



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكرو فيلم

# بسم الله الرحمن الرحيم



**HANAA ALY**



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# شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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# جامعة عين شمس

## التوثيق الإلكتروني والميكروفيلم

### قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها  
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



### يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



**HANAA ALY**



# **Platelet Glycoprotein VI Genetic Polymorphism T13254C in Neonatal Sepsis**

*A thesis*

*Submitted for Partial Fulfillment of M.D. Degree  
in Clinical Pathology*

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# List of Abbreviations

Abb.	Full term
ACS .....	Acute coronary syndrome
ADP .....	Adenosine diphosphate
aPTT.....	Activated partial thromboplastin time
CD.....	Cluster of differentiation
CONS .....	Coagulase-negative Staphylococcus
COX-1 .....	Cyclooxygenase-1
CRP .....	C-reactive protein
CXCL .....	Chemokine (C-X-C motif) ligand
DAMPs.....	Damage associated molecular patterns
DIC .....	Disseminated intravascular coagulation
dNTPs.....	Deoxyribonucleotide triphosphates
DVT .....	Deep vein thrombosis
EDTA .....	Ethyl diamine tetra-acetic
EOS .....	Early-onset sepsis
ESR.....	Erythrocyte sedimentation rate
FMASU .....	Faculty of Medicine, Ain Shams University
FcR $\gamma$ .....	Fc receptor $\gamma$ chain
FiO <sub>2</sub> .....	Fraction of inspired Oxygen
GAG .....	Glycosaminoglycans
G-CSF .....	Granulocyte-colony stimulating factors
GP.....	Glycoprotein
GBS .....	Group B streptococcus
GIT .....	Gastrointestinal tract
GNB3.....	Guanine nucleotide-binding protein beta-3 subunit variant
GPO.....	Glycine– proline–hydroxyproline
IAP .....	Intrapartum antibiotic prophylaxis.
ICAM-1 .....	Soluble Intercellular Adhesion Molecule 1
ICU.....	Intensive care unit

# List of Abbreviations *(Cont...)*

Abb.	Full term
IFN- $\gamma$ .....	Interferon gamma
IL-1.....	Interleukin 1
INR.....	International normalization ratio
ITAM .....	Immunoreceptor tyrosine-based activation motif
ITG .....	Integrin
ISTH.....	International Society on Thrombosis and Hemostasis
IQR.....	Inter-quartile range
LAT .....	Linker of activated T cells
LOS .....	Late-onset sepsis
MAC.....	Membrane attack complex
MGB.....	Minor groove binder
MMP9 .....	Metalloproteinase 9
MPs.....	Microparticles
NETs.....	Neutrophil extracellular traps
NF- $\kappa$ B .....	Nuclear factor kappa- light- chain enhancer of activated B cells
NICU .....	Neonatal intensive care units
NOS2 .....	Nitric Oxide Synthase 2
PAMPs .....	Pathogen associated molecular patterns
PARs.....	Protease Activating Receptors
PCR .....	Polymerase chain reaction
PCT .....	Procalcitonin
PF4 .....	Platelet factor 4
PG.....	Proteoglycans
PLC $\gamma$ 2 .....	Phospholipase C $\gamma$ 2
PMN .....	Polymorphonuclear neutrophils
PMNL-MPs .....	Polymorphonuclear leucocyte-derived microparticle
PolyP .....	Polyphosphates
PR .....	Purinogenic receptor
PSGL-1.....	P-selectin glycoprotein ligand 1
PT .....	Prothrombin time

# List of Abbreviations *(Cont...)*

Abb.	Full term
<b>PTGS1</b> .....	Prostaglandin-endoperoxide synthase 1
<b>RANTES</b> .....	Regulated upon activation normal T cell expressed and secreted
<b>RGD</b> .....	Arginine-glycine-aspartic acid
<b>ROM</b> .....	Rupture of membranes
<b>ROS</b> .....	Reactive oxygen species
<b>SD</b> .....	Standard deviation
<b>SH3</b> .....	Src homology 3
<b>SIC score</b> .....	Sepsis induced coagulopathy score
<b>SIRS</b> .....	Systemic inflammatory response syndrome
<b>SNAP II score</b> .....	Score for neonatal acute physiology II
<b>SNPs</b> .....	Single nucleotide polymorphisms
<b>SOFA</b> .....	Sequential organ failure assess
<b>Spa</b> .....	Staphylococcus aureus protein A
<b>SPSS</b> .....	Statistical package for Social Science
<b>SrpA</b> .....	Serine-rich protein A
<b>TBXA2R</b> .....	Thromboxane A2 receptor
<b>TLRs</b> .....	Toll-like receptors
<b>TF</b> .....	Tissue factor
<b>TNF-alpha</b> .....	Tumor necrosis factor alfa
<b>TPO</b> .....	Thrombopoietin
<b>TxA2</b> .....	Thromboxane A2
<b>VLBW</b> .....	Very low birthweight
<b>vWF</b> .....	Von Willebrand factor
<b>WBC</b> .....	White blood cell count

# INTRODUCTION

**N**eonatal sepsis is a systemic infection occurring in infants at  $\leq 28$  days of life (*Edwards and Baker, 2004*). It is classified into two clinical patterns of illness, that of early and late onset. Early-onset sepsis (EOS) is more fulminant, it is commonly diagnosed within the first 48 hours and almost always during the first week of life (*Chacko and Sohi, 2005*).

Several risk factors for EOS have been recognized, including preterm birth, low birth weight, rupture of membranes for longer than 18 hours, chorioamnionitis and meconium passed (*Good and Hooven, 2019*). However, associations between each individual risk factor and EOS are weak, and some risk factors are inconsistently diagnosed (*Adatara et al., 2018*). It is a common and devastating cause of neonatal mortality and morbidity (*Camacho-Gonzalez et al., 2013*) with life-long impact plagued by a lack of accurate diagnostic and prognostic testing. Management options and outcomes have not been changed for the last 30 years (*Wynn, 2016*).

Platelet activation plays an important role in the development of sepsis. During sepsis, platelet activation leads to endothelial cell injury and promotes neutrophil extracellular traps (NETs) and microthrombus formation, exacerbating septic coagulation and inflammatory reactions. The resultant induction of disseminated intravascular coagulation (DIC) leads to organ damage (*Wang et al., 2018*).

The GPVI protein is the platelet activator receptor for collagen (*Watkins et al., 2006*). It was found to support the host defense and modulate inflammation, platelet influx, activation, and platelet–leukocyte complex formation at the primary site of infection during gram-negative derived sepsis (*Claushuis et al., 2018*). It also has been confirmed as possible participants in the process of platelet-induced NETs formation (*Wang et al., 2018*).

In terms of prognostic information; *Asafi et al. (2019)* identified a significant difference in the morbidity outcome for pediatric sepsis patients with different GPVI haplotypes. Also, *Montague et al. (2018)* proved it to be an important marker for platelet activation that predicts sepsis progression and mortality in injured patients.

Changes to genes of sepsis mediators (polymorphism and mutations) have an important role in the susceptibility to the severity and outcome. With the advance of molecular genetic methods, genetic testing and screening of patient groups at high risk of sepsis may become reality in the future (*Elek et al., 2017*). Mapping the genetic basis of human diseases and their risk factors is important in the current trend of individualization of patient care (*Sionova et al., 2017*). This, however, necessitates further research to clarify in detail the role of most powerful predictors in neonatal sepsis.