# 

# بسيم الله الرحمن الرحيم

وَإِنَ يَمْسَسُكَ اللَّهُ بِضُرٍّ فَلاَ كَاشِفَ لَهُ إِلاَّ هُوَ وَإِن يُرِدُكَ بِحَثِيرٍ فَلاَ مَرَا ذَ لَفَضْلِهِ يُصِيبُ بِهِ مَن يَشَاء مِنْ عِبَادِهِ وَهُوَالْغَفُوسُ الرَّحِيبِ مُ

# حدق الله العظيم

سورة يونس الأية (١٠٧)

#### **Dedication**

To my teachers

Who gave me the gifts of sharing their minds and experiences, so as to be a creative one

To the soul of my father

Who gave me advices and support through the years till his departure. I am very grateful for everything you have done for me

To my mother

Who continually encourage me to success, made me a man and show the meaning of love

To my wife, beloved

For her patience, support, and efforts to make my life shiny, I truly appreciate this.

To my lovely children

Who make happiness and fun in my home and my whole life, may all of my dreams for you come true.

To my colleagues and dear friends

Who always being by my side through good times and bad

With my faithful love and best wishes

### Acknowledgement

By the grace of Allah and his help I completed this study, all praise to him,

I would like to express my appreciation to my advisory committee.

Thanks for giving me the opportunity to discuss this work

Special thanks to

#### Dr. Munsoor Mohammed Munsoor

my supervisor for his time, patience, and understanding, he helped me so much to complete this research, it has been an honor to work with you. Also, thanks and appreciation to the staff of hematology department for all their roles in my Master study

My gratitude also goes to the office of Dr Khalda Dean of Medical laboratory science Faculty for their cooperation

Special thanks to the laboratory and nursing staffs in Dr. Selma Center for Renal Diseases, there are no enough words to describe your excellent work.

#### **Abstract**

This is a descriptive, cross-sectional and analytical study aimed at determining the changes induced by renal failure and hemodialysis in CBC, PT, APTT and Fbg level among 50 patients attending Dr. Selma center for kidney diseases in Khartoum State in June 2011. Male comprises 66 % of patients with age ranged from 16 to 77 years. A questionnaire was used to obtain patient's information as age, gender, duration of dialysis, treatment with Erythropoietin, Folic acid and Iron.

Five ml of venous blood was collected from patients (pre and post hemodialysis) and from 50 normal healthy persons as control, after their consent, dispensed into trisodium citrate and EDTA containers respectively. CBC and coagulation tests were performed using autoanalyzers.

Renal failure caused a statically significant decrease in RBC, Hb, PCV, MCHC, and lymphocyte (P. value 0.000 for all), a significant increase in MCV, RDW, eosinophil (P. value 0.000 for all) and neutrophils (P. value 0.006). Coagulation tests revealed significant reduction in PLT count and MPV (P. value 0.000 for all), a significant increase in PT and APTT (P. value 0.000 for all).

Hemodialysis caused a significant increase in RBC (P. value 0.001), Hb (P. value 0.001), PCV (P. value 0.007), and APTT (P. value 0.000).

### ملخص الأطروحة

هذه دراسة تحليلية وصفية لمقطع مستعرض. تهدف إلى قياس التغيرات التى أحدثها الفشل الكلوى و الغسيل الدموى على التعداد الكامل الدم، زمن البروثرومبين، زمن الثرومبوبلاستين الجزئى المنشط، و مستوى الفبرينوجين عند ٥٠ مريضا يخضعون للعلاج بالغسيل الدموى بمركز د. سلمى لأمراض الكلى بولاية الخرطوم و ذلك في يونيو ٢٠١١. شكل الذكور 77% من المرضى الذين تتراوح أعمار هم بين ١٦ و ٧٧ سنة.

تم جمع المعلومات عن المرضى بواسطة الأستبيان كالعمر، النوع، فترة الغسيل الدموى و الأدوية الداعمة الستعملة كالإرثروبوبيتين و حامض الفوليك و الحديد.

تم سحب ٥ مل من الدم الوريدى من كل مريض (قبل وبعد الغسيل الدموى) و من أشخاص طبيعيين صحيا بعد موافقتهم، وزعت على حاويتى سترات ثلاثية الصوديوم و EDTA بالتساوى و على الترتيب، تم أداء التعداد الكامل الدم و إختبارات التجلط بواسطة أجهزة تحليل أوتوماتيكية.

أحدث الفشل الكلوى إنخفاضا ذو دلالة إحصائية في تعداد الخلايا الحمراء، تركيز خضاب الدم، حجم الخلايا المتراكمة، متوسط تركيز خضاب الدم في الخلايا، و الخلايا اللمفاوية (P. value 0.000 للكل). كما أوضح إرتفاعا ذو دلالة إحصائية في كل من متوسط حجم الخلية ، RDW، و الحمضات (P. value 0.000 للكل) و للعدلات (P. value 0.006).

أظهرت إختبارات التجلط إنخفاضا ذو دلالة إحصائية في تعداد الصفائح الدموية و متوسط حجم الصفيحة الدموية ( P. value ) كما أظهرت زيادة ذات دلالة إحصائية في زمن البروثرومبين و زمن الثرومبوبلاستين الجزئي المنشط ( P. value 0.000 للكل).

P.) تركيز خضاب الدم (P. value 0.001)، تركيز خضاب الدم (P. value 0.001)، تركيز خضاب الدم (P. value 0.000)، حجم الخلايا المتراكمة (P. value 0.000) و زمن الثرومبوبلاستين الجزئى المنشط (value 0.000).

#### **Abbreviations**

ADP Adenosine diphsophate AKI Acute kidney disease

AML Acute myeloid leukaemia

APTT Activated Partial Thromboplastin Time

βTG B-thromboglobulin

ATP Adenosine triphosphate

BFU-E Burst-forming unit, erythroid

BUN Blood urea nitrogen
CBC Complete Blood Count
CD Cluster of differentiation

CFU-E Colony-forming unit, erythroid

CKD Chronic kidney disease
CRF Chronic renal failure
CV Co-efficient of variation

DIC disseminated intravascular coagulation

DNA Deoxyribonucleic acid EBV Epstein-Barr virus

EDTA Ethylene diamine tetra acetic acid eGFR Estimated Glomerular filtration rate

EPOR Erythropoietin receptor ESRD End Stage Renal Disease

Fbg Fibrinogen

FDPs Fibrinogen degradation products

G-CS granulocyte-colony-stimulating factor

GFR Glomerular filtration rate

GM-CSF Granulocyte-macrophage colony-stimulating factor

GP 1b Glycoprotein 1b Hb Hemoglobin HD Hemodialysis

HIV Human immunodeficiency virus HMWK High-molecular weight kininogen

HLA Human leucocyte antigen

Ig E Immunoglobulin E

IL-1 Interleukin-1

MCH Mean Cell Hemoglobin

MCHC Mean Cell Hemoglobin Concentration
M-CSF Macrophage- colony-stimulating factor

MCV Mean Cell Volume

MDRD Modification of diet in renal disease

mRNA Messenger ribonucleic acid

MPV Mean platelet volume

NAP Neutrophil alkaline phosphatase

NCKDS National Center For renal Diseases and Surgery

NK Natural killer cell

PAI-1 Plasminogen activator inhibitor-1

PCV Packed Cell Volume PCV

PD Peritoneal dialysis

PDGF Platelet-derived growth factor

PF4 Platelet factor 4
PLT Platelets count

pmp per million population
PT Prothrombin Time
RBC Red blood cell count

RDW Red blood cell count

RDW Red cell distribution width rh EPO Recombinant erythropoietin

RNA Ribonucleic acid

SLE Systemic lupus erythematosus

SPSS Statistical package for social sciences

TCR T-cell receptor
TF Tissue factor

TFPI Tissue factor pathway inhibitor

TNF Tumour necrosis factor

t-PA Tissue plasminogen activatorTWBC Total white blood cell count

TxA2 Thromboxane A2
URR Urea reduction ratio
VWF von Willebrand factor

## **Contents**

Chapter	One
---------	-----

The state of the s		
Introduction and literature review Pa		
1.1 Introduction		
re review	3	
The urinary system	3	
The kidneys	3	
Internal structure of the kidney	4	
The nephron	5	
Renal Corpuscle	5	
Renal Tubule	5	
Functions of the kidneys	6	
Measurement of Kidney function	7	
Renal failure	8	
Causes of renal failure	8	
Acute Kidney injury	9	
	9	
Replacement therapy for kidney failure	9	
Dialysis	9	
Transplantation	12	
Hemopoiesis	12	
Erythropoiesis	13	
Regulation of Erythropoiesis	14	
Granulopoiesis	14	
Control of granulopoiesis: myeloid growth factors	15	
Platelet production (Thrombopoiesis)	15	
	15	
	16	
	17	
<u> </u>	17	
	18	
	19	
	19	
	19	
	20	
	21 21	
*	21	
<u>*</u>	21 22	
· · · · · · · · · · · · · · · · · · ·	22	
	22	
	n and literature review ction Tre review The urinary system The kidneys Internal structure of the kidney The nephron Renal Corpuscle Renal Tubule Functions of the kidneys Measurement of Kidney function Renal failure Causes of renal failure Acute Kidney injury Chronic kidney disease Replacement therapy for kidney failure Dialysis Transplantation Hemopoiesis Erythropoiesis Regulation of Erythropoiesis Granulopoiesis: myeloid growth factors	

1.2.7.4	Basophils	23
1.2.7.4.1	Basophil leucocytosis (basophilia)	23
1.2.7.5	Lymphocytes	24
1.2.7.5.1	B and T lymphocytes	24
1.2.7.5.2	Natural killer cells	24
1.2.7.5.3	Lymphocytosis	25
1.2.7.5.4	Lymphopenia	25
1.2.8	Normal hemostatic mechanisms	26
1.2.8.1	Endothelium and the vascular system	26
1.2.8.2	The role of platelets	27
1.2.8.3	The role of blood coagulation	28
1.2.8.4	Formation of Fibrin	29
1.2.8.5	PT, PTT, and Fibrinogen Assays: Use and Interpretation	30
1.2.8.5.1	The PT Assay	31
1.2.8.5.2	The PTT Assay	31
1.2.8.5.3	Fibrinogen Assays	32
1.2.9	Hemostasis in renal disease	33
Rationale		34
Objectives		35
-		
	_	
Chapter T		
2	Materials and methods	36
2.1	Approach	36
2.2	Study type and design	36
2.3	Study area	36
2.4	Study population	36
2.5	Study variables	36
2.6	Sampling and sample size	36
2.7	Data collection methods and tools	36
2.7.1	Data collection	36
2.7.2	Specimen collection	37
2.8	Laboratory procedures	37
2.8.1	Complete Blood Count (CBC)	37
2.8.1.1	Principle	37
2.8.1.2	Sample material	38
2.8.1.3	Test procedure	38
2.8.2	PT, APTT and Fibrinogen	38
2.8.2.1	Detection principle for coagulation method	38
2.8.2.1.1	PT assay principle	38
2.8.2.1.2	APTT assay principle	39
2.8.2.1.3	Fibrinogen assay principle	39
2.8.2.2	Sample material	39
2.8.2.3	Reagents	39
2.8.2.4	Test procedures	39
2.8.2.3.1	PT procedure	39

2.8.2.3.2	APTT procedure	40
2.8.2.3.3	Fibrinogen assay procedure	40
2.9	Validity of reagents and instruments	40
2.10	Ethical consideration	40
2.11	Data processing and analysis	40
Chapter Thre	e	
Results		41
<b>Chapter Four</b>		
Discussion		48
Conclusion		50
Recommendatio	on and the same of	51
References		52
Appendices		
Appendix (1)	Questionnaire	54
Appendix(2)	Sysmex KX-21	55
Appendix $(3)$	Sysmex CA-50	56

## **List of Figures**

### **Chapter One**

Figure (1.1): The urinary system shown in anterior view	3
Figure (1.2): A coronal section through the kidney showing the cortex and medulla	4
Figure (1.3): The structure of the kidney showing the nephron and its vascular	6
Chapter Three	
Figure (3.1): Frequency of gender of study group	41
Figure (3.2): Frequency of age groups of patients and control group	42
Figure (3.3): Frequency of hemodialysis duration of patients	42
Figure (3.4): Comparison of study group pre hemodialysis (pre HD) and control group on	45
RBC, Hb, PCV, MCHC, and RDW	
Figure (3.5): Comparison of study group pre hemodialysis (pre HD) and control group on	45
TWBC, neutrophils, lymphocytes, monocytes, and eosinophils	
Figure (3.6): Comparison of study group pre hemodialysis (pre HD) and control group on	46
PLT, MPV, PT, APTT and Fbg level	
Figure (3.7): Comparison of study group pre (pre HD) and post hemodialysis (post HD) on	46
RBC, Hb, PCV, and red cell indices	

## **List of Tables**

Chapter One	
Table 1.1: White cells: normal blood counts	19
Table 1.2: Causes of neutrophil leucocytosis	20
Table 1.3: Causes of monocytosis	22
Table 1.4: Causes of eosinophilia	23
Table 1.5: Causes of lymphocytosis	25
Chapter Three	
Table 3.1: Comparison of Complete blood count and coagulation tests of study group	43
according to gender	
Table 3.2: Comparison of red cell indices, TWBC, and Eosinophil of study group	44
according to the duration of hemodialysis	
Table 3.3: Comparison of red cell indices, PTT, and Fbg of study group according to age	44
Table 3.4: Comparison of study group pre (pre HD) and post hemodialysis (post HD) on	47
TWBC, PLT, PT, APTT, and Fbg level	
Table 3.5: Comparison of effect of erythropoietin, iron, and folic acid intake on Hb	47
concentration	