Pain, Sleep Disturbance and Depression in Chronic Kidney Disease Patients

Thesis

Submitted for partial fulfillment for master degree in internal medicine

By

Diana Danial Lamee M.B.B.Ch

Supervised by

Prof. Dr. Howayda Abdelhameed Elshinnawy

Professor of Internal Medicine and Nephrology Faculty of Medicine- Ain shams University

Dr. Waleed Anwar Abdel-mohsen

Assistant Professor of Internal Medicine and Nephrology Faculty of Medicine- Ain shams University

Dr. Ramez Reda Moustafa

Assistant Professor of Neurology Faculty of Medicine- Ain shams University

Faculty of Medicine
Ain shams University
2016



سورة البقرة الآية: ٣٢

Aeknowledgment

- First, thanks are all due to Allah for Blessing this work until it has reached its end, as apart of his generous help throughout our life.
- It was an honor to work under the supervision of eminent professors, who lent me their whole hearted support and immense facilities as is their usual with their juniors. To them, I owe more than I can record. I would like to express my deepest gratitude and highest appreciation to professor Dr. Howayda Abdelhameed Elshinnawy, Professor of Internal Medicine and Nephrology, Faculty of Medicine, Ain shams University, for her continous encourgement and generous support, no word can express my gratitude.
- I would like to express my scincere gratitude to Dr. Waleed Anwar Abdel-mohsen, Assistant Professor of Internal Medicine and Nephrology, Faculty of Medicine, Ain shams University, who supervised this work with great interest and who gave me unlimited support throughout the work.
- I would like to express my scincere gratitude to Dr.Ramez Reda Moustafa, Assistant Professor of Neurology, Faculty of Medicine, Ain shams University, who supervised this work with great interest and who gave me unlimited support throughout the work.
 - am greatly honored to express my deep gratitude and faithfulness to Prof. Dr. Ashraf Donia, Professor of Nephrology, National Institute of Nephrology and Uorology, for his continous help and kind sympathy. And to all my professors and collegues in the National Institute of Nephrology and Uorology, for their continues help and support.
 - Finally, no words can express my deepest appreciation and gratitude to my family for their never ending supportr and care.

Contents

Subjects Pa	age
List of Abbreviations	I
• List of Tables	IV
• List of Figures	VII
• Introduction	1
• Aim of the Work	4
• Review of literature	
- Chapter (1): Chronic Kidney I	Disease5
- Chapter (2): Pain, Depression	and Sleep Disorder42
Patients and Methods	71
• Results	98
• Discussion	123
• Summary	138
• Conclusion	141
Recommendations	142
• References	143
• Appendix	175
Arabic Summary	

List of Abbreviations

ESKD : End – stage kidney diaease

ACEIs : Angiotensin converting enzyme inhibitors

ADA : American Diabetes Association

ADPKD: Autosomal dominant polycystic kidney

disease

ARBs : Angiotensin receptor blockers

AVF : Arteriovenous fistula

AVG : Arteriovenous graft

BDI-II : Beck Depression Inventory -II

BMI : Body mass index

Bp : Blood pressure

CHD : Chronic hemodialysis

CKD : Chronic kidney disease

CKD- : Chronic kidney disease-mineral bone

MBD disease

CVD : Cardiovascular disease

DFO : Desferrioxamine test

DM : Diabetes Mellitus

DSM-IV: The Diagnostic and Statistical Manuel of

Mental Disorders -IV

eGFR : Estimated glomerular filtration rate

EMA : European Medicine Agency

EpiFunD : Epidemiology of functional disorders

Study study

🕏 List of Abbreviations Z

ESA : Erythrocyte-stimulating agents

ESRD : End- stage renal disease

FDA : Food and Drug Administration

GCKD : German Chronic kidney disease

study

HB : Hemoglobin

HMG-Co: 3-hydroxy-3-methyl-glutaryl- CoA

A

HRQOL : Health related quality of life

HT : Hypertension

IV : Intravenous

KDIGO: The Kidney Disease: Improving Global

Outcomes

KDOQI: The Kidney Disease Outcomes Quality

Initiative

MDD : Major depressive disorder

MDRD : Modification of Diet Renal Disease

NICE : National Institue for Clinical Excllence

Non-REM: Non-rapid eye movement

NSAID : Non steroidal anti inflammatory

OSA : Obstructive sleep apnea

OTC : Over the counter

PLM : Periodic limb movement

PSGN: Post-streptococcal glomerular nephritis

PSQI : Pittsburgh Sleep Quality Index

PTH : Parathyroid hormone

QOL : Quality of life

🕏 List of Abbreviations 🗷

RA : Rheumatoid Arthritis

REM : Rapid eye movement

RLS: Restless legs syndrome

RRT : Renal Replacement Therapy

RTA : Renal tubular acidosis

S. Ca : Serum calcium

S. Po4 : Serum phosphorus

SC : Subcutaneous

SLE : Systemic lupus erytheromatosis

UAE : Urinary albumin excretion

List of Tables

Table	Title	Page
No		No
1	The KDOQI classification of the stages of CKD	5
2	Albuminuria categories in CKD	6
3	Guide to frequency of monitoring (number of times per year) by GFR and albuminuria category	7
4	The clinical stages of diabetic nephropathy	8
5	Other important but less frequently encountered causes of CKD are briefly presented, sub-divided into 2 divisions based on age and ethinicity	9
6	Prevalence rate of risk factors associated with chronic kidney disease	12
7	The percentages reflect the prevalence of anemia	18
8	Features of high and low turnover renal bone disease	21
9	Imaging options in CKD	27
10	A list of Erythropoiesis stimulating agents	39

11	Pain symptoms of common non-	47
	neuropathic and neuropathic pain	
	syndromes	
12	Pain management in patients with	49
	chronic kidney disease	
13	The Diagnostic and Statistical Manual	52
	of Mental Disorders-IV(DSM-IV)	
	defines major depression according to	
	different criteria	
14	Uremia-associated losses and	55
	dependence	
15	Safety profiles and dose adjustments	59
	recommended for different classes of	
	antidepressants in patients with CKD	
	and ESKD	
16	Diagnostic criteria for chronic insomnia	64
	in adults. Synthesis of criteria from	
	American Academy of sleep medicine	
17	Von korff questionnaires	74
18	Interpretation of von korff questionnaires	74
19	Demographic data for all studied groups	92
20	Hemodialysis characteristics of group 4	102
21	Patients clinical assessment in all studied	103
	groups	
22	Comparison between study groups as	105
	regard laboratory Work-up	
23	Prevalence of sleep disorders, depression,	111
	and pain in different stages	

🕏 List of Tables 🗷

24	Completions between DCOL DDL von	115
24	Correlations between PSQI, BDI, von	115
	korff, and other qualitative parameters	
25	PSQI regression model in all studied	116
	groups	
26	BDI regression model in all studied	117
	groups	
	6 1	110
27	Von korff pain score regression model in	118
	all studied groups	

List of Figures

Figure	Title	Page
No		No
1	Algorithm for proteinuria and	24
	microalbuminuria screening in the patient	
	with risk factors for chronic kidney	
	disease	
2	Depression and adverse clinical outcomes	56
3	Treatment of depression	58
4	Age (years)	99
5	Follow up duration(years)	99
6	Percentage of patients living alone %	100
7	Prevalence of DM as comorbedities	100
8	Prevalence of HCV infection	101
9	Mean BMI in different stages	104
10	Mean systolic blood pressure	104
11	Mean serum hemoglobin level	106
12	Mean serum albumin	107
13	Mean serum creatinine	107
14	Mean serum urea	108
15	Mean serum calcium	108
16	Mean serum phosphorus	109
17	Mean serum uric acid	109
18	Mean serum PTH	110
19	Mean Ca xPo4 products	110
20	PSQI	113

🕏 List of Figures 🗷

21	BDI	113
22	VON KORFF pain assessment	114
23	Relationship between sleep disorders and depression	119
24	Relationship between sleep disorders and pain	119
25	Relationship between serum albumin and sleep disorders	120
26	Relationship between serum UA and sleep disorders.	120
27	Relationship between S.PTH and sleep disorders	121
28	Relationship between S. Ca and pain	121
29	Relationship between S.UA and pain	122

Introduction

Chronic kidney disease (CKD) is a term that encompasses all degrees of decreased renal function, and is considered a worldwide public health problem (*Levey et al.*, 2012).

The kidney Disease: Improving Global Outcomes (KDIGO) established a definition and classification of CKD. The KDIGO defines CKD as abnormalities of kidney structure or function, present for > 3 months, with implications for health and CKD is classified based on cause, GFR category, and albuminuria category (CGA) (Stevens and Levin 2013).

Pain is a multidimensional phenomenon with physical, psychological, and social components. Failure to treat pain adequately could be expected to lead to disruption in many aspects of life, such as functional status, mood and sleep (*Cohen et al.*, 2007).

Body pain is one of the most important qualitative parameters for evaluating patients' quality of life. To improve quality of care provided to CKD patients, it is important to understand and relieve body pain (*Pham et al.*, 2010).

It has been reported that 82% of CKD patients undergoing dialysis had chronic pain and 35-70% of patients had moderate to severe pain. Chronic pain is common in CKD patients, especially in patients with end stage renal disease. Few studies have focused on chronic pain in early stage CKD patients (*Golan et al.*, 2009).

Chronic muscloskeletal pain was indpendetly and significantly associated with hyperuricemia as comorbidity, and with the (calcium x phosphate) product levels in early and late stage CKD patients who were not on dialysis (*Heng et al.*, 2014).

Sleep disturbance is common and bothersome to patients with chronic kidney disease (CKD) including those on long term dialysis. The natural history of sleep disturbance in these patients has not been adequately studied (*De Santo et al.*, 2010).

Patients with CKD not on dialysis had disruption of sleep that was independent of several risk factors. However those on hemodialysis had sleep disruption that was of much greater severity than that found amoung those with CKD not on dialysis (*Agarwal et al.*, 2011).

Clinical depression and subthreshold depressive symptoms are associated with increased mortality rate in dialysis patients. However, little is known about the association between elevated depressive symptoms with a decline in kidney function in patients who are not on dialysis (*Willem et al.*, 2011).