsia **(Han et al., 2012).**

Associated fetal risks of GDM include fetal death, macrosomia, shoulder dystocia, neonatal hypoglycemia, respiratory distress syndrome, and childhood obesity**(Fong et al., 2014).**

GDM also carries an economic burden that results in an increase of 25-34% in maternity care costs and a 49% increase in neonatal intensive care unit costs, compared with those pregnancies without GDM (**Richard et al., 2013; Gillespie et al., 2013).**

Identification and treatment of even mild GDM may reduce adverse pregnancy outcome, which underscores the need to screen properly for and diagnose this important comorbidity **(Landon et al., 2009).**

Screening and diagnosis of GDM is frequently delayed until 24–28 weeks of pregnancy based on the assumption that the diabetogenic effects of pregnancy increase as gestation advances **(Middleton et al., 2012).**

However prediction of gestational diabetes in early pregnancy has been the subject of many studies with the aim of initiating early treatment and lifestyle changes **(Yeralet al., 2014).**

HbA1c became firmly established as a critical diabetes control measure through the findings of the land-mark diabetes control and complications trial which conclusively demonstrated that a sustained lowering of HbA1c was associated with significantly fewer microvascular complications. Glycated haemoglobins are formed when glucose in the blood spontaneously reacts with the amino groups of the haemoglobin protein **(Ozgu-Erdinc et al., 2014).**

Glycated hemoglobin (HgbA1c) is aform of hemoglobin that characterizes apatient's plasma glucose over a prolongedperiod of time. It is typically used in thenonpregnant population as both ascreening tool for diabetesmellitus and asa tool to assess the glycemic control ofknown diabetic patients (**American Diabetes Association,2012).**

Normalvalues for HgbA1c in pregnancy innondiabetic women identified anormal reference interval of 4.3-5.4% inthe first trimester. In the nonobstetricpopulation, it has been shown that anHbgA1C value of 5.7-6.4% indicatesimpaired glucose tolerance and a highrisk of future diabetes**(O'Connor et al.,2012).**

Risk of malformations in a group of newborns born to mothers is varied with respect to HbA1C, if the HbA1C level during the first trimester of pregnancy did not exceed a value of 8.5% the risk of malformation was 3.4% and if the maternal HbA1C from the first trimester exceeded 9.5% then this was related to a 22.0% risk of malformation**(Miller et al., 2001)**.

The effectiveness of preconception care in reducing congenital malformations is impressive and has practical implication considering the recent report of the Confidential Enquiry into Maternal and Child Health (CEMCH) which showed that congenital malformations rate in infants of diabetic mothers in England, Wales and Northern Ireland is more than twice the background population rate. This finding is also of a paramount importance to many communities in the Middle East, North Africa and some communities in Asia where the burden of congenital malformation is very high due to many causes including maternal diabetes (**Jaouad et al., 2009)**.

Key differences observed in the recommendations are target levels of HbA1C to be achieved prior to pregnancy. Aiming the HbA1C level at < 1% above the upper limit of