



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



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شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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Hydroxychloroquine Therapy in Women with Autoimmune Recurrent Pregnancy Loss Refractory to Low Dose Aspirin and Heparin: A Randomized Controlled Trial

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

لَسْبَّانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Abbreviations

Abb.	Full term
aCL	<i>Anticardiolipin</i>
anti-β2GP1	<i>Anti-β2-glycoprotein-1</i>
ANXA2	<i>Annexin A2</i>
ANXA5	<i>Annexin A5</i>
aPL	<i>Antiphospholipid antibodies</i>
ApoER2	<i>Apolipoprotein E receptor 2</i>
aPS	<i>Anti- phosphatidylserine</i>
APS	<i>Antiphospholipid antibody syndrome</i>
aPT	<i>Anti-prothrombin</i>
ART	<i>Assisted reproductive techniques</i>
CAPS	<i>catastrophic APS</i>
CD	<i>Celiac disease</i>
CVD	<i>Cardiovascular disease</i>
DAMPs	<i>Damage associated molecular patterns</i>
DOA	<i>Direct oral anticoagulants</i>
dRVVT	<i>Diluted Russel viper venom</i>
EC	<i>Endothelial cell</i>
Elisa	<i>The enzyme-linked immunosorbent assay</i>
EULAR	<i>European League Against Rheumatism</i>
GFD	<i>Gluten-free diet</i>
HCQ	<i>Hydroxychloroquine</i>
HLA	<i>Haplotype human leukocyte antigen</i>
IL-1β	<i>Interleukin-1β</i>
IL-6	<i>Interleukin 6</i>
IL-8	<i>Interleukin-8</i>
INR	<i>International normalised ratio</i>
IRAK1	<i>Interleukin-1 receptor-associated kinase 1</i>
IRAK-1	<i>The interleukin-1 receptor (IL-1R) associated kinase 1</i>
ISTH	<i>International Society on Thrombosis and Haemostasis</i>
LA	<i>Lupus anticoagulant</i>

List of Abbreviations *cont...*

Abb.	Full term
LDA	<i>Low dose aspirin</i>
LMWH	<i>low molecular weight heparin</i>
LPS	<i>Lipopolysaccharide</i>
MAP kinase	<i>Mitogen-activated protein kinase</i>
MyD88	<i>Myeloid differentiation factor 88</i>
NADPH	<i>Nicotinamide adenine dinucleotide phosphate-oxidase</i>
NETs	<i>Neutrophil extracellular traps</i>
NF-κB	<i>Nuclear factor κB</i>
OAPS	<i>Obstetric AntiPhospholipid Syndrome</i>
PA	<i>Phosphatidic acid</i>
PAMPs	<i>Pathogen-associated molecular patterns</i>
PE	<i>Phosphatidylethanolamine</i>
PI	<i>Phosphatidylinositol</i>
PIGF	<i>Placental growth factor 6</i>
PS	<i>Phosphatidylserine</i>
PT	<i>Prothrombin</i>
RCT	<i>Randomized controlled trial</i>
RM	<i>Recurrent Miscarriage</i>
RPL	<i>Recurrent pregnancy loss</i>
sENG	<i>Anti-angiogenic factor soluble endoglin</i>
sFlt-1	<i>Soluble fms-like tyrosine kinase-1</i>
SGA	<i>Small for gestational age</i>
SLE	<i>Systemic lupus erythematosus</i>
STAT3	<i>Signal transducer and activator of transcription 3</i>
TF	<i>Tissue factor</i>
TGAAb	<i>Anti-thyroglobulin antibody</i>
TLRs	<i>Toll-like receptors</i>
TNF-α	<i>Tumor necrosis factor-α</i>
Tpa	<i>Tissue plasminogen activator</i>
TPOAb	<i>Anti-thyroperoxidase antibody</i>

List of Abbreviations *cont...*

Abb.	Full term
<i>TRAF6</i>	<i>Tumor necrosis factor receptor-associated factor 6</i>
<i>TSHrAb</i>	<i>Anti-thyroid stimulating hormone receptor antibody</i>
<i>UFH</i>	<i>Unfractionated heparin</i>
<i>VEGF</i>	<i>Vascular endothelial growth factor</i>
<i>VKA</i>	<i>Vitamin K antagonists</i>
<i>αβ2GPI</i>	<i>αβ2-glycoprotein-1</i>

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INTRODUCTION

Pregnancy loss represents a common obstetric complication occurring in about 15%-25% of all clinically recognized pregnancies. Approximately 80% of all cases of sporadic pregnancy losses occur within the first trimester, and about 50% result from random numeric chromosome errors (*Wang et al., 2003*).

The most common risk factors identified among women who have experienced pregnancy loss are advanced maternal age and prior pregnancy loss (*Andersen et al., 2000*).

The recurrence of pregnancy loss identifies a distinct clinical entity, that is, recurrent pregnancy loss (RPL), which occurs in about 2%-4% of cases (*Practice Committee of American Society for Reproductive Medicine., 2013*), (*American College of Obstetricians and Gynecologists, 2002*).

Several factors, including age, parental chromosomal abnormalities, certain uterine anomalies, heritable and/or acquired thrombophilias, untreated hypothyroidism, uncontrolled diabetes mellitus, other hormonal and metabolic disorders, infections, sperm quality, and lifestyle issues, are involved in RPL (*Pereza et al., 2017*).

The definition of recurrent pregnancy loss is debated, ranging from *two clinical miscarriages*, not necessarily consecutive, according to the American Society for

Reproductive Medicine (ASRM) (*Practice Committee of American Society for Reproductive Medicine., 2013*) and a joint International Committee for Monitoring Assisted Reproductive Technology and World Health Organization glossary (*Zegers-Hochschild et al., 2009*), to *three consecutive pregnancy losses* (not necessarily intrauterine) as defined by both the European Society for Human Reproduction and Embryology (*Jauniaux et al., 2006*) and the Royal College of Obstetricians and Gynaecologists (*RCOG Green Top Guideline, 2011*).

We recommend the term recurrent pregnancy loss be used to describe repeated pregnancy demise, and the term recurrent miscarriage be used when all pregnancy losses have been confirmed as intrauterine miscarriages, by ultrasound or histology. As mentioned, the definition of recurrent pregnancy loss and recurrent miscarriage is controversial, but it is our opinion that the accurate reporting of clinical data is the first step towards an evidence-based definition of recurrent pregnancy loss (*Kolte et al., 2015*).

To date, the association between RPL and the autoantibodies positivity, regardless of the presence of a clinically overt autoimmune disease, has been reported in several studies, even though the strength of such association is not reported unanimously in the scientific literature (*Pereza et al., 2017*).