

Thrombocytopenia During Pregnancy

Thesis

Submitted for Partial Fulfillment of Master Degree in Intensive care

By

Dina Khairy Hemaya Gerguis

M.B., B.Ch. Faculty of Medicine-Ain Shams University

Supervised by

Prof. Dr. Samia Ibrahim Sharaf

Professor of Anaesthesia and ICU Faculty of Medicine - Ain Shams University

Prof. Dr. Hatem Saeed Abdel-hamid

Professor of Anaesthesia and ICU Faculty of Medicine - Ain Shams University

Dr. Hany Victor Zaki

Lecturer of Anaesthesia and ICU Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2016

Abstract

Introduction: Pregnancy is associated with physiological and

pathological changes in platelet numbers and function, which can be

of clinical concern because of risks for maternal and fetal or neonatal

bleeding.

Aim of the Work: To illustrate the causes for thrombocytopenia with

pregnancy and their management.

Methodology: Overall, about 70 – 80% of cases are due to

gestational thrombocytopenia, 6 % secondary to hypertensive

disorders; 3–4% due to an immune process, and the remaining 1–2%

made up of rare constitutional thrombocytopenias, infections and

malignancies.

Conclusion: The mode of delivery should be based on obstetric

considerations given there is no evidence that Caesarean section is

safer for the fetus with thrombocytopenia than an uncomplicated

vaginal delivery, which is usually safer than caesarean section for the

mother.

Keywords: Thrombocytopenia, During Pregnancy, management



First of all, thanks to Allah whose magnificent help was the main factor in completing this work.

No words can express my deep sincere feelings Towards Prof. Dr. Samia Ibrahim Sharaf, Professor of Anaesthesia and ICU, Faculty of Medicine–Ain Shams University for her continuous encouragement, guidance and support she gave me throughout the whole work. It has been a great honor for me to work under her generous supervision.

I would like to express my deepest appreciation, respect and thanks to Prof. Dr. Hatem Saeed Abdel-hamid, Professor of Anaesthesia and ICU, Faculty of Medicine-Ain Shams University, for his continuous guide in all aspects of life beside his great science, knowledge and information.

I would like to express my deepest appreciation, respect and thanks to Dr. Hany Victor Zaki, Lecturer of Anaesthesia and ICU, Faculty of Medicine-Ain Shams University, for his continuous guide in all aspects of life beside his great science, knowledge and information.

Last but not least, sincere gratitude to My Family for their continuous encouragement and spiritual support.

Contents

Subjects	Page
List of abbreviations	II
List of figures	V
List of tables	VI
• Introduction	1
Aim of the work	4
• Chapter (1): Haematological Changes During	
Pregnancy	5
• Chapter (2): Thrombocytopenia in Pregnancy	27
• Chapter (3): Management of Thrombocytopeni	a
During Pregnancy	61
• Summary	105
• References	108
Arabic Summary	

List of Abbreviations

K: The clot formation time

MA : The clot strength or Maximum Amplitude

R : The reaction time to initiation of the clot

α : The clot formation rate

ACL : AntiCardiolipin Antibodies

ADAMTS13: A Disintegrin And Metalloproteinase with a

ThromboSpondin type 1 motif member 13, also

known as Von-Willebrand factor - cleaving

Protease

ADP : Adenosine 5' DiPhosphate

AFLP : Acute Fatty Liver of Pregnancy

ALT : Alanine Transaminase

Anti – **β2GP1** : Anti- Beta2 Glycoprotein 1

Anti D : RH (D) immunoglobulin

Anti HLA Ab: Anti Human Leucocyte Antigen Antibodies

APA : Anti-Phospholipid Antibodies

APC : Acquired Activated Protein C

APS : Anti-Phospholipid Syndrome

aPTT : Activated Partial Thromboplastin Time

ASH : American Socitey of Hematology

List of Abbreviations

AST : Aspartate Transaminase

ATP : Autoimmune Thrombocytopenic Purpura

BCSH : British Committee for standards in Hematology

BUN : Blood Urea Nitrgen

DIC : Disseminated Intravascular Coagulopathies

DIT : Drug Induced Thrombocytopenia

FDP : Fibrin Degradation Products

FFP: Fresh Frozen Plasma

GT : Gestational Thrombocytopenia

HCQ : HydroxyChloroquine

HCT : Hematocrite

HEELP: Hemolysis Elevated Liver Enzymes Low Platelets

HIT : Heparin Induced Thrombocytopenia

HUS : Hemolytic Uremic Syndrome

ITP : Immune Thrombocytopenic Purpura

IUGR : Intra Uterine Growth Restriction

IVIG : Intra Venous Immuno Globulin

LA : Lupus Anticoagulant

LDH : Lactate Dehydrogenase

LY60 : Reduction in maximum amplitude in 60 minutes

MAHA : MicroAngiopathic Hemolytic Anemia

List of Abbreviations

MCHC: Mean Corpuscular Hemoglobin Concentration

MCV : Mean Corpuscular Volume

PAI : Plasminogen Activator Inhibitors

PEX : Plasma Exchange

PGE2 : Prostaglandins E2

PT : Prothrombin Time

RBCs : Red Blood Cells

RCO: Ristocetin Cofactor Activity

SLE : Systemic Lupus Erythematosis

TAFI: Thrombin Activatable Fibrinolysis Inhibitors

TAT : Thrombin – Antithrombin complexes

TEG: ThromboElastography

TEG CI: TEG coagulation index

TEG MA: TEG Maximum Amplitude

TMAs : Thrombotic Microangiopathies

TT : Thrombin Time

TTP : Thrombotic Thrombocytopenic Purpura

VWF : Von Willebrand Factor

WBCs : White Blood Cells

List of Figures

No.	<u>Figure</u>	Page
<u>1</u> -1	Thromboelastograph trace (a) pregnant (b) non-pregnant, showing shortened R and K times and increased maximum amplitude in pregnancy. The highest TEG CI values have been found during active labor. Parameters return to baseline by 4 weeks postpartum13	22
<u>1-2</u>	Interval plot of maximum amplitude vs. weeks' postpartum after normal delivery	23

List of Tables

No.	<u>Table</u>					
<u>1-1</u>	Red cell indices during pregnancy and the puerperium.					
<u>1-2</u>	Coagulation factors during pregnancy and the early puerperium.					
<u>1-3</u>	Natural anticoagulant factors during pregnancy and the early puerperium.	18				
<u>1-4</u>	Natural anticoagulants and markers of fibrinolysis.	19				
<u>3-1</u>	Medical Management of ITP in Pregnancy – ASH and BCSH Guidelines.	66				



Introduction

Pregnancy is associated with physiological and pathological changes in platelet numbers and function, which can be of clinical concern because of risks for maternal and fetal or neonatal bleeding (Stirling et al., *1984*).

Thrombocytopenia in pregnancy is frequently encountered and may be due to increased platelet turnover and plasma dilution, immune-mediated mechanisms, or a complication of a more severe underlying pregnancyrelated disorder such as preeclampsia (Fay et al., 1983).

Inherited defects in platelet function and number may also manifest during pregnancy with the risk of bleeding dependent on the underlying problem. In some women, the diagnosis of thrombocytopenia will precede pregnancy but in others, the problem is first identified when routine pregnancy blood tests are performed (Crowther et al., 1996).

An accurate diagnosis and risk assessment in the antenatal period are essential for developing specific plans for any antenatal interventions and for management of delivery and the postpartum periods, and the neonate. Management of pregnant women with platelet disorders



multidisciplinary requires a approach and close collaboration between the obstetric and hematology teams. Thrombocytopenia, or a low blood platelet count, is encountered in 7-8% of all pregnancies. Women are more commonly diagnosed with platelet disorders during pregnancy since screening is done as part of the initial clinic evaluation with automated blood counts (Kadir & McLintock, 2011).

Thrombocytopenia is defined as a platelet count of less than 150×10^9 /l. Normal pregnancy is generally thought not to affect the platelet count,' but it has been suggested that the normal range is lower in pregnancy, and that the count falls in the third trimester. This review concentrates on causes of thrombocytopenia with particular reference to pregnancy: most of these involve excessive platelet consumption (Fenton et al., 1977).

Demand for folic acid rises to 400-600 mcg/day in normal pregnancy, and dietary deficiency may cause thrombocytopenia, particularly where demand is increased by multiple pregnancy, or by an underlying haemolytic states, combined iron and folate supplements usually provide 350 ug of folate daily (Matthews et al., 1990).

Thrombocytopenia in pregnant women may result from a variety of causes ranging from benign disorders such as gestational thrombocytopenia to life threatening syndrome such as HELLP (hemolysis, elevated liver function tests, and low platelet syndrome), hemolytic uremic syndrome, TTP (Sainio et al., 2000).

Since the clinical features of many of these disorders often overlap making their diagnosis difficult and it is for these complicated cases for which hematologic consultation is taken so thorough knowledge and familiarity of clinical and laboratory features of each of these disorders and differentiation of benign from malignant disorders is required for accurate diagnosis may be achieved so that appropriate treatment instituted well in time (McCrae, *2003*).

Some of these conditions are not associated with adverse pregnancy outcomes others are associated with substantial maternal and/or neonatal morbidity and mortality. However, specific therapies, if instituted promptly, may significantly improve the outcomes of offspring. affected patients and their Particularly management of high risk cases should be co-ordinated in joint obstetric hematology clinics (Samuels et al., 1990).

Aim of the Work

To illustrate the causes for thrombocytopenia with pregnancy and their management.

Haematological Changes During Pregnancy

Normal pregnancy is characterized by profound changes in almost every organ and system to accommodate the demands of fetoplacental unit. There are both slight and signficant changes in hematological parameters during pregnancy and the puerperium, due to changes in the hormonal milieu. Many hematological changes also, occurring during these periods are physiological and are of inconsequential concern to the hematologist. It is also one of the physiological conditions capable of causing remarkable and dramatic changes in haematological variables. A pregnancy is influenced by many factors, some of which include culture, environment, socioeconomic status, and access to medical care. The haematological indices also have an impact on pregnancy and its outcome A thorough understanding of these is important to avoid under-diagnosing both over and abnormalities. Appreciation of the time frame for some of the changes allows sensible planning (Yip, 2000).

Pregnancy is a state characterized by many physiological hematological changes, which may appear to be pathological in the non-pregnant state. The review highlights most of these changes along with the scientific