Role of first Trimester Maternal Serum Uric Acid Concentration in Prediction of Gestational Diabetes

Thesis

Submitted for partial fulfillment of master degree of family medicine

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List of abbreviations

ACHOIS	Australian Carbohydrate Intolerance Study
ADA	American diabetes association
AMP	Adenylic acid
AMPK	Adenosine monophosphate-activated protein kinase
BIAsp	Biphasic insulin aspart
BMI	Body mass index
CFU	Colony forming unit
CGMS	Continuous glucose monitoring systems
CHARGE	Childhood Autism Risks from Genetics and the Environment
CI	Confidence interval
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
DNA	Deoxyribonucleic acid
FDA	Food and Drug Administration
FPG	Fasting plasma glucose
GAD	Glutamic acid decarboxylase
GDM	Gestational diabetes mellitus
GFR	Glomerular filtration rate
HAPO	Hyperglycemia and Adverse Pregnancy
HbA1c	Glycosylated hemoglobin
IADPSG	The International Association of the Diabetes and Pregnancy Study Groups
IMP	Inosinic acid
IRS-1	Insulin receptor substrate-1
IU	International unit
LGA	Large-for-gestational age
MODY	Maturity onset diabetes of the young.
MPC	Model predictive control
NCCWCH	National Collaborating Centre for Women's and Children's Health
NDDG	National Diabetes Data Group
NHS	National Health Service
NICE	National institute for health and care excellence
NPH	Neutral Protamine Hagedorn (Humolin; long acting insulin).
OGTT	Oral glucose tolerance test
OHAs	Oral hypoglycemic agents
OR	Odds ratio
PKA	acid dissociation constant
PE	Pre-eclampsia
PCOS	Poly cystic ovary syndrome
RHI	Regular human insulin
T1DM	Type-1 diabetes mellitus
T2DM	Type-2 diabetes mellitus
TB	Tuberculosis
TRIGR	Trial to Reduce Insulin-dependent Diabetes Mellitus in the Genetically At Risk
UK	United kingdom
WHO	World health organization

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Role of first Trimester Maternal Serum Uric Acid Concentration in Prediction of Gestational Diabetes

ABSTRACT

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Introduction:

. Women who have had GDM are much more likely to develop type 2 DM later in life. Polyhydramnios, preterm labor, pyelonephritis, hypertension and preeclampsia were more frequent in GDM. Maternal hyperglycemia leads to intrauterine hyperglycemia, fetal hyper- insulinemia, shoulder dystocia, hyperbilirubinaemia, respiratory distress syndrome birth injuries, perinatal mortality, polycythaemia, caesarean delivery and congenital anomalies we use new method for screeninig of GDM **Materials and Methods** Cohort study, carried out in the period between March 2015 and April 2016. Pregnant women at first trimester (10-13wks) susceptible to diabetes mellitus attending Al-azhar University Hospital (Damietta) at department of Obstetrics and Gynecology.

. **Results**:The majority of females (80.9%) were from rural area.47.9% had primary education;66% of females were housewives;age ranged from 18 to 45 years with mean of 27.08±5.80 years. Females developed gestational diabetes mellitus were 31 cases (33.3%).There is strong association between high uric acid level in 1st trimestr and subsequent development of GDM in 3rd trimestr with R.R 4.1. The mean age of those who suffered from GDM was signifiecally hiegher than those who were free from it (29.25±5.65 vs 26.01±5.61 respectively).

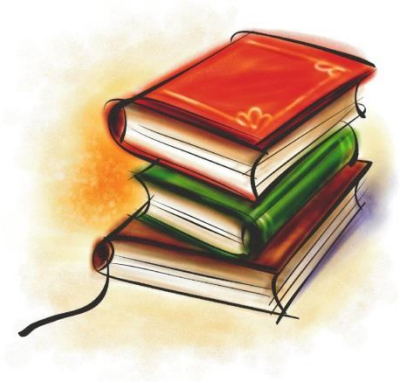
Women with positive family history for hypertension and with past history of GDM suffered from GDM at a higher level than those with negative history and the difference was statisticaly significant.

Although those who had a positive family history of diabetes had a higher level of developing GDM , yet the relation didn't reach the level of the of the statistically significant difference.

The BMI ranged from 22.20 to 72.20 with mean of 32.99±6.70 kg/m^2; and there was significant obesity in positive GDM group when compared to negative GDM group (36.36±6.27 vs 31.33±6.08 respectively).

The serum uric acid ranged from 1.2 to 6.60 with a mean of 3.71±1.19 mg/dl; and there was a significant increase of uric acid conc in positive GDM group when compared to negative GDM group (4.48±0.84 vs 3.33±1.16 respectively).**Conclusion** Elevated first-trimester uric acid concentration was correlated with an increased risk of developing GDM. The risk of developing GDM was 4-fold higher if first-trimester uric acid was ≥ 4mg/dl.The mean BMI was significantly higher in women who developed GDM when compared to women who did not develop GDM[(36.36±6.27vs31.33±6.08 respectively).The mean age of those who suffered from GDM was signifiecally hiegher than those who were free from it (29.25±5.65 vs 26.01±5.61 respectively)

Key words: gestational diabetes,Uric acid,screening .family medicine



Introduction and Aim of the work

Introduction

Gestational diabetes mellitus (GDM), defined as two or more elevated glucose values obtained during a 3-hours oral glucose tolerance test (OGTT[)] **(WHO, 1999).** It affects between 17-27% of pregnancies depending on diagnostic criteria and population **(Gollenberg et al**., **2010)**. GDM is one of the most common medical disorders during pregnancy **(Vibeke et al., 2008).**

GDM prevalence has increased in several racial and ethnic groups during the past 20 year (**Horvath et al., 2010)**. The prevalence of GDM in, the US (4.8%) **(Keshavarz et al., 2005)**, France (12.1%) **(Schneider et al., 2010)** Canada (17.8%) (**Ryan, 2011),** and Australia (9.5%) **(Moses et al., 2011).**

The prevalence in Arab countries is consider high as Qatar was 16.3%**;** In the United Arab Emirates (20.6%) **(Agarwal et al., 2007)** and in Bahrain and Saudi Arabia (12.5%) **(Horvath et al., 2010).**

Women who have had GDM are much more likely to develop type 2 DM later in life. Polyhydramnios, preterm labor, pyelonephritis, hypertension and preeclampsia were more frequent in GDM. Maternal hyperglycemia leads to intrauterine hyperglycemia, fetal hyper-insulinemia, shoulder dystocia, hyperbilirubinaemia, respiratory distress syndrome birth injuries, perinatal mortality, polycythaemia, caesarean delivery and congenital anomalies (**Ryan, 2011)**.

Renal vein thrombosis has also been reported to result from polycythaemia. The fetal lung maturation will be delayed in diabetics **(Cheema et al., 2010).**

GDM is associated with poor pregnancy outcomes; also less severe forms of glucose intolerance are associated with increased feto-maternal morbidity **(Shand et al.,** 2008**).** Perinatal mortality was noted in approximately 2.8% and congenital malformations in 6.4% **(Horvath et al**., **2010).**

The complications associated with GDM can affect both the mother and the fetus which can be avoided by early prediction **(Dabela et al**., **2005**).Several studies have now shown that, compared to their peers, women who go on to develop GDM later in pregnancy have biochemical abnormalities that can be detected in the first trimester including increased levels of uric acid (**Hedderson et al., 2008).**

Uric acid is the end product of purine metabolism and is synthesized by the enzyme xanthine oxidas **(Dincer et al., 2002):** Uric acid is associated with insulin resistance in non pregnant women **(Modan et al**., **1987**).

Outside of pregnancy, hyperuricemia is also associated with the markers of metabolic syndrome, including obesity and dyslipidemia **(Güngör et al., 2006).**

Uric acid is an independent risk factor for developing type-2 diabetes within 10 years in non-pregnant women, an association that was stronger in women compared to men **(Masuo et al**., **2010**).

During pregnancy, the glomerular filtration rate (GFR) increases by ~50%, thereby decreasing the serum creatinine and the uric acid levels. However, the creatinine levels towards the upper limit of the normal range are a warning sign of impending renal disease in GDM. The raised uric acid levels in GDM are a component of the metabolic syndrome that reflects insulin resistance **(Masuo et al**., **2010**).

Alongside the development of new guidance for diabetes in pregnancy concluded that screening and treatment for GDM was cost-effective for the National Health Service (NHS) (**Coutinho et al**., **2007**).

The American Diabetes Association, the American College of Obstetricians and Gynecologists , and the World Health Organization recommend screening most pregnant women for gestational diabetes between 24 and 28 weeks' gestation and screening high-risk pregnant women **(Jensen et al., 2011).**

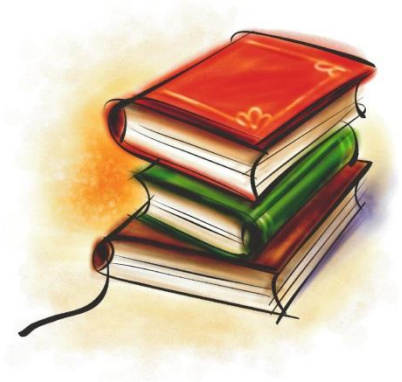
The Hyperglycemia and Adverse Pregnancy outcome (HAPO) group sought to identify new screening values that would better identify pregnancies at risk for perinatal complications. The HAPO study demonstrated a positive linear relationship between screening glucose values and adverse perinatal outcomes **(NCCWCH, 2008).**

Some groups have demonstrated that current screening protocols fail to identify many at-risk pregnancies **(Landon et al., 2011).**

Given the many changes that adopting a new strategy for GDM screening may have on our health care system, it is critical to assess the costs and effects of the approach, it would impact over 4 million pregnant women and result in over 500,000 additional diagnoses of GDM annually in the U.S. alone **(Cowie et al**., **2010**). Also there is a gap of knowledge about the relation between both of uric acid and GDM , we go on through this study aiming to increase our knowledge about it.

Aim of the study

The aim of this study is to determine the role of first trimester maternal serum uric acid concentration in predicting the subsequent development of gestational diabetes mellitus for high risk female.



Review of Literature

Gestational diabetes

Gestational diabetes is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy whether or not insulin is used for treatment **(ACOG, 2013).** It is diagnosed by two or more elevated glucose values obtained during a 3-hours oral glucose tolerance test (OGTT) **(WHO, 1999).**

Epidemiology:

GDM prevalence has increased in several racial and ethnic groups during the past 20 year (**Horvath et al., 2010)**. The prevalence of GDM in, the US (4.8%) **(Keshavarz et al., 2005)**, France (12.1%) **(Schneider et al., 2010)** Canada (17.8%) (**Ryan, 2011),** and Australia (9.5%) **(Moses et al., 2011).**

The prevalence in Arab countries is consider high as Qatar was 16.3%**;** In the United Arab Emirates (20.6%) **(Agarwal et al., 2007)** and in Bahrain and Saudi Arabia (12.5%) **(Horvath et al., 2010).**

The number of adults diagnosed with diabetes in the United States has tripled from 6.9 million in 1991 to 20.9 million in 2011. Diabetes mellitus is the commonest medical condition complicating pregnancy, affecting up to 5% of pregnancies in England and up to 25% of pregnancies in Asia. Prevalence of GDM is increasing all over the world due to increased incidence of risk factors for the development of GDM **(Bellamy et al., 2009)**.

Risk factors:

- Women with a history of gestational diabetes have also increased risk of developing gestational diabetes in subsequent pregnancies **(Bottalico, 2007)**