

**EFFECT OF HEPATITIS C INFECTION ON
PLATELET
FUNCTION IN HEMODIALYSIS PATIENTS**

Thesis

**Submitted for partial fulfillment
Of master degree of internal medicine**

By
Aida Osama Mohamed Zeidan
M.b.b.ch

Supervised by
Professor Dr. Mohamed El Tayeb Nasser
Professor of internal medicine and nephrology
Faculty of medicine Ain Shams University

Dr. Walid Ahmed Bichari
Lecturer of internal medicine and nephrology
Faculty of medicine. Ain Shams University.

**Ain shams University
Faculty of medicine**

2011

تأثير الإصابة بفيروس ج على وظائف الصفائح الدموية لدى
مرضى الفشل الكلوى المزمن المعاشون على الإستصفاء
الدموى

رسالة

توطئة للحصول على درجة الماجستير فى
أمراض الباطنة

مقدمة من

الطبيبة/ عايدة أسامة محمد زيدان

بكالوريوس الطب والجراحة العامة- كلية الطب جامعة عين شمس

تحت إشراف

الأستاذ الدكتور/ محمد الطيب ناصر

أستاذ أمراض الباطنة والكلى

كلية الطب جامعة عين شمس

الدكتور/ وليد أحمد بشرى

مدرس أمراض الباطنة والكلى

كلية الطب جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١١

Summary

HCV has been proven to affect platelet function (aggregation and adhesion) in chronic renal failure patients and increase bleeding tendency in uremic patients on regular hemodialysis this hemostatic effect has been related to the decrease in aggregation and adhesion tests especially adhesion and ristocin aggregation test.

Furthermore, a decrease in platelet aggregation in some patients have reported in uremic patients with negative HCV Abs.

Our study was to analyze the possible effect HCV on platelet function in uremic patients under regular hemodialysis. 30 patients, 11 woman and 19 men, with clinically stable end stage renal failure, who received maintenance hemodialysis 3 times weeks, with an age range between 24-67 years old, were enrolled in the study.

Individual base line values for Hb, and platelet count, and platelet aggregation tests using ristocin, ADP (in concentration of 0.5 – m & 2.5 – m), and Epinephrine, were performed, there were significant decrease in platelet aggregation by using ristocin, ADP significant decrease by using Epinephrine and significant, ADP in concentration There

CONTENTS

	Page
List of Abbreviation	i
List of Tables	iii
List of Figures.....	iv
Introduction and Aim of the Work	1-3
Review of the literature	4
Physiology of platelet	4
Hemostasis & platelet function	4
Platelet abnormalities in chronic kidney disease Pathophysiology	26
Abnormalities of coagulation and fibrinolysis and thrombotic tendency in uremia	34
Clinical presentations of uremic bleeding	36
Prevention of uremic bleeding	37
Relation between parathyroid dysfunction and platelets in chronic renal failure	40
Effect of hepatitis c on platelet function in hemodialysis patients	54
Effect of HCV infection on platelet function	75
Patients and Methods	83
Results	91

CONTENTS

	Page
Discussion	104
Summary	110
Conclusion	112
Recommendations	113
References	114
Arabic Summary	123

List of abbreviations

vWF	von willebrand factor
(No)	nitric oxide
(CGMP)	cyclic guanosine monophosphate
(CKD)	chronic kidney disease
ADP	adenosine diphosphate
(AGA)	the american gastroenterological association
(CBC).	Complete blood counts
rh EPO	recombinant human EPO
(ASA)	acetylsalicylic acid
Tx A₂	thromboxane A ₂
PGI₂	prostaglandin I ₂
(TNF α)	tumor necrosis factor alpha
(GSA)	guanidinosuccinic acid.
(ACH)	adsorbable collagen hemostat
(PCR)	polymerase chain reaction
(TMA)	transcription mediated amplification
(B-DNA)	branched DNA
(TXA)	tranexamic acid
HCV	hepatitis c virus
DDAVP	(1-deamino-8-d-arginine vasopressin)
PTH	parathyroid hormone
(TMA)	transcription mediated amplification
TXB₂	2,3 dinor-thromboxane B ₂
HD	Hemodialysis

List of Tables

	Page
Table 1 Factors involved in the uremic bleeding tendency	29
Table 2 clinical presentations of uremic bleeding	36
Table 3 cure rates by genotype of Hcv	67
Table 4 distribution of the studied group as regard general data	83
Table 5 distribution of the studied groups as regard etiology of CRF	92
Table 6 distribution of the studied group as regard complications	93
Table 7 distribution of the studied group as regard HCV infection	94
Table 8 comparison between HCV negative and positive groups as regard general data	94
Table 9 distribution of the studied cases as regard platelets functions tests	95
Table 10 comparison between HCV negative and positive group as regard bleeding time , and PTT – INR	97
Table 11 comparison between HCV negative and positive group as regard complications	99
Table 12 comparison between HCV negative and positive group as regard capillary fragility	100
Table 13 comparison between negative and positive groups as regard platelets aggregation tests	101

List of Tables

	Page
Table 14 comparison between HCV negative and HCV positive group as regard platelets adhesion test	102
Table 15 comparison between HCV negative and HCV positive group as regard bleeding time , INR, and PT	103

List of Figures

	Page
Figure (1) Over view of platelet activation mechanisms	21
Figure (2) different pathways involved in platelet activation	22
Figure (3) shows that majority of cases had HTN and idiopathic	92
Figure (4) shows that majority of cases had prolonged AV Fistula closure	93
Figure (5) shows that 66,7 % of the studied cases had abnormal adhesion test , while 33,3% had normal platelet adhesion test	96
Figure (6) table shows that serum calcium level was lower among HCV positive group compared to HCV negative group	98
Figure (7) shows no statistically significant difference between both groups as regard capillary fragility test by using fisher exact test.	100
Figure (8) Comparison between HCV positive and HCV negative group as regard ADP – ristocitin and Epinephrine	101
Figure (9) Comparison between HCV positive and HCV negative group as regard adhesion test.	102

O

أَلَا سُبْحَانَكَ لَا عِلْمَ لَنَا
بِأَعْلَمَتِنَا إِنَّكَ أَنْتَ الْعَلِيمُ
الْحَكِيمُ

صدق الله العظيم

سورة النقرة والآية

INTRODUCTION

Hemostasis is the process that maintains the integrity of the circulatory system after vascular damage. It is a dynamic and tightly regulated process that we are just beginning to understand. Under normal circumstances, vessel wall injury rapidly initiates a series of coordinated events designed to seal the breach generated by the injury.

These events lead to clot formation and require both platelet recruitment and activation as well as the generation of thrombin and fibrin. (*Furie and Furie 2008*)

In addition, this process is modulated by multiple mechanisms that contain it, thus preventing the otherwise imminent vascular inflammation and tissue damage (*Lane et al., 2005*).

Deficiencies of platelet function or of the coagulation cascade typically lead to bleeding disorders, whereas platelet hyperreactivity and abnormalities in the regulatory mechanisms may result in excessive thrombin formation and pathological thrombosis. (*Boccardo et al., 2004*)

Patients at various clinical stages of chronic kidney disease (CKD) display a wide range of derangements in all three aspects of hemostasis, and they experience a wide spectrum of clinical manifestations that lead to considerable morbidity and mortality in this patient population, one that

spans prothrombotic tendency leading to excessive cardiovascular events, as well as platelet dysfunction leading to increased bleeding tendency. (*Boccardo et al., 2004*).

This review summarizes the current knowledge on normal hemostasis, abnormalities in hemostatic pathways that have been described in CKD patients, and the different therapeutic options for these individuals as well as their effectiveness. (*Boccardo et al., 2004*)

Aim of the Work

This study aims to assess platelet function in chronic renal failure patients on regular haemodialysis to show the prevalence of platelet dysfunction in this group of patients in relation to hepatitis c status.

Review Of The Literature

Physiolog of Platelets :

Hemostasis & platelet function:

The participation of platelets in hemostasis is a fundamental component of this physiologic process. The reactions involved include adhesion to the cut end of a blood vessel, spreading of adherent platelets on the exposed subendothelial surfaces, secretion of stored platelet constituents (Including molecules involved in hemostasis and wound healing), and formation of large platelet aggregates. (*Johnson et al., 2008*)

Production and kinetics:

The platelets develop in the inter medullary components of bone marrow. The platelet precursor of megakaryocyte undergoes a number of nuclear divisions leading in general to a 16 lobed cell which then begins to produce platelets.

When platelets mature , they circulate for approximately 10 days . During this time , they decrease in size and increase in density primarily because of the loss of plasma membrane . (*George and Lewis,2008*)

Studies showed age related changes in platelet survival , and a rough correlation between shortened survival and vascular disease suggesting that increased platelet turnover may result from vascular lesions (*Abrahamsen, 2007*).

Morphology Of Blood Platelets:-

Platelets are small non nucleated discoid cells about 3M long and 1M thick, In stained blood films , the clear, blue cytoplasm is seen to contain a few granules , but the electron microscope reveals a very complex system of membranes , microtubules and organelles. Under the electron microscope platelets appear to be formed of 4 distinct divisions *(Thompson, 2006)*

- 1- The peripheral zone .
- 2 - The sol-gel zone.
- 3 - The organelle zone.
- 4 - The membrane systems.

Under the peripheral membrane, there are helical coiled bundles of microtubules which are involved in platelet contraction. A gel like matrix embes the organelles and microfilaments.

There is a system of channels by which it is possible that the products of secretory granules reach the organelles. The metabolic requirements of the platelets are maintained by the mitochondria *(Thompson, 2006)*