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PRURITUS IN PATIENTS ON MAINTENANCE HAEMODIALYSIS AT KENYATTA NATIONAL HOSPITAL: QUALITY OF LIFE AND ASSOCIATED FACTORS

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A project done in partial fulfillment of the requirements for the award of

Fellowship in Nephrology of The University of Nairobi

DECLARATION

Student's Declaration

This project write-up is my original work. It shall not be reproduced without my permission as the author.

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ABSTRACT

Background: Dialysis associated pruritus causes impairment in quality of life and increases mortality. Even then, it is not well characterized and hence lacks effective treatment.

Objectives: To estimate the extent and disability impact of haemodialysis associated itch, and their relationship with clinical and laboratory characteristics among patients on maintenance haemodialysis at a tertiary health facility.

Study design: A cross sectional survey was conducted among patients on maintenance haemodialysis at Kenyatta National Hospital renal unit.

Sample size and sampling technique: One hundred and nine participants were enrolled, determined using Daniel's formula for finite populations. Total population purposive sampling technique was adopted.

Methodology: Researcher-administered questionnaire, aimed at collecting relevant patients' biodata, haemodialysis vintage, average number of dialysis hours per week and co-morbid conditions, was used. Pruritus was diagnosed by a score of > 5 on a 5D itch scale that was administered to those who reported to experience itching. Chart review was carried out to collect the following laboratory information; haemoglobin, mean corpuscular volume, calcium, phosphorus, creatinine, urea and albumin. Prevalence of pruritus, and pruritus disability scores were ascertained. Analysis was done to interrogate the relationship between pruritus and highlighted variables. The same was done for pruritus disability score categories.

Results: One hundred and nine participants were enrolled, 51.4% being male. The mean age was 46.6(SD: 15.9) years. The commonest cause of ESRD was chronic glomerulonephritis (35.8%), followed by diabetes mellitus (24.8%), then hypertension (21.1%). Thirty-seven (33.9%) participants had pruritus. Among those with pruritus,18.9 % had pruritus disability scores > 3. Xerosis was significantly associated with pruritus (75.7% vs 29.2%, P<0. 001). There was no association between laboratory characteristics and pruritus. Urine output < 200mLs in 24 hours was associated with higher pruritus disability scores (52.1% vs 6.7%, p=0.001). Likewise, absence of anaemia correlated positively with higher pruritus disability scores, (14.3% vs 0.0%, p = 0.046).

Conclusions: The prevalence of pruritus among patients on maintenance haemodialysis at Kenyatta National Hospital is 33.9%. Xerosis predicted the occurrence of pruritus. Urine output < 200mLs in 24 hours and absence of anaemia predicted higher pruritus disability scores, reflecting significant impairment in quality of life.

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LIST OF ABBREVIATIONS

CKD-MBD	Chronic kidney disease-Mineral and bone disorder
CRP	C- reactive protein
DM	Diabetes mellitus
EDTA	Ethylenediaminetetraacetic acid
EQC	External quality control
ESRD	End stage renal disease
GLA	Gamma linolenic acid
HD	Haemodialysis
IFSI	International Forum for the Study of Itch
IL2	Interleukin 2
iPTH	intact Parathyroid hormone
IQR	Interquartile range
KNH	Kenyatta National Hospital
MCV	Mean corpuscular volume
pH	Potential for hydrogen
QC	Quality control
QOL	Quality of Life
RRT	Renal replacement therapy
SD	Standard deviation
Th1	T - helper lymphocytes subtype 1
UECs	Urea, electrolytes and creatinine
UNL	Upper normal limit
UP	Uraemic pruritus
UVB	Ultraviolet B Light
VAS	Visual Analogue Scale

CHAPTER 1: INTRODUCTION

1.1 Background

Pruritus is one of the most disturbing symptoms experienced by patients receiving haemodialysis. Rising kidney morbidity (1–3), to recent global prevalence rates of between 11% to 13% (4), means a consequent requirement for haemodialysis (HD). As such, haemodialysis-associated pruritus is a commonly encountered phenomenon in clinical practice.

The trend of global growth of maintenance dialysis has been exponential. Thomas *et al* reported 170% rise in proportion of patients that were on maintenance dialysis in countries that had universal access and 154% increase in countries that did not yet have universal access, in the years 1990 to 2000 (5)**.** In tandem with this, the reported prevalence of haemodialysis associated pruritus has been equally high. In a study of 19,226 patients receiving maintenance haemodialysis across 11 countries, the prevalence of pruritus was 40.6%(6). Another cross-sectional study carried out across eleven countries, involving 18,000 haemodialysis patients estimated the prevalence of moderate to extreme pruritus to be 42% (7).

Haemodialysis associated pruritus has been shown to be positively associated with poor sleep, impairment in quality of life, depression and increased mortality (7,8). It is therefore an important problem that ought to be sought for, properly characterized and managed appropriately.

1.2 Problem statement

Despite high prevalence, and life-altering consequences, haemodialysis associated pruritus remains poorly characterized. It often escapes the attention of many clinicians, and hence lacks effective treatment. There is no local data on the prevalence of pruritus and associated clinical and laboratory chracteristics among patients on maintenance haemodialysis, most of who receive twice

weekly haemodialysis which is deemed inadequate for symptom control. Majority of these patients are not on any symptom ameliorating treatment for uraemic pruritus.

1.3 Justification

The study sought to inform the health care providers, involved in management of chronic kidney disease, the extent of haemodialysis associated pruritus in patients they interact with daily. By knowing the scale of this problem, it is hoped that they will be more alert and proactive in inquiring about its existence and taking appropriate steps towards its management.

The study also sought to determine the factors that may be positively associated with pruritus. This information is important in guiding health care personnel to better manage pruritus through intervening on such factors where possible.

Better characterization of haemodialysis associated pruritus will guide appropriate use of available therapeutic interventions that have been shown to reduce pruritus, including intensifying haemodialysis.

1.4 Study question

The study would answer the following question; What is the prevalence of pruritus in patients on maintenance haemodialysis at Kenyatta National Hospital, and how does haemodialysis associated pruritus relate with clinical and laboratory characteristics in these patients?

1.5 Objectives

1.5.1 Broad objective:

Broad objective was to establish the prevalence of haemodialysis-associated pruritus, and to determine its relationship with clinical and laboratory characteristics in patients on maintenance haemodialysis at Kenyatta National Hospital.

1.5.2 Specific objectives:

1. To determine the prevalence of haemodialysis associated pruritus in patients on maintenance haemodialysis at Kenyatta National Hospital.
2. To determine the relationship between haemodialysis associated pruritus and patients' clinical and laboratory characteristics.
3. To determine the relationship between pruritus disability scores and patients' clinical and laboratory characteristics.

CHAPTER 2: LITERATURE REVIEW

Introduction

Pruritus can be defined as unpleasant feeling on the skin that provokes the need to scratch (9). Most patients on maintenance haemodialysis (HD) for end stage kidney disease (ESRD) will experience this disturbing symptom. It can be caused by primary skin diseases or various systemic diseases. Renal impairment is reported as the most common systemic disorder that is associated with pruritus (10). The proportion of HD patients experiencing pruritus, as reported by several studies ranged widely from 40% to 84% (7,8,11,12). A number of metabolic disorders associated ESRD in dialyzing patients are speculated to be responsible for pruritus but its specific cause remains unknown.

The features of uraemic pruritus in patients with ESRD vary over time and in individual patients. Haemodialysis associated pruritus is frequent, almost daily occurring itch that is sensed on expansive, symmetrical skin surfaces. Pruritus can vary from a localized itch affecting the face, back and arms to a generalized itch. The severity of itch ranges from mild intermittent discomfort to severe persistent restlessness (12–14).

Impact of haemodialysis-associated pruritus on quality of life

Suffering from chronic pruritus often significantly interferes with sleep, sexual life, social life and mental health of patients. Incremental rise in the intensity of haemodialysis-associated pruritus has been shown to correlate with concurrent and proportional drop in morbidity-associated quality of life (13,15,16). Dialysis outcomes and practices patterns(DOPPS) investigators demonstrated that haemodialysis patients experiencing significant pruritus were more prone to have fatigue and to have poor quality sleep (11). Furthermore, haemodialysis associated pruritus is associated with

17% increased risk of all-cause mortality (11). These observations underscore the fact that haemodialysis-associated pruritus ought to be regarded as an important health problem.

Pathophysiology of haemodialysis associated pruritus

The mechanisms of pruritus are not well elucidated and not all pruritogens involved have been clearly identified. Even though many factors and mechanisms are thought to contribute to pruritus, strong evidence has pointed towards a central role of immune system and opioidergic system abnormalities (17).

It has been proposed that uraemic pruritus is a consequence of pro-inflammatory state and ensuing imbalance in T helper lymphocytes type 1(Th1) cytokines. To corroborate this postulation, serum C-reactive protein was found to be higher in a cohort of patients with haemodialysis-associated pruritus compared to those without (18–20). Kimmel and co-investigators found that haemodialysis patients experiencing pruritus had more enhanced Th1 cytokines and interleukin 6 (IL 6) levels when compared to those without (21). In tandem with this theory, anti- inflammatory therapies have been shown to ameliorate pruritus. Ultraviolet B (UVB) light (22), tacrolimus (23,24) and thalidomide (25) have all been found to ameliorate pruritus. Ultraviolet B light downregulates Th1 lymphocyte cell differentiation and clonal expansion hence attenuating interleukin 2 (IL-2) production. Thalidomide, on the other hand, blocks activation of Th 1 lymphocytes by reducing tumour necrosis factor levels in the blood, whereas tacrolimus downregulates T- lymphocyte activation through interfering with the activity of calcineurin phosphatase.

According to opioidergic theory, itching can occur when there is dysregulation in endogenous opioids and their receptors. It proposes that there exists hyperactivity of mu-opioid receptors and hypoactivity of kappa opioid receptors in skin cells and lymphocytes. The kidneys are

responsible for partial excretion of endogenous opioids and serum beta endorphin levels rise in the setting of renal function impairment. Opioids cause mast cells to degranulate resulting in pruritus (26). Naltrexone, a mu-opioid antagonist has been shown to alleviate pruritus (27). Likewise, nalfurafine, a kappa receptor agonist has been demonstrated to have beneficial results in the treatment of severe uraemic pruritus (28).

Chronic kidney disease-Mineral and bone disorder (CKD-MBD) is also thought to contribute to pruritus. It has been demonstrated that plasma levels of calcium, magnesium and inorganic phosphorus are much more elevated among pruritic patients. High levels of these divalent ions trigger degranulation of mast cells with subsequent release of histamine and serotonin, which are pruritogenic (29).

Dry skin/xerosis is common in haemodialysis patients (30). The impact of xerosis on pruritus was assessed by Morton *et al* who showed that among patients receiving haemodialysis, those who had significantly lower skin hydration status were more likely to have pruritus. It is thought that uraemic xerosis, even though it may not be the primary cause of pruritus, has a worsening effect by lowering the threshold for itch (31).

Inefficient removal of middle-molecule uraemic toxins with regular haemodialysis has been proposed as another possible reason for haemodialysis associated pruritus. This is supported by observation that high flux haemodialysis with convective clearance alleviates pruritus (32). On the other hand, higher efficacy removal of small molecules like urea by standard assessment of Kt/V has not been shown to improve pruritus, and has, in fact been associated with worsening of pruritus (33).

Severity of pruritus tends to be more during, or immediately after haemodialysis treatment session in a significant proportion of patients. It has been proposed that this could probably be due to antigen sensitization derived from dialysis membrane (34,35). Haemodialysis using polysulphone membranes was shown to be more commonly associated with pruritus than using cuprophane or haemophane membranes (36). On the other hand, the intensity of pruritus was higher in haemodialysis patients using cellulose membranes compared to those using polysulphone even though clearance achieved using either membranes is similar (37). Polymethylmethacrylate dialysis membranes and high-flux polyacrylonitrile membranes have the least incidences of pruritus (38,39).

There exists a positive co-relation between pruritus and neuropathy in haemodialysis patients. Peripheral neuropathy is almost an invariable feature in these patients. The efficacy of capsaicin, lidocaine and gabapentin in alleviating haemodialysis-associated pruritusis is in favour of this theory. In patients with pruritus, there are new changes in nerve fibers in skin as well as in central nervous system resulting in low threshold for perception of itch (40). It has been demonstrated, for instance, that there exists sprouting of neuron specific enolase immunoreactive nerve fibers throughout epidermis in haemodialysis patients, a feature that was not seen in healthy controls (41). Nervous system dysregulation, particularly the somatic component, is related to occurrence of haemodialysis associated pruritus (42,43).

Scales for measuring pruritus

Pruritus is a subjective symptom that has multiple dimensions. It is therefore often difficult to quantify pruritus. Many methods for assessing pruritus are limited by being uni-dimensional, only measuring intensity without quantifying other important aspects of pruritus like the impact it has on quality of life. Visual analogue scale (VAS) has been used for a long time and adequately

assesses the severity of pruritus (44). It does not, however, address other aspects of pruritus. Other validated scales recommended by International Forum for the Study of Itch (IFSI) for use in assessing haemodialysis-associated pruritus include Brief Itch Inventory, Medical Outcome Study and Skindex-10 (45). These scales incorporate a comprehensive assessment of psychometric properties of pruritus and are therefore more informative unlike the VAS. In recent time, a more refined multidimensional scale has been specifically designed and validated for assessing chronic pruritus. This 5D itch scale evaluates the five domains of pruritus which include severity, duration, direction, site and impact on quality of life in aspects such as sleep, leisure/social life and household chores. Compared to other scales, it is reliable, more specific and sensitive in assessing pruritus(46,47).

Treatment modalities for haemodialysis associated pruritus

Despite haemodialysis associated pruritus being a common and often debilitating symptom in patients with kidney failure, available evidence for its specific treatment is weak and only supported by small studies. General measures such as wearing loose clothing, cool environment and use of topical emollients are very important(48). Topical gamma linolenic acid (GLA) has been demonstrated to exert anti-pruritic effect, via modulatory effect on lymphocytes and lymphokines (49). Other topical agents that have demonstrated efficacy, though in small trials include capsaicin and pramoxene (50).

More convincing body of evidence, including in placebo-controlled trials, has been found for effectiveness of gabapentin and pregabalin in the treatment of haemodialysis-associated pruritus (51,52). Some studies have demonstrated non-inferiority of desloratadine compared to gabapentin and have suggested that it could be preferably used in view of its less sedating effect (53). Second

generation sedating antihistamines have been used historically for treatment of haemodialysis associated pruritus, even though there are no studies confirming their efficacy.

Certain modalities of extracorporeal renal replacement therapies have proven effective in ameliorating pruritus. High flux haemodialysis, haemofiltration and haemoperfusion have been found to be significantly better in improving pruritus intensity (54–56). Likewise, controlling calcium and phosphorus levels tightly is important in reducing the severity of pruritus (57).

Th1 lymphocyte immunomodulating approaches have been shown to have a role in treatment of uraemic pruritus. Broad band UVB downregulates Th1 lymphocyte differentiation and clonal expansion hence decreasing IL-2 production (58,59). Thalidomide interferes with Th1 lymphocyte activation by lowering tumour necrosis factor alpha activation (25). Calcineurin inhibitors like tacrolimus and cyclosporin suppress T- lymphocyte activation by inhibiting the activity of phosphorylase enzyme calcineurin phosphatase. Local application of tacrolimus 0.03% or 0.1% was demonstrated to improve pruritus by Kuypers *et al* (24).

Naltrexone, oral μ-opioid antagonist, has been studied with some positive outcomes although other studies did not prove efficacy (60,61). Montelukast, a leukotriene receptor antagonist has been compared to placebo, and it significantly improved uremic pruritus (62). Likewise, mast cell stabilizers like cromolyn sodium have demonstrated efficacy in uraemic pruritus (63). Other agents that have been tried include doxepin, ondansetron and pentoxifylline (64,65).

CHAPTER 3: MATERIALS AND METHODS

3.1 Study population

This consisted of patients with end stage renal disease on long term renal replacement therapy by haemodialysis, and patients who remained haemodialysis dependent for a period exceeding one month after an episode of acute kidney injury, at Kenyatta National Hospital. There are approximately 110 patients receiving haemodialysis on a long-term basis at KNH renal unit.

3.2 Study area

The study was carried out at Kenyatta National Hospital, Renal Unit. Kenyatta National Hospital is a tertiary referral hospital located in the capital city of Kenya, Nairobi, with a capacity of 2000 beds. Renal unit is equipped to provide in-hospital dialyisis to patients needing both acute and long-term maintenance haemodialysis. Clinical and nutritional reviews are provided to these patients as well. It also hosts renal transplant clinic where pre-transplant evaluation and post-transplant follow up of patients is conducted. There are 26 haemodialysis stations, 2 water treatment plants and a dedicated renal laboratory in the unit. Besides patients needing acute haemodialysis, there are about 110 patients on long term maintenance haemodialysis, most of who come from Nairobi, and are scheduled to attend a minimum of two sessions per week.

3.3 Study design

Cross sectional survey was carried out to find out the prevalence of pruritus, its disability impact and associated clinical and laboratory factors among patients with ESRD on dialysis.

3.4 Inclusion criteria

All patients with end stage renal disease on maintenance haemodialysis and all patients who remained haemodialysis dependent beyond one month after an episode of acute kidney injury.

3.5 Exclusion criteria

Failure to obtain consent.

Presence of primary dermatological disease, unrelated to renal failure.

3.6 Sample size

There are approximately 110 patients on maintenance haemodialysis at KNH renal unit. This constituted a finite study population. As such, the formula with finite population correction was adopted for this study(66).

Thus: $$n = \frac{NZ^2 P(1-P)}{d^2(N-1) + Z^2 P(1-P)}$$

Where,

n = Sample size with finite population correction,

N = Population size,

Z = Z statistic for a level of confidence,

P = Expected proportion/prevalence (in proportion of one),

d = Precision (in proportion of one).

From previous data, prevalence of uraemic pruritus has been estimated to be 40% (0.4)(11). Adopting Z statistic of 1.96 corresponding to 95 % level of confidence, and precision of 0.05, substituting into the formula above yielded a sample size of 85 at minimum.

Being a population survey, we aimed at recruiting all the patients meeting the inclusion criteria. 109 participants were enrolled into the study.

3.7 Sampling technique

A total population purposive sampling was adopted for this study.

3.8 Recruitment and consenting procedure

All patients on maintenance haemodialysis as a result of end stage renal disease or haemodialysis dependency for a period exceeding one month after an episode of acute kidney injury were identified by reviewing haemodialysis register at renal unit. They were then listed according to the day and time they are scheduled to dialyze. They were assessed for eligibility by the principal investigator through a brief clinical history and examination in a private examination room at the unit. This was done as they came for haemodialysis. All those eligible were introduced to the intended study by the principal investigator and consenting done.

3.9 Study procedure

Researcher administered questionnaire was filled for all consenting patients. This was aimed at collecting relevant patients' bio-data, dialysis vintage, average number of dialysis hours per week in the previous one month, and capturing co-morbid conditions that led to, or existed with chronic kidney disease. A subjective inquiry about the presence of pruritus was made for each patient. For those who answered in affirmative, pruritus was qualified by a score of more than 5 on a 5D itch scale (appendix 3) that was administered to each of them.

Chart review was carried out to collect the following laboratory information, if it had been done on blood samples collected within the previous one month as part of routine care: haemoglobin, mean corpuscular volume, serum calcium, phosphate, creatinine, urea and albumin.

3.10 Data management and analysis

3.10.1 Data collection

Data collection was executed by the researcher on a composite data entry form. Each data entry form was allocated a unique identifier, which was the participant's number. Data was later transferred to computer epi-data software. The following variables were captured;

Independent - Age, gender, duration since initiation of dialysis, number of dialysis hours per week in the previous one month, haemoglobin, mean corpuscular volume, calcium, phosphate, creatinine, albumin and co-morbid conditions that included xerosis, neuropathy, diabetes mellitus, hypertension and chronic glomerulonephritis.

Dependent- Presence of pruritus and pruritus disability score.

Operational definition of some variables:

Xerosis- Rough, dry and scaling skin, described by the patient and elicited through examination of entire skin surface.

Neuropathy- Symptoms arising from a disorder in the function of peripheral nerves. In this study, the symptoms that we considered included temporary or permanent numbness, tingling, prickling, burning sensation, and increased sensitivity to touch and/or pain.

Chronic glomerulonephritis- This was determined based on any or all of the following:

1. History of hypertension, proteinuria, haematuria, edema, and progressive loss of kidney function ending up in renal failure.
2. Sonographically small kidneys with loss of corticomedullary differentiation.
3. Hypertension in the setting of end stage renal disease, in a person younger than 46 years, where all other secondary causes have been considered unlikely, and with no history of diabetes mellitus.

4. Documented kidney biopsy results revealing glomerulosclerosis.

3.10.2 Statistical analysis

We used STATA version 13 to analyze data. Descriptive statistics including mean with corresponding standard deviation (SD) and median with corresponding interquartile range (IQR) were used to summarize continuous variables such as age, calcium, urea and creatinine among others. The Gaussian assumptions were assessed using histograms, normal probability plots, and Shapiro-Wilk test. Whenever the assumptions were satisfied, mean and SD were used to summarize the continuous variables, otherwise median and the IQR were used.

Frequencies and corresponding percentages were used to summarize categorical variables such as sex, presence or absence of pruritus among others.

Association between independent categorical variables like sex, hypertension, diabetes mellitus, and pruritus status was assessed using Pearson's Chi Squared test. Independent sample t-test was used to compare the means, and two sample-Wilcoxon rank sum test was used to compare the medians between those who were qualified to have pruritus and those who did not have.

Binary logistic regression model was used to study the variables associated with pruritus status. The variables included in the multivariable logistic regression model were chosen using backward selection method.

3.11 Ethical considerations

3.11.1 Approval

Approval of the study was sought from Kenyatta National hospital/University of Nairobi Ethical and Research Committee. Authorization was obtained from Kenyatta National Hospital administration as well.

3.11.2 Risks

There were no actual or anticipated risks paused to the participants in this study.

3.11.3 Informed consent and confidentiality

Decision to participate in the study was voluntary and those who declined to consent were not discriminated against in any way. All willing participants were required to provide prior signed informed consent, and assent where applicable.

Confidentiality of participants was observed. Interviews and clinical examinations were conducted in private and quiet rooms by principal investigator. When necessary, a chaperon nurse was availed during examination. The participants' information was kept confidential through de-identification, where actual names or file chart numbers were not used at data entry. Access to entered data was restricted via a password.

CHAPTER 4: RESULTS

One hundred and eleven patients on maintenance haemodialysis were assessed for eligibility. Two were excluded due to presence of primary cutaneous disease; one had psoriasis and the other had herpes zoster with neuralgia. A total of 109 participants were enrolled. The mean age was 46.6 (SD: 15.9) years with a range of 18 and 87 years. 51.4% were male.

Table 1: Demographic characteristics of the participants

Variable	N	n (%) or Mean (SD)
Age (Years), Mean (SD)	109	46.6 (15.9)
Range		16 – 87
Gender, n (%)		
Male	109	56 (51.4%)
Female		53 (48.6%)

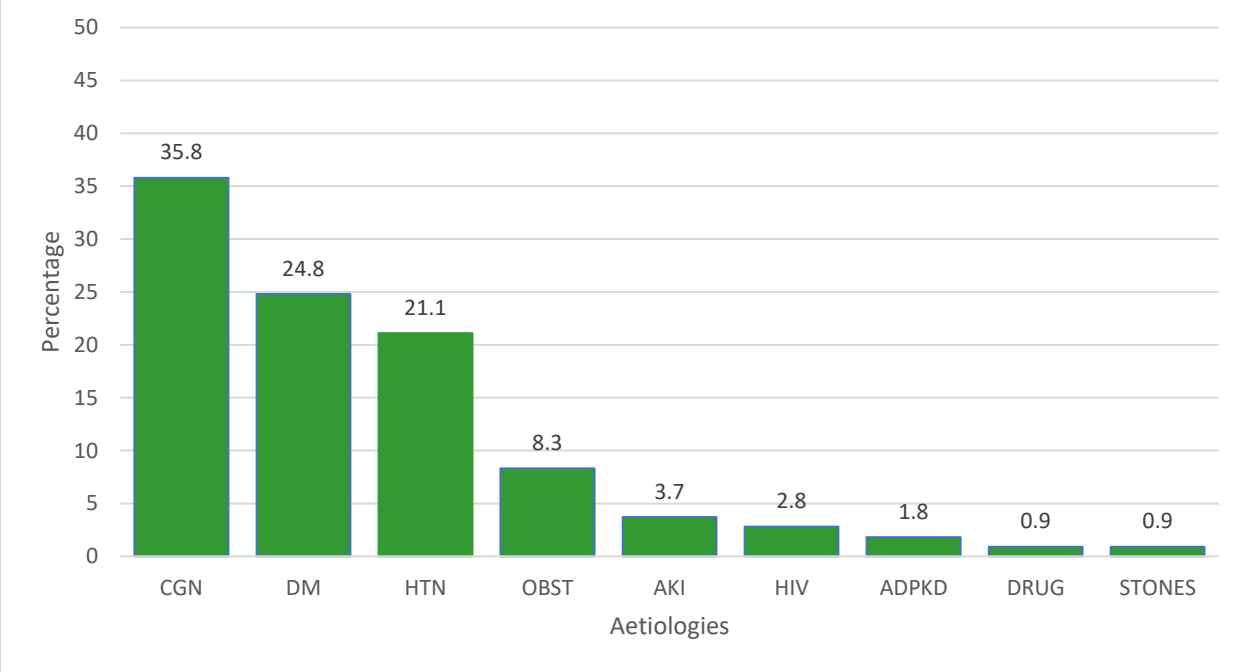

Figure 1: Aetiologies of ESRD

Majority (35.8%) of the participants had chronic glomerulonephritis (CGN) contributing to ESRD. Diabetes mellitus and hypertension contributed 24.8% and 21.1% respectively. Obstructive causes accounted for 8.3 %. There were 3.7% and 2.8% with dialysis dependence beyond one month following acute kidney injury and HIV-associated kidney disease respectively.

Table 2: Clinical characteristics

Variable	n (%) or Median (IQR)
Anuria, n (%)	25 (22.9%)
Xerosis, n (%)	49 (45.0%)
Neuropathy, n (%)	52 (47.7%)
Functioning AVF, n (%)	23 (21.1%)
HD vintage (Months), Median (IQR)	8 (4, 12)
Range	1.5 – 132
Weekly HD (Hours >8)	5 (4.6%)

Out of all participants, 22.9 % had urine output less than 200 mililitres in 24 hours, 45.0% had xerosis and 47.7% experienced neuropathy. Only 21.1% had functioning AVF.

The median haemodialysis vintage was 8 (IQR: 4.0, 12.0) months with a range of 6 weeks to 132 months. The proportion of participants having more than 8 dialysis hours per week was 4.6%.

Table 3: Laboratory characteristics

Variable	n (%) or Median (IQR)
Urea (mmol/L), Median (IQR)	19.1 (14.4, 24.3)
Range	5.8 - 55.8
Creatinine (µmol/L), Median (IQR)	606.0 (457.0, 800.0)
Range	278 - 1841.9
Calcium (mmol/L), Median (IQR)	2.1 (1.9, 2.4)
Range	0.9 - 2.95
Phosphorus (mmol/L), Median (IQR)	1.1 (0.9, 1.6)
Range	0.3 - 4.6
Albumin (g/L), Mean (SD)	36.9 (7.8)
Range	15.5 - 60.0
Hypoalbuminaemia, n (%)	40 (37.0%)
MCV (fL), Mean (SD)	90.0 (7.7)
Range	69.4 - 107.0
HB (g/dL), Median (IQR)	9.3 (7.8, 10.5)
Range	6.0 - 16.7
Anaemia, n (%)	99 (90.8%)

More than one third (37.0%) of the participants had hypoalbuminemia. The median hemoglobin was 9.3 (IQR: 7.8, 10.5) g/dL. 90.8 % of participants had anaemia.

Table 4: Outcome variables

Variable	N	n (%) or Median (IQR)
Pruritus, n (%)	109	**37 (33.9%)**
Pruritus DS	37	2 (2, 3)
Range		1 – 5
Pruritus DS>3(severe pruritus), n (%)	37	**7 (18.9%)**

Out of 109 participants, 37 (33.9%) had pruritus according to 5D itch scale and of these, only 2 (5.4%) were on symptom-ameliorating treatment. Median pruritus disability score was 2.0 (IQR: 2.0, 3.0) in a score range of 1 to 5. Amongst the participants with pruritus, 18.9% had pruritus disability score that was > 3, indicating severe impairment in quality of life.

Table 5: Association between demographic and clinical characteristics, and pruritus status

	Pruritic		
	No	Yes	P-value
Variable	N=72 (66.1%)	N = 37 (33.9%)	
Age (Years), Mean (SD)	46.7 (16.7)	46.6 (14.5)	0.979ϕ
Gender, n (%)			
Male	38 (52.8%)	18 (48.7%)	
Female	34 (47.2%)	19 (51.4%)	0.683†
DM, n (%)			
Yes	22 (30.6%)	5 (13.5%)	
No	50 (69.4%)	32 (86.5%)	**0.051**†
HTN, n (%)			
Yes	13 (18.1%)	10 (27.0%)	
No	59 (81.9%)	27 (73.0%)	0.277†
CGN, n (%)			
Yes	23 (31.9%)	16 (43.2%)	
No	49 (68.1%)	21 (56.8%)	0.244†
Others (Obst, HIV, AKI, Drugs, ADPKD, & Stones), n (%)			
Yes	14 (19.4%)	6 (16.2%)	
No	58 (80.6%)	31 (83.8%)	0.680†
Anuria, n (%)			
Yes	19 (26.4%)	6 (16.2%)	
No	53 (73.6%)	31 (83.8%)	0.232†
Xerosis, n (%)			
Yes	21 (29.2%)	28 (75.7%)	
No	51 (70.8%)	9 (24.3%)	**<0.001**†
Neuropathy, n (%)			
Yes	31 (43.1%)	21 (56.8%)	
No	41 (56.9%)	16 (43.2%)	0.175†
Functioning AVF, n (%)			
Yes	17 (23.6%)	6 (16.2%)	
No	55 (76.4%)	31 (83.8%)	0.370†
HD Vintage (Mo), Median (IQR)	8.0 (3.5, 12.5)	9.0 (4.0, 12.0)	0.751φ
Weekly HD Hours >8			
Yes	3 (4.2%)	2 (5.4%)	

ϕ - t test, †- Chi Square, φ- Wilcoxon-rank Sum

The proportion of participants with diabetes mellitus among those who had pruritus was low (13.5%) compared to among those without pruritus (30.6%), (P=0.051). The participants who had xerosis were significantly higher (75.7%) among those with pruritus, compared to those without pruritus (29.2%), p <0.001. The other demographic and clinical variables did not depict significant association with pruritus status.

Table 6: Association between laboratory characteristics and pruritus status

	Pruritic		
	No	**Yes**	**P-value**
Variable	**N=72 (66.1%)**	**N = 37 (33.9%)**	
Urea *(mmol/L)*, Median (IQR)	18.7 (14.2, 24.2)	19.6 (15.4, 25.6)	0.639ᵠ
Creatinine *(µmol/L)*,Median (IQR)	582.5 (440.0, 775.7)	658.0 (457.0, 882.0)	0.243ᵠ
Calcium *(mmol/L)*,Median (IQR)	2.1 (1.9, 2.3)	2.2 (1.9, 2.5)	0.123†
Phosphorus *(mmol/L)*, Median (IQR)	1.1 (0.9, 1.6)	1.2 (0.9, 1.5)	0.647ᵠ
Albumin *(g/L)*, Mean(SD)	37.4 (7.8)	37.2 (7.9)	0.921ᵠ
MCV *(fL)*, Mean (SD)	90.3 (8.2)	89.3 (6.4)	0.470ᵠ
HB *(g/dL*) Median (IQR)	9.3 (7.7, 10.9)	9.3 (8.1, 10.5)	0.830ᵠ
Hypoalbuminaemia*(g/L)*, n (%)			
Yes	23 (37.1%)	11 (36.7%)	
No	39 (62.9%)	19 (63.3%)	0.968†
Anaemia, n (%)			
Yes	61 (87.1%)	33 (97.1%)	
No	9 (12.9%)	1 (2.9%)	0.108†

ᵠ - t test, †- Chi Square, ᵠ- Wilcoxon-rank Sum

There was no evidence of association between laboratory characteristics and presence or absence of pruritus (p>0.05).

Table 7: Logistic regression model assessing the factors associated with pruritus

Variable	N	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Xerosis			
No		Reference	Reference
Yes	109	7.56 (3.05, 18.71)	**7.56 (2.83, 20.25)**
DM			
No		Reference	Reference
Yes	109	0.36 (0.12, 1.03)	0.60 (0.13, 2.78)
HTN			
No		Reference	Reference
Yes	109	1.68 (0.66, 4.31)	1.91 (0.44, 8.35)
CGN			
No		Reference	Reference
Yes	109	1.62 (0.72, 3.68)	2.14 (0.52, 8.89)
Neuropathy			
No		Reference	Reference
Yes	109	1.74 (0.78, 3.86)	1.24 (0.48, 3.18)
Age (Years)	109	1.00 (0.97, 1.03)	1.00 (0.96, 1.04)
Sex			
Female		Reference	Reference
Male	109	0.85 (0.38, 1.87)	1.09 (0.39, 3.00)

Adjusted for diabetes mellitus, hypertension, CGN, neuropathy, age, and sex, xerosis remained associated with more than seven times increased odds for occurrence of pruritus, Adjusted OR: 7.56 (95% CI: 2.83, 20.25).

Table 8: Association between demographic and clinical characteristics, and pruritus disability score

	Pruritus disability score ≤ 3	**Pruritus disability score > 3**	**P-value**
Variable	N = 30 (81.1%)	N = 7 (18.9%)	
Age (Years), Median (IQR)	47.2 (14.1)	43.9 (16.7)	0.589[ϕ]
Gender, n (%)			
Male	15 (50.0%)	3 (42.9%)	
Female	15 (50.0%)	4 (57.1%)	0.734[†]
DM, n (%)			
Yes	4 (13.3%)	1 (14.3%)	
No	26 (86.7%)	6 (85.7%)	0.947[†]
HTN, n (%)			
Yes	8 (26.7%)	2 (28.6%)	
No	22 (73.3%)	5 (71.4%)	0.919[†]
CGN, n (%)			
Yes	13 (43.3%)	3 (42.9%)	
No	17 (56.7%)	4 (57.1%)	0.982[†]
Others (Obst, HIV, AKI, Drugs, ADPKD, &Stones), n (%)			
Yes	5 (16.7%)	1 (14.3%)	
No	25 (83.3%)	6 (85.7%)	0.878[†]
Urine output < 200mLs, n(%)			
Yes	2 (6.7%)	4 (57.1%)	
No	28 (93.3%)	3 (42.9%)	**0.001**[†]
Xerosis, n (%)			
Yes	21 (70.0%)	7 (100.0%)	
No	9 (30.0%)	0 (0.0%)	0.096[†]
Neuropathy, n (%)			
Yes	16 (53.3%)	5 (71.4%)	
No	14 (46.7%)	2 (28.6%)	0.384[†]
AVF, n (%)			
Yes	4 (13.3%)	2 (28.6%)	
No	26 (86.7%)	5 (71.4%)	0.325[†]
HD Vintage (Months), Median (IQR)	8.0 (4.0, 12.0)	12.0 (3.0, 12.0)	0.626[φ]
Weekly HD hours >8			
Yes	2 (6.7%)	0 (0.0%)	
No	28 (93.3%)	7 (100.0%)	0.482[†]

ϕ - t test, †- Chi Square, φ- Wilcoxon-rank Sum

There was evidence of association between urine output less than 200 millilitres in 24 hours and higher pruritus disability score (p=0.001). A higher proportion of participants who had pruritus disability score > 3 had urine output < 200mLs in 24 hours, 57.1% compared to 6.7% among those who had a pruritus disability score of 3 or less.

Table 9: Association between laboratory characteristics and pruritus disability score

	Pruritus disability score ≤ 3	Pruritus disability score > 3	P-value
Variable	**N = 30 (81.1%)**	**N = 7 (18.9%)**	
Urea*(mmol/L)*, Median (IQR)	20.5 (15.8, 25.0)	16.9 (12.0, 26.2)	0.479[φ]
Creatinine*(µmol/L)*, Median (IQR)	639.0 (453.0, 855.5)	677.0 (507.0, 962.0)	0.571[φ]
Calcium*(mmol/L)*, Median (IQR)	2.2 (2.0, 2.5)	2.2 (1.9, 2.5)	0.463[†]
Phosphorus*(mmol/L)*, Median (IQR)	1.1 (0.9, 1.5)	1.3 (0.9, 1.9)	0.418[φ]
Albumin *(g/dL)*, Mean (SD)	38.5 (7.7)	32.8 (7.4)	0.094[ɸ]
MCV *(fL)*, Mean (SD)	88.7 (6.6)	91.4 (5.6)	0.209[ɸ]
HB *(g/dL)*, Median (IQR)	9.2 (7.4, 10.5)	9.6 (8.2, 10.5)	0.831[φ]
Hypoalbuminaemia *(g/L)*, n (%)			
Yes	8 (34.8%)	3 (42.9%)	
No	15 (65.2%)	4 (57.1%)	0.698[†]
Anaemia, n (%)			
Yes	27 (100.0%)	6 (85.7%)	
No	0 (0.0%)	1 (14.3%)	**0.046**[†]

ɸ- t test, †- Chi Square, φ- Wilcoxon-rank Sum

All participants who had pruritus disability of score ≤ 3 were anemic compared to 85.7% among those who had pruritus disability score > 3 (p = 0.046).

CHAPTER 5: DISCUSSION

This cross-sectional survey was conducted among patients receiving maintenance haemodialysis. It constituted a relatively young population, with a median age of 46 years, which ties up with the fact that glomerulonephritides have been shown, in previous surveys, to be the leading cause of chronic kidney disease in Africa. The phenotype of glomerulonephritis in Africa has been described. It tends to occur in relatively young people, often being aggressive disease that responds poorly to treatment, ultimately leading to end stage renal disease (67,68). The diagnosis of chronic glomerulonephritis (CGN) among our participants was inferred from a consideration of factors that included a relatively young age less than 45years, sonographically small kidneys with loss of corticomedullary differentiation, history of edema, hematuria, proteinuria and relatively rapid progression to requirement for renal replacement therapy. In our study, the contribution of CGN to ESRD was the highest at 35.8% followed by diabetes mellitus at 24.8% and hypertension at 21.1%.

There was no difference in the proportion of haemodialysis-requiring ESRD among either sex. The median dialysis vintage was 8 months, which would appear short considering low transplantation rate in Kenya. With the roll-out of Managed Equipment Services (MES) programme by the Government of Kenya, availing dialysis services across many parts of the country, many patients initiated on haemodialysis in a tertiary referral centre like Kenyatta National Hospital are sent to continue haemodialysis in other facilities once they become stable. The short median dialysis vintage may also reflect the high mortality that occur in haemdialysis population especially in low and middle income countries(LMIC), like ours, where access to transplantation is still a challenge for many (69,70).

Traditionally, a total of 12 haemodialysis hours per week has been recommended as adequate. Most (95.4%) of the participants in this study fell short of this, and were on 8 hours per week. This is majorly because of scheduling convenience and financial convenience for patients, as well as ensuring equity of haemodialysis services that are still only in-centre in our Kenya. Twice weekly haemodialysis has been practiced widely particularly among patients with low morbidity burden, good residual kidney function and those with financial constraints. Generally, it has not impaired the quality of life when compared to three times weekly haemodialysis (71). Dialyzing for 8 hours in a week or more than 8 per week did not have any statistically significant relationship with pruritus status or its disability scores in our study.

The aim of this survey was to evaluate the extent of, and disability scores associated with pruritus among haedmodialysis patients at Kenyatta National Hospital and to correlate these with clinical and laboratory characteristics. Using 5D-itch scale, the prevalence of pruritus was 33.9%. This is high, considering the negative health consequences like increased rate of depression, poor sleep and even mortality that have be shown to be associated with pruritus (11). Generally, the proportion of pruritus among haemodialysis patients has varied widely, from 40% to 84% (6–8). This has been so, most likely, because of various reasons including the changing haemodialysis practices over time, non-uniform haemodialysis practices in different centres and different scales used for determining pruritus status and intensity among others.

Among the participants with pruritus, 18.9% had significant impairment in quality of life. This was based on a disability score of >3, in a scale of 1 to 5, when we assessed the impact of pruritus on the following aspects of patient lives; sleep, leisure/social activities, housework/errands and work/school performance. Our finding regarding the impact of pruritus on quality of life, that parallels severity of pruritus, compared to that reported by Rayner *et al* where they found 18%

significant pruritus in their survey (7). In the same survey, a high rate of reporting of itch problem to the health worker for treatment was noted, with only18 % of people with pruritus not being on symptom-ameliorating treatment. This is in contrast to observation in our study, where about 95 % of participants with pruritus were not on any symptom ameliorating treatment. The study did not interrogate the reasons for this observation. Pruritus associated with haemodialysis may have been largely ignored, and its impact on morbidity, quality of life and mortality has not captured the attention of many clinicians.

We sought to correlate a number of important clinical and laboratory characteristics of participants, with pruritus. Uraemic xerosis, clinically characterized by rough, dry and scaling skin is a common phenomenon in patients with ESRD and increases to 50% to 85% after initiation of maintenance haemodialysis. The rate of uraemic xerosis in our study participants was 45%. Participants who had uraemic xerosis were significantly higher (75.7%) among those with pruritus, compared to those without (29.2%), $p < 0.001$. Other studies have established a less direct relationship between uraemic xerosis and uraemic pruritus. Whereas xerosis do not seem to cause pruritus, its presence has been shown to aggravate the severity of existing pruritus, both therefore, contributing to declining scores in quality of life (72,73). The interaction between xerosis and pruritus is not clear. Skin is a reservoir of up to 20% of body water, and disturbed volume equilibrium in dialysis patients over-stretches homeostatic mechanisms at the expense of skin, making it dry and vulnerable to external irritants and hence pruritus.

Polyneuropathy, regardless of cause, has been positively correlated with occurrence of pruritus, and this has led to use of drugs like gabapentin and pregabalin in treating uraemic pruritus. Pruritus was shown to be common among patients with diabetes mellitus and it has been postulated to be related to diabetic polyneuropathy (74). It would be reasonable to hypothesize that haemodialysis

patients with diabetes mellitus would have higher odds for developing pruritus. A surprising finding in our study, however, was a higher tendency for those without diabetes mellitus to have pruritus (p=0.051). This is a difficult to explain finding, but we hypothesize that polyneuropathy due to ureamia distributed evenly in the study population regardless of comorbid disease, was a competing reason for pruritus. Afsar *et al* demonstrated that even in non-diabetic haemodialysis patients, HbA1c levels were independently related to uraemic pruritus (75). In non-diabetic patients on haemodialysis, disturbed glucose metabolism as demonstrated by relatively high HbA1c levels, may have a role in the development of neuropathy, cancelling out the role of polyneuropathy that is attributable to diabetes mellitus per se. If this is the case, it is plausible to hypothesize that, perhaps, haemodialysis patients with diabetes mellitus may have an impaired perception of itch and therefore would report less of pruritus.

Derangements in a number of laboratory variables have been associated with occurrence of pruritus. Patients with pruritus are likely to have high calcium, high phosphorus, high parathyroid hormone, high ferritin, high c- reactive protein, low albumin among other parameters. Our study did not find a relationship between any of the selected laboratory characteristics and pruritus. This may point to the possible multi-factorial aetiology of pruritus that operate variedly in different populations.

Using disability domain of 5D-itch scale, we rated the extent to which pruritus contributed to disability, and examined whether certain variables contributed to higher pruritus disability scores. Urine output less than 200 milliliters in 24 hours was associated with higher pruritus disability scores. Similar observation was reported by Ming-Hui Liu *et al* (76). This underscores the importance of residual kidney function in patients with ESRD on haemodialysis. Residual urine in haemodialysis patients, is a reasonable surrogate indicator of residual kidney function. Residual

kidney function is associated with better control of volume status, electrolytes including divalent ions, more efficient clearance of middle molecules and protein bound solutes, and less inflammation. Generally, patients with residual kidney function seem to have a less morbidity burden, including pruritus, and have better quality of life.

Majority (90.8%) of our participants had anaemia. We found out that anaemia was associated with lower pruritus disability scores. Whether it is in the context of iron repletion therapies or inflammatory states, excess serum ferritin has been associated with development of, and severity of pruritus in haemodialysis patients (77). There have been conflicting reports, though, regarding direct contribution of high serum ferritin level to occurrence of pruritus, in the context of treatment of iron deficiency anaemia among dialyzing patients. Yen-Lin Chiu and co-workers did not find an association between ferritin and pruritus or its severity, after controlling for normal C- reactive protein levels (18). Almost all patient in our population used parenteral iron without regular monitoring. We hypothesize that even though iron therapy has an important role in the treatment of anaemia, lack of proper monitoring of iron status may have led to high blood ferritin levels and worsening of pruritus. This is likely to be the reason as to why absence of anaemia was associated with higher pruritus disability scores in the present study.

Limitations:

This study was not without limitations. The domains of 5D-itch scale were scored based on participants' recall of prior events. This could have potentially introduced some recall bias that may have potentially skewed the data.

The diagnosis of chronic glomerulonephritis (CGN) was inferred since most patients had not had kidney biopsies before progressing to end stage renal disease. There is a potential overlap between CGN and primary hypertension and we are cognizant of the fact that this may have a bearing on

the relative contribution of various aetiologic categories to end stage renal disease as reported as reported in our study.

CHAPTER 6: CONCLUSIONS

From this study, the following conclusions are drawn:

1. The prevalence of pruritus among patients on maintenance haemodialysis at Kenyatta National Hospital was 33.9%. This is high considering the health consequences of pruritus that include depression, impairment in quality of life and mortality. Majority of patients with pruritus are not on any symptom relieving treatment.
2. Xerosis, characterized by rough, dry and scaly skin was diagnosed in 45% of the patients, and was found to be associated with occurrence of pruritus. Likewise, absence of diabetes mellitus was positively correlated with occurrence of pruritus.
3. Laboratory charateristics, which included haemoglobin, mean corpuscular volume, serum urea, serum creatinine, serum calcium, serum phosphorus and serum albumin, were not associated with occurrence of pruritus.
4. Among participants with pruritus, only 18.9% were scored as having high disability scores, reflecting significant impairment in quality of life as a result of pruritus. Urine output less than 200mLs in 24 hours and absence of anaemia were positively correlated with increased pruritus disability scores/severity.

CHAPTER 7: RECOMMENDATIONS

From this study, the following recommendations are made:

1. Given the high prevalence of haemodialysis associated pruritus, health care providers ought to be more vigilant in order diagnose and manage it appropriately.
2. Uraemic xerosis, which is common and has been demonstrated to be associated with occurrence of pruritis among haemidialysis patients, should be sought for and treated with therapies like topical emollients.
3. Practices that preserve residual kidney function should, at all times, be incorporated in the management of haemodialysis patients since preserved function is associated with less incidence of pruritus. Such practices include avoidance of excess ultrafiltration, avoidance of nephrotoxic drugs and agents, judicious use of diuretics among others.

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APPENDIX 1: STUDY APPROVAL DOCUMENT

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KENYATTA NATIONAL HOSPITAL APPROVED 13 JUN 2018 KNH/UoN-ERC P.O. Box 20723-00202 NRB.

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KENYATTA NATIONAL HOSPITAL
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Ref: KNH-ERC/A/229

June 13, 2018

Dr. Peter Kipruto Koech
Reg. No.H114/10160/2018
(Nephrology Fellowship student)
East Africa Kidney Institute
College of Heath Sciences
University of Nairobi

Dear Dr. Koech

RESEARCH PROPOSAL – PRURITUS AMONG PATIENTS ON MAINTENANCE HAEMODIALYSIS AT KENYATTA NATIONAL HOSPITAL; QUALITY OF LIFE AND ASSOCIATED FACTORS (P227/04/2018)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is from 13th June 2018 – 12th June 2019.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director, CS, KNH
The Chairperson, KNH-UON ERC
The Assistant Director, Health Information, KNH
Prof. S.O. McLigeyo(UoN, Dr. Ahmed Sokwala (Aga Khan University Hospital)

APPENDIX 2: DATA COLLECTION FORM

Identifier/study number _____

Age: _____ years Gender: Male, ☐ Female, ☐

Section A- Participants interview questions:

What has the doctor told you/what do you know, is the cause of chronic kidney disease?

_____

Are there other concurrent illnesses you have?

1) _____

2) _____

3) _____

4) _____

How long have you been dialyzing? _____ months

How many hours do you dialyze per week? _____ hours

Do you experience dryness of skin on near daily basis in the last one month?

Dryness qualified through examination YES, ☐ NO, ☐

Do you experience tingling, pins and needles, burning on near daily basis in the last one month?

YES, ☐ NO, ☐

Do you experience itching on daily or near daily occasions in the last one month?

Itching present (qualified using 5D- itch scale) YES, ☐ NO, ☐

Are you on any specific treatment for your itching problem? YES, ☐ NO, ☐

Section B- Chart abstraction data:

Haemoglobin	_____	g/dl
Mean corpuscular volume	_____	fL
Corrected calcium	_____	mmol/L
Phosphate	_____	mmol/L
Albumin	_____	g/L
Urea	_____	mmol/L
Creatinine	_____	µmol/L

APPENDIX 3: 5D -ITCH SCALE

Duration: During the last 2 weeks, how many hours a day have you been itching?

Less than 6 hrs/day	6-12 hrs/day	12-18 hrs/ay	18-23 hrs/day	All day
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

Degree: Please rate the intensity of your itching over the past 2 weeks: -

Not present	Mild	Moderate	Severe	Unbearable
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

Direction: In the last 2 weeks, has your itching got better or worse compared to previous month: -

Completely resolved	Much better but still present	Little bit better but still present	Unchanged	Getting worse
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

Disability: Rate the impact of your itching on the following activities over the last 2 weeks: -

	N/A	Never affects	Occasionally affects	Frequently affects	Always affects
Leisure/social	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
Housework/errand	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
Work/school	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

Sleep	Never affects sleep	Occasionally delays falling asleep	Frequently delays falling asleep	Delays falling asleep and occasionally wakes me up at night	Delays falling asleep and frequently wakes me up at night
	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

Distribution: Mark whether itching has been present in the following parts of your body over the last 2 weeks. (If the body part is not listed, choose the one that is closest anatomically): -

Head/scalp	☐	Tops of feet/toes	☐
Face	☐	Soles	☐
Chest	☐	Palms	☐
Abdomen	☐	Tops of hands/fingers	☐
Back	☐	Fore arms	☐
Buttocks	☐	Upper arms	☐
Thighs	☐	Groins	☐
Lower legs	☐	Points of contact with clothing (e.g. waist band, undergarments)	☐

Note:

Single-item domain scores (duration, degree and direction) are equal to the value indicated below the response choice range (1–5). The disability domain includes four items that assess the impact of itching on daily activities: sleep, leisure/social activities, housework/errands and work/school. The score for the disability domain is achieved by taking the highest score on any of the four items. For the distribution domain, the number of affected body parts is tallied (potential sum 0 to16) and the sum is scored as follows: sum of 0-2 = score of 1, sum of 3-5 = score of 2, sum of 6-10 = score of 3, sum of 11-13 = score of 4and sum of 14-16 ==score of 5.

APPENDIX 4: CONSENT EXPLANATION FORM

Hallo! My name is Dr. Peter Kipruto Koech. I am a student at University of Nairobi School of Medicine/East Africa Kidney Institute. I am carrying out a study titled: '**Pruritus in patients on maintenance haemodialysis at Kenyatta National Hospital: quality of life and associated factors'**

Why have I been invited to take part?

I am interested in enumerating the extent, severity and factors related to itch among patients on maintenance haemodialysis at Kenyatta National Hospital. This is in order to better understand and hence plan for its treatment.

What am I needed to do?

This will involve asking you questions relevant to occurrence of itching, for which we expect you to answer accurately, and entering the answers you provide on the data entry sheet. We shall also review your chart to find information on results of relevant laboratory tests.

How do I benefit from the study?

The information obtained from this study will add onto the knowledge and understanding of itching that occur in patients undergoing haemodialysis and hence help improve its treatment. There will be no monetary compensation. If you will be found to have features and/or laboratory parameters that are out of recommended ranges for management of your condition, you will be informed and treatment interventions shall be offered.

Risks of participating

There are no risks in participating in this study.

Confidentiality

Records relating to your participation in this study will remain confidential. Your name will not be used in any report resulting from this study. You will receive a signed copy of this consent form.

Do I have to take part in the study?

Your participation is by free will. You may decide not to participate, and you remain free to withdraw consent at any stage during the study without prejudice.

APPENDIX 5: CONSENT FORM

I ……. (Name of patient), do hereby agree to participate in the research study. The purpose, methods and means by which the study will be conducted; and the risk which may be reasonably expected have been explained to me by .....……. (Researcher's name).

I have been given the opportunity to ask questions concerning this study and any such questions have been answered to my full and complete satisfaction.

I understand that I may at any time during the course of this study revoke this consent and withdraw from the study without prejudice.

Patient's signature …… Date…….

For additional information, you may contact the following:

Dr. P. K. Koech

Principal investigator,

P.O Box 4797-30100, ELDORET

Telephone: 0711601759

Prof. M. L. Chinda

Secretary, KNH-UoN ERC

P.O Box 20723 – 00202, NAIROBI

Telephone: 254-020-726300 Ext 9

APPENDIX 6: MAELEZO KUHUSU UTAFITI

Mada

Jina langu ni Daktari Peter Kipruto Koech. Ninasomea shahada ya Fellowship ya utabibu wa magonjwa ya figo katika Chuo Kikuu cha Nairobi, Kitivo cha Afya/ East Africa Kidney Institute.

Niko na nia ya kufanya utafiti kwa ajili ya kukusanya takirimu kuhusu ugonjwa wa kujikuna kwa wanaofanyiwa usafishaji wa damu, yaani dialysis katika Hospital Kuu ya Kitaifa ya Kenyatta. Kichwa cha utafiti huu ni; **'Viuzishi vya, na hadhari za tatizo la kujikuna miongoni mwa wagonjwa wa figo wanaofanyiwa matibabu ya usafishaji damu kwenye Hospitali Kuu ya Kitaifa ya Kenyatta'.**

Je, nimealikwa kujiunga kwa nini?

Matarajio ya utafiti huu ni kuchunguza kama kuna sababu fulani kwenye historia yako, ama damu yako yanayochangia kuwepo au kuzidi kwa tatizo la kujikuna. Hii itasaidia kuhelewa na hivyo basi kupanga matibabu ya shida hii.

Nitahitajika kufanya nini?

Tutakuuliza maswali kadhaa yanayo ambatana na ugonjwa wako na tutahitaji kuchukua damu ili kupima viwango vya vipimo kadhaa muhimu kwa ugonjwa uliyonayo.

Je, nitanufaika kivipi kwa kujiunga na utafiti huu?

Manufaa yataanzia kwenye kupata mawaidha kuhusu magonjwa ya figo. Iwapo utapatikana kuwa na ishara ya itilafu kupitia historia au vipimo vya damu, utashauriwa na matibabu utapewa.

Hakutakuwepo na malipo yeyote utakayopewa kwa kujiunga na utafiti huu.

Je kuna madhara yatakayonipata?

Hakuna madhara tunayotarajia kuwakumba watakaoshiriki kwenye utafiti huu.

Je, rekodi yangu binafsi na matokeo ya vipimo vyangu yatawekwa siri?

Damu itatumika kwa sababu iliyotajwa pekee, wala si kwa sababu zingine zozote. Maswala yote yanayokuhusu yatawekwa siri na wala hautatambuliwa kwa jina au njia nyingine yeyote.

Je, ni lazima kujiunga na utafiti huu?

Kujiunga ni kwa hiari yako wewe mwenyewe. Waweza kuamua kutojiunga au waweza kujiondoa kwenye utafiti huu kwa wakati wowote, wala hautadhulumiwa kwa kufanya maamuzi kama hayo.

APPENDIX 7: CHETI CHA IDHINI

Mimi (jina la mhusika), ……, nimesoma na kukubaliana na maelezo niliyopewa kuhusu utafiti huu. Maswali yangu yote yamejibiwa kwa ukamilifu.

Nimekubali kuingia utafiti huu.

Sahihi…… Tarehe……

Shaidi ……. (mtafiti mkuu au msaidizi wake)

Tarehe……..

Kwa maelezo zaidi, unaombwa uwasiliane na:

Daktari. P. K. Koech

Mtafiti mkuu

Sanduku La Posta 4797-30100, ELDORET.

Nambari ya simu 0711601759

Prof. M.L. Chinda

Katibu wa idhaa ya uadilifu kwenye utafiti

Hospitali Kuu ya Kenyatta

Sanduku La Posta 20723 – 00202, NAIROBI

Simu ya ofisi: 254-020-726300 Ugani 9

APPENDIX 8: SPECIMEN HANDLING AND PRINCIPLES OF ANALYSIS

Specimen collection, handling and transport

The procedure was explained to the patient/participant and verbal consent sought. Universal safety precautions were observed. A tourniquet was then applied 5 cm proximal to the selected venipuncture site. The site was cleaned with methylated spirit starting from the centre and working outwards then allowed to dry. The patient's arm was grasped firmly using the thumb to keep the skin taut and anchor the vein. A sterile needle mounted on the sterile syringe was inserted gently into the lumen of the vein at an angle of 15- 30º, and approximately 4 mLs of blood drawn. 2 mLs each was then emptied into a plain and a citrated/EDTA specimen bottles. After adequate blood was drawn the tourniquet was released and a swab applied at the site under pressure for a minute. The containers were labelled with the study number of the participant. All tests were done within 2 hours of blood collection.

Equipment used in analysis

The machines used for sample analysis included the BioLis Clinical Chemistry Analyzer for serum albumin, phosphorus, calcium, electrolytes, urea, creatinine and C-reactive protein; the Cobas® Analyser from Roche diagnostics for intact parathyroid hormone and the Sysmex® Blood cell Counter from Hass Scientific for haemoglobin and MCV. These were stationed at the renal unit laboratory and biochemistry laboratory, both at Kenyatta National Hospital.

Quality control and quality assurance

The laboratories actively run quality control (QC) materials on a daily basis to ensure the quality of results is guaranteed at all times. Laboratories also actively participate in external quality control (EQC) programme provided by Riqas®Company.

Albumin measurement principle

At a slightly acid pH (pH=4.2), serum albumin combines with bromocresol green to produce coloured complex whose intensity at 570 nm is directly proportional to the concentration of albumin.

Calcium measurement principle

Arsenazo III reagent reacts with calcium to form a bluish-purple coloured complex. The amount of colour formed is measured by an increase in absorbance of the reaction mixture at 630 nm. The intensity of colour is directly proportional to calcium present in the sample.

Inorganic phosphorus measurement principle

Ammonium molybdate combines with phosphate in presence of sulphuric acid to produce a phosphomolybdate complex. The absorbency increase is directly proportional to the concentration of phosphate.

Urea measurement principle

The determination of urea is based on coupled enzymes (Urease/glutamate Dehydrogenase [GLDH]), which is a quantitative kinetic type of analysis. The rate of decrease in absorbance measured at 340 nm wavelength is directly proportional to the urea concentration in the specimen.

Creatinine measurement principle

The determination of serum creatinine is based on Jaffe reaction. The reaction occurs between creatinine and picrate ion in an alkaline medium; a red-orange colour complex whose intensity is measured at 510 nm is directly proportional to the concentration of creatinine.

Blood cell count principle

Complete blood count is performed by an automated analyser that counts the numbers and types of different cells within the blood. It aspirates a very small amount of the sample through the narrow tubing. Within this tubing, there are sensors that count the number of cells going through it and using a diode laser bench. Fluorescent flow cytometry provides the sensitivity needed for measuring and differentiating cell types in whole blood and body fluid samples. For detection, light detectors are used as well as the measurement of electrical impedance. One way the instrument can tell what type of blood cell is present is by size. The parameters measured in full blood count included: red blood cells, white blood cells, platelets count, haematocrit and haemoglobin concentration; absolute and differential counts for neutrophils, lymphocytes, eosinophils, monocytes and basophils; red blood cell indices (mean corpuscular volume, mean corpuscular haemoglobin concentration, mean corpuscular haemoglobin).