Association between Plateletcrit and Preeclampsia

Thesis

Submitted for partial fulfillment of Master Degree in Obstetrics and Gynecology

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2018

سورة البقرة الآية: ٣٢

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. Magdy Mohammed Kamal,*** *Professor of Obstetrics and 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 ***Assist. Prof. Adel Shafik Salah El-Din****, Assistant professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance through out this work.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients participated in this study.

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List of Abbreviations

Abb.	Full term
ADP	Adenosine 5∂-diphosphate
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AT1	Type-1 angiotensin II receptor
ATP	Adenosine 5- triphosphate
BUN	Blood urea nitrogen
CBC	Complete blood count
CI	Confidence interval
CTG	Cardio topography
CV	Cardiovascular
DBP	Diastolic blood pressure
DM	Diabetes mellitus
ER	Endoplasmic reticulum
FHR	Fetal heart rate
Fl	Femtoliters
Hb	Hemoglobin
INR	International normalized ratio
IPF	Immature platelet fraction
ITP	Immune thrombocytopenia
IUGR	Intrauterine growth restriction
KIRs	Killer cell immunoglobulin-like receptors
MBP	Mean blood pressure
MPC	Mean platelet component
MPM	Mean platelet mass

List of Abbreviations (Cont.)

Abb.	Full term
MPV	Mean platelets volume
OCS	Open canalicular system
OR	Odds ratio
PCDW	Platelet component distribution width
PCT	Plateletcrit
PDW	Platelets distributed width
PE	Preeclampsia
Pg	Picogram
PI	Platelet indices
P-LCR	Platelet larger cell ratio
PlGF	Placental growth factor
RR	Relative risk
SBP	Systolic blood pressure
SPSS	Statistical Package for the Social Sciences
sVEGFR-1	Soluble vascular endothelial growth factor receptor 1
TGF-β3	Transforming growth factor β3
VEGF	Vascular endothelial growth factor

INTRODUCTION

Preeclampsia (PE) is a multifactorial disease, characterized by the presence of high blood pressure and proteinuria after the 20th week of pregnancy. PE occurs in 5–8% of pregnancies worldwide and is an important cause of maternal and fetal death. Its prevalence varies in different populations and in different ethnic groups ***(Trogstad et al., 2011)***.

Diagnosis is made primarily based on blood pressure measurement and determination of the proteinuria and clinical data ***(Yang et al., 2014)***.

It is classified into mild and severe preeclampsia according to severity of symptoms:

- Severe PE was diagnosed using the following: a blood pressure elevation with a systolic blood pressure of ≥ 160 mm Hg or a diastolic blood pressure of ≥110 mm Hg and proteinuria >3+ on a urine dipstick.
- For the diagnosis of mild PE, a systolic blood pressure between 140 and 160 mmHg and a diastolic blood pressure between 90 and 110 mmHg, and proteinuria >1+ or 2+ on a urine dipstick was considered significant. A minimum of two consecutive positive measurements was required for the diagnosis ***(Freitas et al., 2013).***

Preeclampsia is one of the most important causes of maternal and fetal morbidity and mortality. Many theories are proposed for the pathophysiology of pre-eclampsia. The formation of a utero placental vasculature insufficient to supply adequate blood to the developing fetus results in fetoplacental hypoxia, leading to imbalances in the release and metabolism of prostaglandins, endothelin and nitric oxide by placental and extra placental tissues. As well as enhanced lipid peroxidation and other undefined factors contribute to the hypertension, platelet activation and systemic endothelial dysfunction characteristics of preeclampsia. Activation of coagulation system in small vessels and increased platelet aggregation is present in preeclampsia. It is clear that preeclampsia is one of the causes of maternal thrombocytopenia and the platelet count increases rapidly after the delivery. There are studies suggesting the storage of platelet in the areas with endothelial damage as the cause of thrombocytopenia. The platelet counts were lower, while the mean platelet volume, platelet distribution width and platelet large cell ratio were increased in preeclampsia as compared to control group ***(Annam et al., 2011)***.

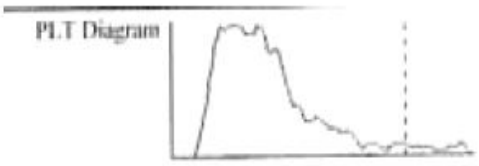
Platelets are anuclear cell fragments derived from the cytoplasm of bone marrow megakaryocytes that circulate in the blood stream of humans for 7-10 days. The function of platelets is to prevent excess bleeding and also play an important role in maintaining the integrity of the endothelium through the release

of proangiogenic cytokines and growth factors ***(Kaplan and Jackson, 2011)***.

Occurrence of endothelial damage can cause increased activation of platelets which has an important role of appearing thrombus on the region and because of increased platelet activation, increased platelet consumption and thus, increased joining of new and big volume, more reactive platelet occurs ***(Ariöz et al., 2007)***.

Evaluation of platelet indices can be a useful screening test for early identification of preeclampsia as its estimation can be considered as early, economical and rapid procedures of assessment of severity of preeclamptic cases and have a significant impact on maternal and perinatal outcome ***(Vijaya et al., 2014)***.

Plateletcrit (total platelet mass), which corresponds to the volume that platelets have in 100ml of total blood, is the product of platelet count and MPV ***(Freitas et al., 2013)***. It can be mentioned to be analogous to the hematocrit. PCT is the most physiologically relevant parameter in hemostasis and in regulation of hematopoiesis ***(Butkiewicz et al., 2006)***.



$$PCT\ \% = \frac{MPV * PLT * 10^9/l}{10}$$

The aim of this study, therefore, to investigate the association between reduced PCT and preeclampsia even in women with normal platelet count ***(Dadhich et al., 2012; Han et al., 2014; Yang et al., 2014; Mondal et al., 2015)*** one large prospective study has been showed that PCT is significant predicator of development of preeclampsia ***(Yang et al., 2014)***.

The aim of the current study was to investigate the relationship between platelets count and platelet indices, and severity of PE.

Chapter 1
PLATELET PHYSIOLOGY

Platelets are small anucleate cell fragments that circulate in blood playing crucial role in managing vascular integrity and regulating hemostasis. Platelets are also involved in the fundamental biological process of chronic inflammation associated with disease pathology. Platelet indices like mean platelets volume (MPV), platelets distributed width (PDW), and plateletcrit (PCT) are useful as cheap noninvasive biomarkers for assessing the diseased states. Dynamic platelets bear distinct morphology, where and dense granule are actively involved in secretion of molecules like GPIIb, IIIa, fibrinogen, vWf, catecholamines, serotonin, calcium, ATP, ADP, and so forth, which are involved in aggregation. Differential expressions of surface receptors like CD36, CD41, CD61 and so forth have also been quantitated in several diseases. Platelets activation and dysfunction have been implicated in many diseases ***(Ghoshal and Bhattacharyya, 2014)***.

The term thrombocyte (clot cell) came into use in the early 1900s and is sometimes used as a synonym for platelet; but not generally in the scientific literature, except as a root word for other terms related to platelets (e.g. thrombocytopenia meaning low platelets) ***(BMA, 2013)***. Platelets were discovered by Giulio Bizzozero in 1882 ***(Ribatti and Crivellato, 2007)***, but for many decades the dynamic and multifunctional nature of

platelets remained a field of interest only for biologists. Anucleate, discoid platelets are the smallest blood particles which unveil their dynamicity through their morphology. Primarily they are associated with hemostasis, which is to initiate blood coagulation. Although very dynamic, they usually prefer to remain in inactive state and get activated only when a blood vessel is damaged. But hemostasis or blood coagulation is not the sole function of platelets; rather it is employed in several multifunctional attributes monitoring the homeostasis of the body **(Figure 1)**. Its high sensitivity to different disease states eventually assigned it to be one of the most accessible markers ***(Cerletti et al., 2012)***. Platelet reactivity for different disease pathogenesis is widely dependent upon some biologically active markers like CD36, CD41, CD42a, CD42b, and CD61. These include some active surface receptors and platelet secretory products. Platelet tends to alter the expression and signaling of these markers in different disease diagnosis and prognosis, providing a huge field to explore disease progression ***(Ghoshal and Bhattacharyya, 2014)***.