Serum Visfatin Level in Women with Gestational Diabetes Mellitus

Thesis

Submitted for Partial Fulfillment of Master's Degree in Endocrinology and Metabolism

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2018

سورة البقرة الآية: ٣٢

Acknowledgment

Firstly, I wanted to thank Allah for granting me the opportunity to continue my learning path and accomplish one of my biggest goals.

I would like to express my appreciation and profound gratitude to ***Prof. Dr. Nehad Shokry Shoeib,*** *Professor of Internal Medicine and Endocrinology-Faculty of Medicine, Ain Shams University, for her support, kind supervision, valuable advice and continuous encouragement, which made the completion of this work possible.*

I also wanted to express my deepest gratitude to ***Dr. Maram Mohamed Maher Mahdy,*** *Assistant Professor of Internal Medicine and Endocrinology- Faculty of Medicine, Ain Shams University, for her care, continuous supervision, valuable instructions, constant help and great assistance throughout this whole process.*

I am deeply thankful to ***Dr. Nesma Ali Ibrahim,*** *Lecturer of Internal Medicine and Endocrinology- Faculty of Medicine, Ain Shams University, for her continuous guidance, support, encouragement and active participation, she has been a role-model and an older sister, being very patient and kind through every step.*

I wanted to express the deepest respect and gratitude to ***Prof. Hanan Amer,*** *Professor of Internal Medicine and Enocrinology- Faculty of Medicine, Ain Shams University, and* ***Prof. Nouran Ghandour,*** *Professor of Internal Medicine and Endocrinology Faculty of Medicine, Cairo University, for their kindness, supervision and cooperation.*

I would like to express my deepest gratitude to ***Dr Mohammed Halawa,*** *Professor of Internal Medicine and Endocrinolgy-Faculty of Medicine, Ain Shams University, for his guidance and support.*

Last but not least, I wanted to thank my ***twin sister*** *Amina Negm,* ***my mother*** *Nevine Khaled,* ***and my father*** *Aly Negm. They have stood by me, supported me, guided me and helped me accomplish everything I have ever wished for; I would be nothing without them. I wanted to thank my grandparents, Samia and Khaled Hussein, who have been my biggest blessing. I wanted to thank all my family and friends for their continuous support through-out the whole process, they make this world a better place.*

I wanted to wish my sincere appreciation to all the patients, the statistician, the pathologist, and the publisher that helped and participated in our work, it would not have been possible without them.

Eman Negm

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List of Abbreviations

Abb.	Full term
AIT	*Autoimmune thyroiditis*
BMI	*Body mass index*
CRP	*C-reactive protein*
DNL	*De Novo Lipogenesis*
EDTA	*Ensure mixing of anticoagulant*
ELISA	*Enzyme Linked-Immunosorbent Assay*
GDM	*Gestational diabetes mellitus*
HDL	*High-density lipoproteins*
HRP	*Horseradish Peroxidase*
IG	*Impaired glucose*
IL-6	*Interleukin-6*
IQR	*Interquartile range*
IR	*Insulin resistance*
LDL	*Low-density lipoproteins*
MAPK	*Mitogenactivated protein kinase*
MAPK	*Mitogenactivated protein kinase*
NAD	*Nicotinamide adenine dinucleotide*
NAFLD	*Nonalcoholic fatty liver disease*
NASH	*Non-alcoholic steatohepatitis*
OGTT	*Oral glucose tolerance test*
PBEF	*Pre-B-cell colony-enhancing factor*
PCOS	*Polycystic Ovary Syndrome*
PIK3	*Phosphotidylinositol 3-kinase*
SD	*Standard deviation*
SPSS	*Statistical package for Social Science*
SST	*Serum separator tube*
T2DM	*Type 2 diabetes mellitus*
VLDL	*Very-low-density lipoproteins*
WTHR	*Waist to hip ratio*

INTRODUCTION

Pregnancy presents a unique situation in which transient physiological insulin resistance, approaching levels observed in type 2 diabetes mellitus patients, often forms in order to facilitate nutrient delivery to the developing fetus ***(Ryan, 2003).***

Notably, pregnancy is also associated with the most dramatic increase in adipose tissue observed during adulthood. Both insulin resistance and reduced insulin secretion in gestational diabetes mellitus (GDM) have been linked to genetic traits, though insulin resistance (IR) is generally considered to play the dominant role ***(Lopez-Bermejo et al., 2006).***

Epidemiologic studies have revealed that the prevalence of gestational diabetes mellitus (GDM) has increased over time, along with the increase in the prevalence of obesity ***(Dabelea et al., 2005)***. Hence, in parallel with the explosion of the obesity and metabolic syndrome in younger adults, incidence of GDM will undoubtedly continue to increase in coming years ***(Rezvan et al., 2012).***

According to a 2014 analysis by the Centers for Disease Control and Prevention, the prevalence of gestational diabetes is as high as 9.2% ***(American Diabetes Association, 2014).***

Women with GDM are at increased risk for developing type 2 diabetes; how-ever, the pathophysiology is still poorly understood. Nonetheless, a variety of abnormalities that are also found in patients with type 2 diabetes are seen early in women in GDM ***(Buchanan and Xiang, 2005).***

Among the factors that might contribute to altered glucose handling are changes in adipocytokines. For example, plasma adiponectin concentrations are lowered and leptin and resistin persistently increased after delivery in women with GDM and are associated with hyperglycemia and insulin resistance ***(Winzer et al., 2004).***

Adipocytokines, the bioactive proteins produced by adipose tissue, have recently been implicated in mediating insulin resistance. It has been suggested that hormones secreted by the placenta and cytokines secreted by adipose tissues are related to the development of IR during pregnancy, possibly playing an important role in the pathogenesis of gestational diabetes mellitus ***(Harlev and Wiznitzer, 2010).***

Visfatin is a newly discovered 52 kDa adipocytokine hormone in humans, it's preferentially produced by visceral adipose tissue ***(Zhao et al., 2014).***

It exerts an insulin-like effect by binding to the insulin receptor-1. A firm correlation has been previously established

between plasma visfatin levels and type 2 diabetes mellitus, and recent research also suggests that circulating maternal visfatin levels could play a role in the development GDM ***(Mazaki-Tovi et al., 2009).***

Though the role of visfatin in human GDM remains controversial, it is likely that visfatin is involved in the pathogenesis of GDM. In fact, circulating maternal visfatin concentrations of the plasma and serum have been reported to be both higher and lower in GDM patients compared with healthy pregnant women by different studies, contributing to the controversial role of visfatin in GDM ***(Karrasch et al., 2014).***

Aim of the Work

The aim of this study was to estimate serum visfatin level among women with gestational diabetes mellitus, and its association with glycemic control, insulin resistance and lipid profile.

Chapter 1

GESTATIONAL DIABETES MELLITUS

Definition and Pathology:

Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy. As such, GDM is the product of routine glucose tolerance screening that is currently carried out in otherwise healthy individuals. Like other forms of hyperglycemia, GDM is characterized by pancreatic β-cell function that is insufficient to meet the body's insulin needs. Available evidence suggests that β-cell defects in GDM result from the same spectrum of causes that underlie hyperglycemia in general, including autoimmune disease, monogenic causes, and insulin resistance. Thus, GDM often represents diabetes in evolution and, as such, holds great potential as a condition in which to study the pathogenesis of diabetes and to develop and test strategies for diabetes prevention ***(Barbour et al., 2007)***.

The full array of causes of hyperglycemia in GDM is not known. However, available data suggest that GDM results from a spectrum of metabolic abnormalities that is representative of the causes of hyperglycemia in relatively young individuals. In many, perhaps most women with GDM, the abnormalities appear to be chronic in nature, detected by routine glucose

screening in pregnancy. They are frequently progressive, leading to rising glucose levels and eventually to diabetes. Thus, GDM can be viewed largely as diabetes in evolution that provides important research and clinical care opportunities. Regarding research, GDM offers a strong opportunity to study the early biology of diabetes. Cross-sectional studies could identify metabolic abnormalities in different subsets of prior GDM, including important ethnic differences in contributions of obesity, adipose tissue biology, insulin resistance, and β-cell dysfunction to the pathogenesis of non-immune diabetes ***(Jarvela et al., 2006)***.

Pathophysiology:

Women with GDM are at increased risk for developing type 2 diabetes; how-ever, the pathophysiology is still poorly understood ***(Buchanan and Xiang, 2005).***

Among the factors that might contribute to altered glucose handling are changes in adipocytokines. For example, plasma adiponectin concentrations are lowered and leptin and resistin persistently increased after delivery in women with GDM and are associated with hyperglycemia and insulin resistance ***(Winzer et al., 2004)***.

One main aspect of the underlying pathology is insulin resistance, where the body's cells fail to respond to the hormone

insulin in the usual way. Several pregnancy hormones are thought to disrupt the usual action of insulin as it binds to its receptor, most probably by interfering with cell signaling pathways. The body then compensates by producing more insulin to overcome the resistance and in gestational diabetes, the insulin production can be up to 1.5 or 2 times that seen in a normal pregnancy ***(National Health Service United Kingdom, 2016).***

Symptoms of gestational diabetes mellitus include:

The condition is usually asymptomatic, but symptoms if available are:

- Excessive thirst with dry mouth.
- Frequent urination.
- Recurrent infections including thrush or yeast infection Weakness.
- Blurred vision.

Gestational diabetes raises the risk of birth complications and future health conditions. Some examples are given below:

- Premature birth.
- Macrosomia.
- Placental abruption, which can be fatal to both mother and baby.
- Trauma during delivery.