

# **NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) IN RELATION TO RENAL ANEMIA OF HEMODIALYSIS PATIENTS**

**A Thesis Submitted In Partial Fulfillment For  
MD Degree in Internal Medicine**

**By**

**Mohamed Ahmed Mohamed Mohamed Khalil**  
**MB,BCh (Dec, 2003) - MSc Internal Medicine (Nov, 2007)**  
**Faculty of Medicine, Ain Shams University**

## **SUPERVISORS**

**Prof. Dr. Gamal El-Sayed Ibrahim Mady**  
**Professor of Internal Medicine,**  
**Faculty of Medicine, Ain Shams University**

**Prof. Dr. Iman Ibrahim Mohamed Sarhan**  
**Professor of Internal Medicine**  
**Faculty of Medicine, Ain Shams University**

**Prof. Dr. Heba Sayed Abdel-Aziz Asal**  
**Professor of Internal Medicine**  
**The National Research Center, Cairo, El-Dokki**

**Dr. Walid Anwar Mohamed Abdel Mohsen**  
**Lecturer in Internal Medicine,**  
**Faculty of Medicine, Ain Shams University**

**Dr. Walid Ahmed Bichari**  
**Lecturer in Internal Medicine**  
**Faculty of Medicine, Ain Shams University**

**Faculty of Medicine, Ain Shams University**

**2013**

# علاقة ليبوكالين النيتروفييل المرتبط بالجيلاتيناز بفقر الدم الكلوي في مرضى الغسيل الدموي

رسالة مقدمة من

الطبيب / محمد أحمد محمد محمد خليل

بكالوريوس الطب والجراحة – ديسمبر 2003

ماجستير في الأمراض الباطنة العامة – نوفمبر 2007

كلية الطب – جامعة عين شمس

توطئة للحصول على درجة الدكتوراه في الأمراض الباطنة العامة

المشرفون

الأستاذ الدكتور / جمال السيد إبراهيم ماضي

أستاذ الأمراض الباطنة - كلية الطب – جامعة عين شمس

الأستاذ الدكتورة / إيمان إبراهيم محمد سرحان

أستاذ الأمراض الباطنة - كلية الطب – جامعة عين شمس

الأستاذ الدكتورة / هبة سيد عبد العزيز عسل

أستاذ الأمراض الباطنة - المركز القومي للبحوث – الدقي

الدكتور / وليد أنور محمد محمد عبد المحسن

مدرس الأمراض الباطنة - كلية الطب – جامعة عين شمس

الدكتور / وليد أحمد بشاري

مدرس الأمراض الباطنة - كلية الطب – جامعة عين شمس

كلية الطب – جامعة عين شمس

2013

## **ACKNOWLEDGEMENT**

First and foremost, thanks to ALLAH, the most beneficent and merciful.

I wish to express my deepest gratitude to Prof. Dr. Gamal El-Sayed Ibrahim Mady, Professor of Internal Medicine, Faculty of Medicine, Ain Shams University, for proposing the study and for his step by step guidance and assistance throughout this work. The words cannot express my thanks to his expertise supervision, fruitful advice and encouragement.

I am very much obliged to the kindness and great help of Prof. Dr. Iman Ibrahim M. Sarhan, Professor of Internal Medicine, Faculty of Medicine, Ain Shams University, for her scientific guidance and assistance throughout this work. I am indebted to her for giving time and guiding with great patience.

No words could express my sincere appreciation and deepest gratitude to Prof. Dr. Heba Sayed Abdel-Aziz Asal, Professor of Internal Medicine, The National Research Center, Cairo, El-Dokki, for her continuous generous guidance, valuable criticism and encouragement throughout the whole research.

I want also to express my sincere gratitude to Dr. Inas Abdel Rasheed, Ass. Prof. of Clinical Pathology and Dr. Salwa Tawfik, Ass. Prof. of Internal Medicine, The National Research Center, Cairo, El-Dokki, for their tremendous effort, valuable help and support throughout this work.

I would like to thank very much Dr. Walid Anwar M. Abdel Mohsen and Dr. Walid Ahmed Bichari, Lecturers in Internal Medicine, Faculty of Medicine, Ain Shams University, for the great help, willing assistance and encouragement they offered me throughout this work.

## **ABBREVIATIONS**

**AKI:** Acute kidney injury  
**ARF:** Acute renal failure  
**BUN:** Blood urea nitrogen  
**CKD:** Chronic kidney disease  
**CRP:** C-Reactive protein  
**D-CTIN:** Drug-induced chronic tubulointerstitial nephritis  
**eGFR:** estimated Glomerular filtration rate  
**EPO:** Erythropoietin  
**ESAs:** Erythropoietin stimulating agents  
**ESRD:** End-stage renal disease  
**Hb:** Hemoglobin  
**HD:** Hemodialysis  
**MA:** Microalbuminuria  
**NAPRTCS:** North American Pediatric Renal Trials and Collaborative Studies  
**NGAL:** Neutrophil gelatinase associated lipocalin  
**NHANES:** National Health and Nutrition Examination Survey  
**NKF-K/DOQI:** National Kidney Foundation's Kidney Disease Outcomes Quality Initiative  
**PD:** Peritoneal dialysis  
**RES:** Reticulo-endothelial system  
**r-HuEPO:** Recombinant human erythropoietin  
**RRT:** Renal replacement therapy  
**SIRS:** Systemic inflammatory response syndrome  
**TIBC:** Total iron binding capacity  
**TSAT:** Transferrin saturation  
**USRDS:** the United States Renal Data System

## LIST OF TABLES

	<b>Page</b>
Table (1) shows % difference in the mean Hb level between HD patients (group 1A and 1B) versus the control group.	53
Table (2): shows the iron study in the group of patients with Hb level < 11 g/dl (Group 1A).	56
Table (3): shows the iron study in the patients of group 1B with Hb level (13 g/dl > Hb ≥ 11 g/dl).	56
Table (4): shows the iron study in the control group (Group 2) having Hb level ≥ 13 g/dl.	56
Table (5): shows % difference in the mean values of serum iron between HD patients (Group 1A & 1B) versus the control group	57
Table (6): shows % difference in mean values of serum ferritin between HD patients (Group 1A & 1B) versus the control group	58
Table (7): shows % difference in the mean values of TIBC between HD patients (Group 1A & 1B) versus the control group	59
Table (8): shows % difference in the mean values of TSAT% between HD patients (Group 1A & 1B) versus the control group	60
Table (9): shows % difference in the mean values of serum CRP between HD patients (Group 1A & 1B) versus the control group	62
Table (10): shows % difference in mean values of serum NGAL between HD patients (Group 1A & 1B) versus the control group	64
Table (11): Correlation between serum NGAL level and the parameters describing the iron status in all studied subjects.	66
Table (12): Correlation between serum CRP (ug/ml) and serum ferritin level (ng/ml) in all studied subjects.	69

## LIST OF FIGURES

	<b>Page</b>
Figure (1) shows mean Hb level between HD patients (group 1A & 1B) versus the control group (group 2).	53
Figure (2): shows comparison of the mean values of serum iron between HD patients (Group 1A & 1B) versus the control group	57
Figure (3): shows comparison of mean values of serum ferritin between HD patients (Group 1A & 1B) versus the control group	58
Figure (4) : shows comparison of the mean values of TIBC between HD patients (Group 1A & 1B) versus the control group	59
Figure (5): shows comparison of the mean values of TSAT% between HD patients (Group 1A & 1B) versus the control group	60
Figure (6): shows comparison of the mean values of serum CRP between HD patients (group 1A & 1B) versus the control group	62
Figure (7): shows comparison of mean values of serum NGAL between HD patients (group 1A & 1B) versus the control group	64
Figure (8): Correlation between serum NGAL level (ng/ml) and Hb level (g/dl) in all studied subjects.	66
Figure (9): Correlation between serum NGAL level (ng/ml) and serum iron (ug/dl) in all studied subjects.	67
Figure (10): Correlation between serum NGAL level (ng/ml) and serum ferritin (ng/ml) in all studied subjects.	67

Figure (11): Correlation between serum NGAL level (ng/ml) and TIBC (ug/dl) in all studied subjects. 68

Figure (12): Correlation between serum NGAL level (ng/ml) and TSAT% in all studied subjects. 68

Figure (13): Correlation between serum CRP (ug/ml) and serum ferritin level (ng/ml) in all studied subjects. 69

## CONTENTS

	Page
ABBREVIATIONS	i
LIST OF TABLES	ii
LIST OF FIGURES	iii
INTRODUCTION & AIM OF THE WORK	1
REVIEW OF LITERATURE:	
Chapter (I): Chronic Kidney Disease	6
Chapter (II): Renal Anemia	15
Chapter (III) NGAL	28
SUBJECTS & METHODS:	
Subjects	45
Methods	46
RESULTS	52
DISCUSSION	70
SUMMARY & CONCLUSION	79
REFERENCES	82
APPENDIX	
ARABIC SUMMARY	



# **ACKNOWLEDGEMENT**

# **INTRODUCION AND AIM OF THE WORK**

# **REVIEW OF LITERATURE**

# **SUBJECTS AND METHODS**

# RESULTS

# **DISCUSSION**

# **SUMMARY AND CONCLUSION**