

Assessment of Platelet Aggregation Function in Women with Unexplained Recurrent Miscarriage

Thesis

Submitted for Partial Fulfillment of Master Degree
in Obstetrics & Gynecology

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
AA	: Arachidonic acid
ACA	: Anticardiolipin antibody
aCL	: Anticardiolipin antibodies
ACOG	: American College of Obstetricians and Gynecologists
ADP	: Adenosine diphosphate
ANA	: Antinuclear antibody
APS	: Anti-phospholipid syndrome
AUC	: Area under the curve
BMI	: Body mass index
cAMP	: Cyclic adenosine monophosphate
CI	: Confidence interval
cMPs	: Circulating microparticles
Coll	: Collagen
COX	: Cyclooxygenase
DAG	: Diacylglycerol
DF	: Degree of freedom
DNA	: Deoxy ribonucleic acid
EPI	: Epinephrine
ESHRE	: European Society of Human Reproduction and Embryology

FcR	: Fragment, crystallizable region
FSH	: Follicle stimulating hormone
Gal-1	: Galectin-1
G-CSF	: Granulocyte colony-stimulating factor
Gd	: Glycodelin
GP	: Glycoprotein
GPL	: G phospholipids (GPL),
hCG	: Human chorionic gonadotropin
IDO	: Indolamine 2-3 deoxy-genase
IgG	: Immunoglobulin G
IL	: Interleukin
IP3	: Inositol triphosphate
IVF	: In vitro fertilization
IVIg	: Intravenous immunoglobulin
LDA	: Low-dose aspirin
LH	: Luteinizing hormone
LMP	: Last menstrual period
LMWH	: Low-molecular-weight heparin
LPD	: Luteal Phase Defect
LTA	: Light transmission aggregometry
MA	: Maximum clot amplitude
MHC	: Major histocompatibility complex

MPA	: Microtitre platelet aggregation
MPL	: M phospholipids
NK	: Natural killer
NO	: Nitricoxide
OC	: Oral contraceptives
OPC	: Outpatient clinic
OR	: Odds ratio
PAR	: Protease activated receptor
PCOS	: Polycystic Ovary Syndrome
PFA	: Platelet function Analyser-100
PGH	: Prostaglandin H
PGI₂	: Prostacyclin
PIBF	: Progesterone-induced blocking factor
PKC	: Protein kinase C
PLA₂	: Phospholipase A ₂
PLC	: Phospholipase C
PPAR	: Peroxisome proliferator-activated receptors
PPP	: Platelet poor plasma
PRL	: Prolactin level
PRP	: Platelet rich plasma
RCOG	: Royal College of Obstetricians and Gynaecologists
RM	: Recurrent miscarriage

ROC	: Receiver-operating characteristic
RPL	: Recurrent pregnancy loss
SD	: Standard deviation
SPSS	: Statistical package for social science
ThXA2	: Thromboxane
TNF-α	: Tumor necrosis factor alpha
TRAP	: Thrombin receptor activating peptide
TSH	: Thyroid stimulating hormone
TX	: Thromboxane
uNK	: Uterine NK
VEGF	: Vascular endothelial growth factor
vWF	: von Willebrand factor

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Abstract

Background: Spontaneous abortion is the most common complication of pregnancy and is defined as the passage of a pregnancy prior to completion of 20 weeks gestation. **Aim of the Work:** The aim of this study is to evaluate the platelet aggregation function in women with unexplained recurrent miscarriage. **Patients and Methods:** his study was an observational case control study which included sixty non pregnant women recruited from Recurrent Miscarriage (RM) outpatient clinic (OPC) of Ain Shams University Maternity Hospital in the period from July 2016 till November 2016. **Results:** This study showed that there was statistical significant difference between both groups regarding aggregation response 0.309 mg/mL AA (P value = 0.009). However, there was no statistical significant difference regarding aggregation responses to other concentrations (2.5 mg/mL AA, 0.625 mg/mL AA, 0.17 mg/mL AA, 1.25mg/ml) (P value = 0.871, 0.533, 0.257, 0.704 respectively). **Conclusion:** It was concluded that patients with a history of unexplained recurrent first trimesteric pregnancy loss have greater platelet aggregation to submaximal dose of AA (0.309mg/ml) compared to control group. **Recommendations:** It is recommended to improve a prothrombotic state in unexplained recurrent miscarriage group by using antiplatelet drugs such as aspirin $\pm$ LMWH as an empirical rationale in management of this clinical condition. It has been thought that it is necessary to assess platelet aggregation function in patients with unexplained recurrent first trimesteric miscarriage.

Key words: spontaneous abortion, gestation, pregnancy, unexplained recurrent miscarriage, platelet aggregation

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Introduction

Miscarriage is one of the most common complications of pregnancy , with recognized miscarriage affecting approximately 15-25% of all conceptions , recurrent miscarriage is defined as three or more consecutive pregnancy losses affects approximately 1% of all couples(**Branch et al.,2010; Jauniaux et al.,2006**).

The risk of having spontaneous miscarriage for the first time is about 15%, And the risk is at least doubled in women experiencing recurrent miscarriage(**Gupta et al., 2007**).

The etiology underlying recurrent miscarriage includes anatomic, endocrine, immunologic, microbiologic and hematologic causes. In spite of the advances in the investigation for miscarriage, more than 50% of women with recurrent miscarriage remain unexplained (**Flood et al., 2010**).

There has been accumulating evidence over decades that some cases of “unexplained” recurrent miscarriage are caused by exaggerated hemostatic response and placental vascular thrombosis, thrombin-antithrombin complexes, circulating microparticles ,and performance of thrombo-elastography in the unexplained recurrent miscarriage population. (**Van Horn et al., 2004**).