

Prevalence of Pruritus Among Patients with Chronic Kidney Disease, Hemodialysis Patients and Posttransplantation

Thesis

*Submitted for Partial Fulfillment of Master Degree
in Internal Medicine*

Presented by

Ahmed Fathy Abd El Haleem
(M.B., B.Ch.)

Under Supervision of

Prof. Dr. Mohamed El Tayeb Nasser
Professor of Internal Medicine
Faculty of Medicine - Ain Shams University

Dr. Yasser Mahmod El Shahawi
Lecturer of Internal Medicine
Faculty of Medicine - Ain Shams University

Dr. Dawlat Hussein Sany
Lecturer of Internal Medicine
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University

2011

List of Contents

Title	Page
♦ Introduction	1
♦ Aim of the Work	3
♦ Review of Literature:	
▪ Chapter 1:	
➤ Dermatologic Manifestations of Renal Disease	4
▪ Chapter 2:	
➤ Uremic Pruritus.....	20
▪ Chapter 3:	
➤ Treatment.....	42
♦ Patients and Methods	83
♦ Results	90
♦ Discussion	120
♦ Summary	152
♦ Conclusion	155
♦ Recommendations	156
♦ References	157
♦ Arabic Summary	--

List of Abbreviations

Abbrev.	
ALT	Alanine aminotransferase
APD	Acquired perforating dermatitis
AQP3	Aquaporin-3
AST	Aspartate aminotransferase
AZA	Azathioprine
b2MG	β 2-micro-globulin
BB-UVB	Broadband ultraviolet B
BCC	Basal cell carcinoma
BUN	Blood urea nitrogen
Ca	Calcium
Ca*pho4	Calcium phosphorus product
CAPD	Continuous ambulatory peritoneal dialysis
CBC	Complete blood count
CKD	Chronic kidney disease
CRP	C-reactive protein
CsA	Cyclosporine A
CXC	Chemokine
CXCR3	Chemokine receptor 3
CYP	Cytochrome P
DM	Diabetes mellitus
DOPPS	Dialysis Outcomes and Practice Patterns Study
ELISA	Enzyme linked immunesorbent assay
ESRD	End stage renal disease
FIR	Far-infrared rays

List of Abbreviations (Cont.)

Abbrev.

GBP	Gabapentin
GLA	Gammalinolenic acid
Hb	Hemoglobin
Hct	Hematocrit
HCV	Hepatitis C virus
HD	Hemodialysis
HLA	Human Leukocyte Antigens
HPV	Human papilloma virus
hsCRP	Highly selective C-reactive protein
IL	Interleukin
iPTH	Intact parathyroid hormone
ITSCC	International Transplant Skin Cancer Collaborative
IV	Intravenous
MCC	Merkel cell carcinoma
MED	Minimal erythema dose
MMF	Mycophenolate mofetil
MW	Molecular weight
NB-UVB	Narrowband ultraviolet B
NIUN	National Institute of Urology and Nephrology
P	Phosphate
PCT	Porphyria cutanea tarda
PD	Peritoneal dialysis
PGB	Pregabalin
PMMA	Polymethylmethacrylate

List of Abbreviations (Cont.)

Abbrev.

PTH	Parathyroid hormone
PUVA	Psoralen Ultraviolet A
RTRs	Renal transplant recipients
SC	Subcutaneous
SCC	Squamous cell carcinoma
SLE	Systemic lupus erthromatosis
SSRIs	Selective serotonin reuptake inhibitors
TAC	Tacrolimus
TNF	Tumor necrosis factor
TSAT	Transferritin saturation
UK	Untied Kingdom
UP	Uremic pruritus
URR	Urea reduction ratio
USRDS	United state renal data system
UV	Ultraviolet
UVA	Ultraviolet A
UVB	Ultraviolet B
UVB	Ultraviolet B
5-HT	5-hydroxy-tryptamine
8-MOP	8-methoxypsoralen
95% CI	95% confidence interval

List of Tables

Table No.	Title	Page
Table (1)	Dermatologic Manifestations of Diseases Associated with the Development of ESRD.....	5
Table (2)	Post-transplantation immunosuppressants and their main cutaneous side effects.....	19
Table (3)	Treatment Options for Chronic Kidney Disease Associated Pruritus.....	43
Table (4)	Treatment options for uraemic pruritus (UP)	81
Table (5)	Comparison between the studied groups as regard demographic characteristics (gender and age).....	90
Table (6)	Comparison between the studied groups as regard causes of chronic kidney disease	90
Table (7)	Comparison between the studied groups as regard pruritus	82
Table (8)	Comparison between the studied groups as regard severity of pruritus.....	93
Table (9)	Comparison between the studied groups as regard location of pruritus	94
Table (10)	Comparison between the studied groups as regard type of pruritus.....	95
Table (11)	Show comparison between cases with itching versus cases without itching as regard age in the studied groups	96
Table (12)	Show comparison between cases with itching versus cases without itching as regard sex in the studied groups	97

List of Tables (Cont.)

Table No.	Title	Page
Table (13)	Show comparison between cases with itching versus cases without itching as regard neuropathy in the studied groups.....	98
Table (14)	Show comparison between cases with itching versus cases without itching as regard xerosis in the studied groups.....	100
Table (15)	Comparison between cases with itching versus cases without itching as regard general data in dialysis group.....	101
Table (16)	Comparison between cases with itching versus cases without itching as regard causes of renal impairment in dialysis group.....	102
Table (17)	Relation between intensity of itching and dialysis session.....	103
Table (18)	Show comparison between cases with itching versus cases without itching as regard labs in dialysis group	105
Table (19)	Correlation between severity of itching versus other variables among dialysis group.....	107
Table (20)	Show comparison between cases with itching versus cases without itching as regard HCV in dialysis group.....	108
Table (21)	Show the most important factors related to pruritus among dialysis group.....	108

List of Tables (Cont.)

Table No.	Title	Page
Table (22)	Show comparison between cases with itching versus cases without itching as regard labs in CKD group.....	110
Table (23)	Show comparison between cases with itching versus cases without itching as regard HCV in CKD	111
Table (24)	Show correlation between pruritus versus all other variables among CKD group.....	112
Table (25)	Comparison between cases with itching versus cases without itching as regard general data in transplantation group.....	112
Table (26)	Show comparison between cases with itching versus cases without itching as regard labs in transplantation group.....	113
Table (27)	Show correlation between pruritus versus all other variables among transplantation group.....	114
Table (28)	Show correlation between pruritus versus all other variables among the three studied groups.....	115
Table (29)	Show effect of treatment received by the patients in the studied groups	116
Table (30)	Shows the effect of different form of treatment on pruritus in the studied groups.....	118

List of Figures

Figure No.	Title	Page
Figure (1)	Proposed pathogenetic model for uremic itch.....	35
Figure (2)	Therapeutic approach to CKD-associated pruritus IPTH= intact parathyroid hormone; Kt/V= urea clearance by dialysis.....	80
Figure (3)	Treatment hierarchy for ureamic pruritus treatment.....	82
Figure (4)	Causes of CKD in group 1.....	91
Figure (5)	Causes of CKD in group 2.....	91
Figure (6)	Causes of CKD in group 3.....	92
Figure (7)	Comparison between the studied groups as regard pruritus.....	93
Figure (8)	Comparison between the studied groups as regard severity of pruritus	94
Figure (9)	Comparison between the studied groups as regard location of pruritus	95
Figure (10)	Comparison between the studied groups as regard type of pruritus.....	96
Figure (11)	Comparison between cases with itching and cases without itching as regard sex in the studied groups.....	97
Figure (12)	Show Comparison between cases with itching and cases without itching as regard neuropathy in the studied groups	99
Figure (13)	Comparison between cases with itching and cases without itching as regard xerosis in the studied groups	101

List of Figures (Cont.)

Fig. No.	Title	Page
Figure (14)	Show relation between intensity of itching and dialysis session	104
Figure (15)	Comparison between cases with itching and cases without itching in dialysis group as regard laboratory investigation (phosphorus, calcium phosphate product and hematocrit)	106
Figure (16)	Show correlation between pruritus versus all other variables among dialysis group	109
Figure (17)	Shows comparison between cases with itching and cases without itching in CKD group as regard laboratory investigation	111
Figure (18)	Show comparison between cases with itching versus cases without itching as regard labs in transplantation group	114
Figure (19)	Show correlation between pruritus versus all other variables among the three studied groups	115
Figure (20)	Shows the effect of treatment of pruritus in the three studied groups	117
Figure (21)	Shows the effect of every treatment separately on pruritus	119

INTRODUCTION

The prevalence and incidence of chronic kidney disease (CKD) has increased drastically during the past several decades worldwide, making it a major public health issue...” In 2003, there were more than 320,000 people with end-stage renal disease in the United States, and the prevalence is predicted to increase to 650,000 by 2010 and 2 million by 2030 (*Robinson, 2006*).

Pruritus, often overlooked by nephrologists, primary care physicians, and health care professionals, is one of the most common and distressing cutaneous symptoms of CKD. CKD-associated pruritus frequently is a disabling and distressing symptom that has a significant impact on the mental and physical capacity of patients, contributing to daytime fatigue, agitation, and depression, also profoundly impacts on sleep (*Hamer and El-Nahas, 2006*).

The prevalence of CKD-associated pruritus varies substantially, ranging from 22% to 90%. In the early 1970s, Young et al. reported that 85% of dialysis patients were affected by CKD itch. In the largest and most recent epidemiological study to date (2006), the prevalence of CKD-associated pruritus was 42% (*Dyachenko et al., 2006*).

We observed no correlation between pruritus intensity and type of dialysis membrane. In addition, CKD-associated pruritus was reported to completely resolve after renal transplantation,

although in our experience, some patients continue to experience pruritus posttransplantation (*Duque et al., 2006*).

In 2000, Yosipovitch et al. developed a questionnaire for the evaluation and measurement of pruritus, based on the McGill Pain Questionnaire. This questionnaire subsequently was tested in 145 hemodialysis patients with CKD-associated pruritus. It proved to be reliable and provided valid data for the sensory, affective, and overall intensity of CKD-associated pruritus (*Yosipovitch et al., 2001*).

This questionnaire, along with other similar questionnaires, subsequently was used in studies that attempted to characterize clinical features of this distressing symptom. The development and use of a standardized questionnaire undoubtedly will provide a better understanding of CKD-associated pruritus, possibly facilitating discovery of a pathophysiological mechanism and allowing valid comparisons of different treatment options (*Zucker et al., 2003*).

AIM OF THE STUDY

The purpose of this work is to study the Prevalence of pruritus among patients with chronic kidney disease, hemodialysis patients and post-transplantation.

DERMATOLOGIC MANIFESTATIONS OF RENAL DISEASE

Introduction

Cutaneous examination of patients with ESRD has shown that 50-100% of patients have at least one dermatologic condition. A high prevalence of cutaneous disorders is expected, since most patients with ESRD have an underlying disease process with cutaneous manifestations. In addition, uremia and conditions associated with renal replacement therapy are fraught with numerous and, often, relatively unique cutaneous disorders (*Reichrath and Nurnberg, 2008*).

Dermatologic manifestations of renal disease may be divided into 3 general categories including:

- (1) Dermatologic manifestations of diseases associated with the development of ESRD.
- (2) Dermatologic manifestations of uremia.
- (3) Dermatologic disorders associated with renal transplantation.

(Reichrath and Nurnberg, 2008)

Table (1): Dermatologic Manifestations of Diseases Associated with the Development of ESRD (*Goldsmith and Black, 2001*).

Systemic Disorder	Renal Disorder	Dermatologic Manifestations
Diabetes mellitus	Diabetic nephropathy	Diabetic dermopathy Necrobiosis lipoidica Acanthosis nigricans Eruptive xanthomas Kyrle disease Scleredema
SLE	Glomerulonephritis Nephrotic syndrome	Purpura Chronic cutaneous lupus Subacute cutaneous lupus Photosensitivity Mucosal ulcers Vasculitis
Henoch-Schönlein purpura	Glomerulonephritis Vasculitis	Purpura
Wegener granulomatosis	Glomerulonephritis Vasculitis	Purpura Subcutaneous nodules Ulcers
Polyarteritis nodosa	Glomerulonephritis Vasculitis	Purpura Subcutaneous nodules Ulcers
Subacute bacterial endocarditis	Renal emboli Glomerulonephritis	Petechiae Purpura
Cholesterol emboli	Renal emboli	Petechiae Livedo reticularis Blue toes
HCV	Glomerulonephritis	Purpura Porphyria cutanea tarda Lichen planus Sclerodermatous plaques Cutaneous polyarteritis nodosa Necrolytic acral erythema
HIV	HIV-associated nephropathy	Eosinophilic folliculitis Oral hairy leukoplakia Bacillary angiomatosis Kaposi sarcoma
Systemic sclerosis	Malignant hypertension	Diffuse scleroderma
Amyloidosis	Nephrotic syndrome	Purpura Macroglossia
Fabry disease	Nephrotic syndrome	Angiokeratomas
Nail-patella syndrome	Renal tubular defects	Absent/displaced patella Absent/pitted nails
Tuberous sclerosis	Renal hamartomas Renal cell carcinoma	Adenoma sebaceum Ash-leaf macule Periungual fibromas Shagreen patch