بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

The Association Between Increase of Serum Fructosamine and Unexplained Recurrent Pregnancy Loss

Thesis

Submitted For Partial Fulfillment of Master Degree in Obstetrics & Gynaecology

By

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Acknowledgment

First and foremost, I feel always indebted to ALLAH, the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to ***Prof. Dr. Ihab Fouad Serag Eldeen Allam,*** *Professor of Obstetrics & Gynecology Faculty of Medicine - Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to ***Prof. Dr. Abdellatif Galal El Kholy,*** *Professor of Obstetrics & Gynecology Faculty of Medicine - Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I am deeply thankful to ***Dr. Gihan El Sayed El Hawwary,*** *Lecturer of Obstetrics & Gynecology Faculty of Medicine - Ain Shams University, for her great help, active participation and guidance.*

Kholoud Ibrahim Ameen Salaama

Dedication

Words can never express my sincere thanks to ***My Family, My Loving Husband Abdellatif and My Loving Son Maher*** *for their generous emotional support and continuous encouragement, which brought the best out of me. I owe them all every achievement throughout my life.*

I would like to express my everlasting gratitude to all ***My Professors, Colleagues and Friends, (special thanks to Laboratory El Mokhtabar)****, so many of them influenced, encouraged and inspired me throughout the years. I wish them the best of all.*

I would like also to thank the ***patients*** *who agreed willingly to be part of my study and without them; I would not have been able to accomplish this work.*

ABSTRACT

Background: Recurrent pregnancy loss (RPL) is one of the most frustrating and difficult areas in reproductive medicine because the etiology is often unknown. Endocrine factors may account for 15 to 60 percent of RPL. Pre-gestational diabetes is associated with an elevated risk of pregnancy loss, but it is unclear whether subclinical glucose intolerance is associated with pregnancy loss or not, especially recurrent pregnancy loss (RPL).

Objective: comparing maternal serum fructosamine in patients with and without RPL to determine whether increase serum fructosamine is associated with RPL**.**

Patients and Methods: This case control study was conducted on Ain Shams University Maternity Hospital, antenatal care clinic and contraception clinic from December 2018 to August 2019. The population of this study was women with recurrent miscarriage attended Ain Shams University Maternity Hospital age 20-40 years with BMI < 30 kg/m2 with two or more unexplained pregnancy losses prior to 20 weeks' gestation with no more than one live birth (cases). Women had at least one uncomplicated full-term delivery (control group) and all the husbands had a spermiogram within normal limits. Maternal serum was analyzed for fructosamine on quantitative spectrophotometry

Results: serum fructosamine was higher in women with RPL compared with controls. Comparative study between RPL group and control shows non-significant difference as regards age, BMI and residence. Serum fructosamine had no relation to BMI in RPL patients**.**

Conclusion: In our study, analysis of data revealed that serum fructosamine was increased in RPL group compared to control group. By using ROC-curve analysis, serum fructosamine level at a cutoff point (>231) predicted women with abortion event, with fair (76%) accuracy, sensitivity= 60% and specificity= 82% ($p < 0.01$). Thus, subclinical glucose intolerance may be associated with an increased risk of RPL. Spearman's correlation analysis shows that; age and serum fructosamine had a highly significant positive correlation with RPLs however parity had a highly significant negative correlation with RPL. Multiple regression analysis shows that; after applying (backward method) and entering some predictor variables; the increase in serum fructosamine; had an independent effect on increasing RPLs. Logistic regression analysis shows that; after applying (backward method) and entering some predictor variables; the increase in serum fructosamine; had an independent effect on increasing the probability of abortion event.

Keywords: Recurrent pregnancy loss, fructosamine, BMI.

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List of Abbreviations

Abb.	Full term
AFC	Antral follicle count
AMH	Anti-müllerian hormone
ANA	Antinuclear antibody
aPL	Antiphospholipid antibodies
APS	Antiphospholipid syndrome
ASRM	American Society for Reproductive Medicine
DIEP	Diabetes In Early Pregnancy
E2	Estradiol
ERA	Endometrial receptivity analysis
ESRD	End stage renal disease
FSH	Follicle stimulating hormone
GA	Glycated albumin
GCT	Glucose challenge test
GDM	Gestational diabetes mellitus
GM-CSF	Granulocyte macrophage-colony stimulating factor
HbA1c	Glycated hemoglobin
hCG	Human chorionic gonadotropin
HLA-G	Human leukocyte antigen-G
HLAs	Human leukocyte antigens
hMG	Human menopausal gonadotropin
HPV	Human papillomaviruses
HSG	Hysterosalpingography
IgG	Immunoglobulin G
IL	Interleukin
IUGR	Intrauterine growth restriction

List of Abbreviations Cont...

Abb.	Full term
IVF	In vitro fertilization
LH	Luteinizing hormone
LMWH	Low-molecular weight heparin
LPS	Lipopolysaccharide
M-CSF	Macrophage-colony stimulating factor
MRI	Magnetic resonance imaging
NGSB	National glycohemoglobin standardization program
NICHD	National Institute of Child Health and Human Development
NQMC	National quality measures clearinghouse
OGTT	Oral glucose tolerance test
PCOS	Polycystic ovary syndrome
pET	Personalized embryo transfer
PGE2	Prostaglandin E2
PGS	Preimplantation genetic screening
QOFG	Quality and outcomes framework guidance
RCOG	Royal College of Obstetricians and Gynaecologists
RPL	Recurrent pregnancy loss
TGF-beta	Transforming growth factor-beta
TLR4	Toll-like receptor 4
TNF-alpha	Tumor necrosis factor-alpha
TPO	Thyroid peroxidase
Tregs	T regulatory cells
TVS	Transvaginal ultrasound
WHO	World Health Organization

Protocol

PROTOCOL OF A THESIS FOR PARTIAL FULFILMENT OF MASTER DEGREE IN OBSTETRICS & GYNAECOLOGY

Title of the Protocol: The association between increase of serum fructosamine and unexplained recurrent pregnancy loss.

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What is already known on this subject? AND What does this study add?

Recurrent pregnancy loss (RPL) is one of the most frustrating and difficult areas in reproductive medicine because the etiology is often unknown. Endocrine factors may account for 15 to 60 percent of RPL. Pre-gestational diabetes is associated with an elevated risk of pregnancy loss, but it is unclear whether subclinical glucose intolerance is associated with pregnancy loss or not, especially recurrent pregnancy loss (RPL).This study compares maternal serum fructosamine in patients with and without RPL.

1.INTRODUCTION/ REVIEW

Recurrent pregnancy loss (RPL) is one of the most frustrating and difficult areas in reproductive medicine because the etiology is often unknown and there are few evidence-based diagnostic and treatment strategies. Studies on the etiology, evaluation, and management of RPL are often flawed ***(Christiansen et al., 2005).***

The definition of RPL varies, which makes studying the phenomenon, and determining which couples to counsel or treat, more challenging. As examples, varying definitions have included:

- Two or more failed clinical pregnancies as documented by ultrasonography or histopathologic examination ***(ASRM, 2013).***
- Three consecutive pregnancy losses, which are not required to be intrauterine ***(RCOG, 2011).***

In response to these varied definitions, the European Society of Human Reproduction and Embryology released a 2014 consensus statement proposing that RPL describes repeated pregnancy loss, regardless of anatomic location, but they did not recommend the number of losses required for the problem to be defined as recurrent ***(Kolte et al., 2015).***

RPL can be further divided into primary or secondary processes. Primary RPL refers to pregnancy loss in women who have never carried to viability. In contrast, secondary RPL refers to pregnancy loss in a

woman who has had a previous live birth. The prognosis for successful pregnancy is better with secondary RPL ***(Paukku et al., 1999).***

Couples who have had a pregnancy loss have two major concerns: the cause and the risk of recurrence. Unfortunately, the cause of RPL can be determined in only 50 percent of patients ***(Abramson and Stagnaro, 2001).***

Once a woman has a history of two unexplained miscarriages, she and her partner should be evaluated for factors associated with RPL. According to the American Society for Reproductive Medicine's guidelines from 2012, the standard evaluation consists of screening for a maternal or paternal translocation, structural uterine factors, antiphospholipid syndrome, diabetes mellitus, PRL abnormalities, and thyroid disorders. ***(ASRM, 2012)***

One method to assess subclinical diabetes is by testing biomarkers correlated with glucose tolerance such as fructosamine. Fructosamine is an indicator of mean blood glucose similar to glycated hemoglobin (HbA1c). Instead of measuring HbA1c, the fructosamine assay measures glycated serum proteins such as albumin. Fructosamine can be related to blood glucose using the following formula: fructosamine =(HbA1c–1.61)×58.82.4, thus for every 16-mg/dL rise in mean blood glucose (0.5% rise in HbA1c), there is a corresponding 20-μmol/mL rise in fructosamine. Because of the rate of turnover of the relevant glycated proteins, the fructosamine level represents serum glucose averaged over 1–3 weeks. In addition, unlike HbA1c, fructosamine can be reliably measured in frozen/thawed serum samples ***(Delgado et al., 2011).***

Pre-gestational diabetes is associated with an elevated risk of pregnancy loss, but it is unclear whether subclinical glucose intolerance is associated with pregnancy loss or not, especially recurrent pregnancy loss (RPL) ***(Jauniaux et al., 2006).***

2.AIM / OBJECTIVES

1. **Research hypothesis:** In women with RPL there may be no association with subclinical glucose intolerance.

2. **Research question:** In women with RPL is there any association with subclinical glucose intolerance??