OBSTRUCTIVE SLEEP APNEA RISK AND ASSOCIATED FACTORS AMONG PATIENTS WITH END-STAGE KIDNEY DISEASE ON MAINTENANCE HEMODIALYSIS AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM

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OBSTRUCTIVE SLEEP APNEA RISK AND ASSOCIATED FACTORS AMONG PATIENTS WITH END-STAGE KIDNEY DISEASE ON MAINTENANCE HEMODIALYSIS AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM

By

Frank Peter, MD

A Dissertation Submitted in (Partial) Fulfillment for the Requirement of Degree in Master of Medicine in Internal Medicine of the Muhimbili University of Health and Allied Sciences

October, 2024

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled; **"Obstructive sleep apnea risk and associated factors among patients with End-stage kidney disease on Maintenance Hemodialysis at Muhimbili National Hospital, Dar es Salaam"**, in (partial) fulfilment of requirements for the degree of Master of medicine (Internal Medicine) of Muhimbili University of Health and Allied Sciences.

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DECLARATION AND COPYRIGHT

I, Frank Peter declare that this dissertation is my original work and has not been submitted elsewhere for examination, award of a degree, or publication and will not be presented to any other University for a similar or any other degree award. Where other people's work has been used, this has properly been acknowledged and referenced per MUHAS requirements.

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My family; my mother and siblings for standing with me during my postgraduate studies with constant encouragement whenever I was low in spirit, prayers, resources, and unwavering support.

DEDICATION

This dissertation is dedicated to my mother Juliana Kazuzuru for her unending love, support, and encouragement and for the memory of my father the late Peter William Madibu, may his soul continue resting in eternal peace. Amen

ABSTRACT

Background: Obstructive sleep apnea (OSA) is claimed to affect more than 50% of hemodialysis patients, with the reported prevalence being extremely variable. It is known that OSA increases cardiovascular risk in ESRD patients and impairs the QOL with cardiovascular mortality remaining the leading cause of death in these patients.

Aim: To determine the prevalence and associated factors of risk of OSA among ESRD patients on maintenance hemodialysis therapy at Muhimbili National Hospital (MNH).

Methodology: A hospital-based cross-sectional study was conducted among patients with ESRD on maintenance HD between September 2023 and January 2024 at MNH dialysis centre. The patient's sociodemographic and clinical characteristics were recorded. **The** STOP-Bang and ESS questionnaires were administered serially starting with SBQ. The ESS score of ≥ 10 points. Comparison of categorical variables was done using Chi-square and Robust Poisson regression was used to identify factors associated with OSA. A significance level was set at p-value <0.05

Results: A total of 350 ESRD patients were enrolled in the study. The median age was 52.0 IQR (43-59) years with a male-to-female ratio of 2.4:1. The prevalence of risk of OSA was 37.1%. A significantly high prevalence of risk of OSA was seen among hypertensive patients (42.4%) (p=0.001) and diabetic patients (62.2%) (p<0.0001). Independent factors associated with OSA were hypertension (aPR(95%CI) =2.91, (2.09-4.06), p<0.0001) and diabetes (aPR(95%CI) =3.37 (2.68-4.23), p<0.0001). Dialysis vintage, number of HD sessions per week, dialysis adequacy, and laboratory parameters were not independently associated with the risk of OSA.

Conclusion: The risk of OSA is common among ESRD patients on maintenance hemodialysis. Early detection and effective management of those patients with risk of OSA among ESRD patients by nephrologists is of great significance as it will reduce cardiovascular complications and improve the quality of life.

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LIST OF ABBREVIATIONS

AHI	Apnea-Hypopnea Index
aPR	Adjusted Prevalence Ratio
AVF	Arteriovenous Fistula
BMI	Body Mass Index
BQ	Berlin Questionnaire
BUN	Blood Urea Nitrogen
CKD	Chronic Kidney Disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
DM	Diabetes Mellitus
eGFR	estimated Glomerular Filtration Rate
EPO	Erythropoietin
ESKD	End-Stage Kidney Disease
ESS	Epworth Sleepiness Score
Hb	Hemoglobin
HD	Hemodialysis
IJV	Internal Jugular Vein
KDIGO	Kidney Disease Improving Global Outcome
Kt/V	Clearance (K), time (t), Volume (V)
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
OR	Odds Ratio
OSA	Obstructive Sleep Apnea
PI	Principal Investigator
PSG	Polysomnography
SBQ	STOP Bang Questionnaire
SPSS	Statistical Package for Social Sciences
URR	Urea Reduction Ratio
WHO	World Health Organization

DEFINITIONS OF TERMS

The apnea-hypopnea index (AHI) is the total number of apnea and hypopnea occurrences per hour of the total sleep time length(1)

Dialysis adequacy refers to how well toxins and waste products are removed from the patient's blood during a hemodialysis session. In this study dialysis adequacy will be analysed using Kt/V and will be considered to be adequate if Kt/V is >1.2 or URR > 65% (2,3)

Excessive Day time Sleepiness is defined as the inability to maintain wakefulness and alertness during the major waking episodes of the day, with sleep occurring unintentionally or at inappropriate times almost daily for at least three months (1,4)

End-stage kidney disease (ESKD) is an irreversible decline in kidney function, which is severe enough and can lead to fatal complications in the absence of dialysis or kidney transplantation. In this study, ESRD patients referred to those who had eGFR < 15 ml/min/1.73 m^2 and were receiving maintenance hemodialysis therapy(5)

Risk of OSA is defined as having a combined STOP-Bang score ≥ 3 points and ESS≥ 10 points (6)

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

ESRD occurs as an outcome of a progressive decline in kidney function over months or years. The global burden of ESRD is increasing at a rate of about 7% per year and is a leading cause of morbidity and mortality especially in developing countries where the availability of renal replacement therapy is limited as compared to the developed countries. (7)(8) Despite the increase in the burden of ESRD, there is still under-recognition of sleep complaints by health workers including clinicians.(9)

ESRD patients on hemodialysis (HD) frequently experience sleep complaints, with the most prevalent manifestations being insomnia, sleep apnea (including the obstructive and the central forms), and restless legs syndrome. (10) It has been reported that up to 80% of patients receiving hemodialysis (HD) report some level of sleep disturbance(11–13) Unfortunately, little attention has been paid to the impact of these disorders on patients with end-stage renal disease (ESRD) who are on dialysis(14)

Obstructive Sleep Apnea (OSA) is a prevalent sleep disorder characterized by episodes of complete or partial cessation of airflow, known as apneas and hypopneas, respectively, as well as respiratory effort-related arousals (RERAs).(15) The estimated prevalence of OSA in the general population ranges from 3% to 7%, affecting approximately 1 billion people aged 30 to 70 worldwide. The rise in obesity over the past two decades has contributed significantly to the increase in OSA cases. Among End-Stage Kidney Disease (ESKD) patients, the prevalence of OSA is notably higher, exceeding 50%, though there are currently no specific clinical guidelines for screening or managing OSA in this population, resulting in infrequent assessment in clinical practice. (13,16–19)

Research indicates a correlation between declining kidney function and increased prevalence of sleep apnea, with rates of 57% in ESRD patients, 41% in chronic kidney disease (CKD) patients not on dialysis, and 27% in those with an estimated glomerular

filtration rate (eGFR) ≥ 60.(16) OSA is recognized as a significant risk factor for hypertension, cardiovascular disease (CVD), stroke, and mortality. The pathophysiology of OSA involves intermittent hypoxia, which stimulates sympathetic nerve activity, systemic inflammation, and oxidative stress, leading to endothelial dysfunction and arteriosclerosis. (20,21)

Several studies have identified risk factors for Obstructive Sleep Apnea (OSA), including male gender, older age, obesity, increased neck circumference, craniofacial abnormalities, smoking, alcohol use, and comorbidities such as hypertension and endocrine disorders. These risk factors are also prevalent in patients with End-Stage Renal Disease (ESRD) who have sleep-related disorders, particularly older age, male gender, obesity, smoking, and diabetes. (17,22–27)

Typical symptoms of OSA include loud snoring, apnea episodes, morning headaches, and daytime sleepiness, with excessive daytime sleepiness (EDS) being common in 12-65% of patients and linked to higher risks. (4,22,26,28) However, in ESRD patients, these symptoms may overlap with renal failure, requiring higher suspicion and objective monitoring for accurate diagnosis.(29) Untreated OSA worsens ESRD symptoms, further reducing health-related quality of life by increasing fatigue, sleepiness, and cognitive impairment. .(30,31)

1.1.1 Pathogenesis of OSA in ESKD

The mechanisms linking chronic kidney disease (CKD) and OSA are not yet fully understood.(32,33) However, several proposed mechanisms explain the pathophysiology of CKD-related sleep apnea. There is a bidirectional relationship between OSA and end-stage kidney disease (ESKD).ESRD can worsen sleep apnea through fluid redistribution and altered respiratory control, while OSA can damage the kidneys through hypoxia and increased inflammation. (16,27)ESKD contributes to OSA by causing factors such as metabolic acidosis, chemoreceptor insensitivity, and upper airway narrowing due to fluid buildup. (16,33–35)

Pharyngeal narrowing is a major factor in OSA among these patients, especially due to rostral fluid overload during sleep. This fluid shift increases neck circumference, reduces airway size, and raises pharyngeal resistance. .(19,33,36,37)

Chronic uremia-related neuropathy or myopathy, as well as underlying conditions like diabetes, also contribute to airway narrowing. Patients with ESKD are more prone to sensory neuropathy and muscle denervation, worsening the disease process. (20,33,38)

1.1.2 Diagnosis and treatment of OSA

Diagnosing Obstructive Sleep Apnea (OSA) in patients with End-Stage Kidney Disease (ESKD) is challenging due to symptom overlap between OSA and ESKD, which complicates accurate diagnosis. Common OSA symptoms such as loud snoring are less frequent in hemodialysis patients, while hypertension and fatigue are more noticeable. Polysomnography (PSG) remains the gold standard for diagnosing OSA, categorizing its severity based on the Apnea-Hypopnea Index (AHI). (10,18,21,29,39,40)

However, PSG is underutilized for screening due to its high cost and limited availability, with only about 10% of suspected cases receiving this test. Initial screening is often conducted using questionnaires like the Berlin Questionnaire and STOP-BANG, though their specificity is limited in ESKD patients. (17,21,28,29,41–43)

Studies have shown that questionnaire-based screening methods tend to underestimate OSA risk in ESKD patients compared to objective PSG methods. For instance, a meta-analysis in Italy revealed a significant increase in OSA prevalence when PSG was used alongside questionnaires.(43)Similar findings were reported in studies from Italy and India, highlighting that questionnaire methods often fail to capture the true prevalence of OSA, which is more accurately detected through PSG.(31,44) Recent research also indicates suboptimal accuracy of Berlin and SBQ in diagnosing OSA in ESKD patients.(29) To address these challenges, a two-step screening process is sometimes used, combining initial questionnaires with the Epworth Sleepiness Scale (ESS) for better accuracy.(6)

OSA treatment options include weight loss, CPAP, mandibular advancement devices, and, in some cases, surgery or airway stimulation, though the latter can have significant side effects. Early diagnosis and intervention are crucial for managing OSA risks in ESKD patients. (4,23,24,45,46)

1.2 Problem Statement

End-stage kidney disease is a dramatically increasing global health and healthcare burden with about 500 million people reported to have CKD globally where 80% live in developing countries. Due to this high burden, it is suggested that more than 70% of the patients with end-stage kidney disease (ESKD) will be residing in low-income countries by the year 2030. (47,48). In Tanzania, the prevalence of CKD is reported to range between 7% -15%, majority of these patients progress to ESKD needing hemodialysis(30,49,50) However, the prevalence of OSA in patients with ESKD on hemodialysis is 10-fold higher than in the general population resulting in worsening of the clinical manifestations and cardiovascular complications.(10) Mortality in end-stage kidney disease (ESKD) patients undergoing dialysis approaches 20% per year, and the leading cause of mortality is cardiovascular disease (CVD). It is known that OSA increases cardiovascular risk in ESKD patients and cardiovascular mortality remains the leading cause of death in these patients and impairs the QOL. (48,51)

No studies have been done to evaluate the magnitude of OSA among ESKD patients on hemodialysis in Tanzania.

The paucity of local data on the burden of OSA among patients with ESKD on hemodialysis provides less attention to this condition by most of the clinicians hence resulting in the higher prevalence of undiagnosed patients with OSA.(9,20) This study is essential to determine the burden of OSA and the factors associated among patients with ESKD on dialysis.

1.3 Conceptual Framework

As illustrated in the conceptual framework below, different independent factors are related to the prevalence of OSA in ESKD patients. These factors are categorized as

sociodemographic factors and clinical parameters. The sociodemographic factors are sex, age, body mass index, insurance status, employment status, and level of education and clinical and laboratory parameters are BMI, neck circumference, EDS, comorbidities (DM, HTN), hemodialysis factors, plasma calcium, phosphate and hemoglobin levels.

These factors have an immediate impact on the existence of OSA in ESKD patients on

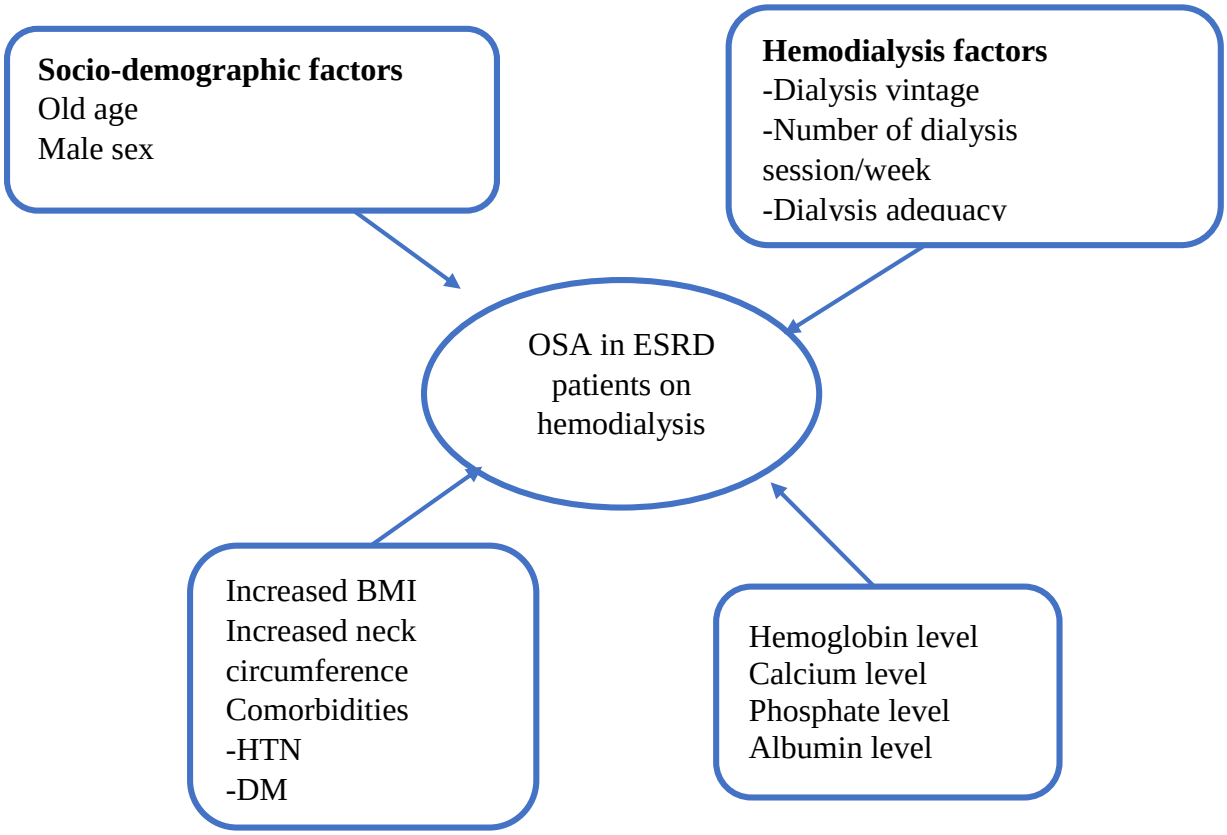


Figure 1: A self-designed conceptual framework showing different factors associated with the risk of OSA in ESKD patients on hemodialysis.

1.4 Rationale

The aim of this study is to shed light on the status of the risk of OSA and its associated factors among ESKD patients on hemodialysis at Muhimbili National Hospital in Tanzania. To date, there are no documented studies available on obstructive sleep apnea risk in this specific population, which underscores the importance and newness of this research.

It is thus expected that the results of this study will help provide valuable crucial insights and raise awareness about the burden and factors associated with risk of OSA in ESKD patients undergoing maintenance HD at MNH. Furthermore, the findings of this study will not only contribute to the existing body of knowledge on risk of OSA but will also serve as a stepping stone for further research in our local setting.

1.4.1 Main Research Question

How common is the risk of OSA and its associated factors among ESKD patients receiving maintenance hemodialysis at MNH?

1.4.2 Specific Research Questions

i. What is the prevalence of risk of OSA among ESKD patients attending maintenance hemodialysis?
ii. What are the factors associated with the risk of OSA among ESKD patients attending maintenance hemodialysis?

1.5 Objectives

1.5.1 Broad Objective

To determine the prevalence of risk of OSA and its associated factors among ESKD patients on maintenance hemodialysis at Muhimbili National Hospital

1.5.2 Specific Objectives

i. To determine the prevalence of risk for OSA among ESKD patients attending hemodialysis at MNH
ii. To determine the factors associated with the risk of OSA among ESKD patients attending hemodialysis at MNH

1.6 Study Hypothesis

The prevalence of risk of OSA among ESKD patients on hemodialysis attending MNH is high

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 PREVALENCE OF OSA AMONG PATIENTS WITH ESKD

The prevalence of OSA rises as chronic kidney disease (CKD) becomes more severe, and it may be up to ten times higher in dialysis patients than in the general community.(51). Obstructive sleep apnea (OSA) is claimed to affect up to 80% of hemodialysis patients, with the reported prevalence being extremely variable depending on the diagnosis method used.(10) Using PSG, more than 50% of patients with a risk of OSA have been reported. (19)

Studies on the prevalence of Obstructive Sleep Apnea (OSA) among patients with End-Stage Kidney Disease (ESKD) across different regions reveal significant variability. In Europe, a multi-center study in Switzerland found 56% of patients had moderate to severe OSA, with 71% identified as high-risk based on the STOP-Bang questionnaire. In contrast, an Italian study reported a much lower prevalence of 23.6%.(10) In Australia, OSA prevalence among ESKD patients ranged from 66% to 89%, depending on the diagnostic method used. Meanwhile, studies in North America showed a broad range of prevalence: from 12% in a U.S. cohort study to 75% and 32% in Canadian studies using different diagnostic criteria. (18,31,34,51–53)

In Asia, studies reveal similarly varied prevalence rates. In Saudi Arabia, the prevalence of high-risk OSA was 44.2% to 64.2%, while in Iran, it ranged from 53.2% to 84.6% based on different questionnaires. Japan reported a 42% prevalence based on polysomnography. (12,13,44,54–56) In Africa, OSA prevalence among ESKD patients ranged from 41.4% to 63.4% based on various studies and diagnostic tools. Studies in Egypt showed high rates of 70.6% using the STOP-Bang questionnaire, whereas prevalence rates in Kenya and Tanzania varied significantly. (11,19,57–62) These differences highlight how factors such as study population, sample size, OSA definitions, and diagnostic methods influence the reported prevalence of OSA among ESKD patients.(43)

Table 1: Prevalence of risk of OSA in hemodialysis patients in different countries

S/N	Author(year)(ref)	Study design	Total No of participants	Prevalence of risk of OSA (%)	Country	Method of diagnosis
1.	Onally et al (2016) (19)	Cross-sectional	115	34.8	Kenya	BQ
2.	Merino et al (2006) (52)	Cross-sectional	883	23.6	Italy	BQ
3.	Ibrahim et al (2011) (60)	Cross-sectional	264	21.6	Egypt	BQ
4.	Tondi et al (2016)(59)	Cross-sectional	127	49.1	Senegal	BQ
5.	Georges et al (2021)(57)	Cross-sectional case control	136	63.4	Cameroon	SBQ
6.	Seck et al (2019)(58)	Cross-sectional	128	41.4	Senegal	BQ
7.	Ogna et al (2015) (52)	Cross-sectional	125	87/71/39	Switzerland	PSG/SBQ /BQ
8.	Huang et al (2017) (34)	Cohort	32	66	Australia	PSG
9.	Kerns et al (2018) (36)	Cohort	558	12	USA	Chart review+PSG
10.	Lyons et al (2016) (18)	Cross-sectional	42	75	Canada	PSG
11.	Mucsi et al (2004)(53)	Cross-sectional	78	32	Canada	BQ
12.	Wali et al (2015)(54)	Cross-sectional	355	44.2/64.2	Saudi Arabia	BQ/SBQ
13.	Al-Jahdali et al (2012) (13)	Cross-sectional	227	70.9	Saudi Arabia	BQ
14.	Amini et al (2018)(55)	Cross-sectional	65	68.3/84.6	Iran	BQ/SBQ
15.	Moradzaeh et al (2020) (56)	Cross-sectional	47	53.2	Iran	SBQ
16.	Tada et al (2007)(63)	Cross-sectional	119	42	Japan	PSG
17.	Chen et al (2006)(12)	Cross-sectional	700	20	China	BQ
18.	Chu et al (2019)	Cross-sectional	107	89	Australia	SBQ

2.2 FACTORS ASSOCIATED WITH OSA

There are various factors associated with OSA among patients with ESKD on hemodialysis as reported in the different studies.

2.2.1 Socio-Demographic Characteristics

2.2.1.1 Age

Aging is known to be a major factor contributing to the risk of OSA as the prevalence of OSA increases with age. OSA prevalence varies with age, from 5 to 15% among middle-aged adults to >20% among elderly individuals, although in a majority of affected adults, the disorder is undiagnosed. People with age >65 years are 2 to 3 times more likely to develop OSA as compared to individuals aged 30 to 64 years. (25,64)

Several studies have explored the relationship between age and the risk of developing Obstructive Sleep Apnea (OSA) in ESKD patients on hemodialysis (HD). A Swiss study by Ogna et al found that patients with moderate to severe OSA had a higher mean age of 65.2 years compared to 57.3 years in those with no to mild OSA, showing a significant association. (10)Similarly, Amini et al's study in Iran found that patients at high risk of OSA were older, with a mean age of 58.67 years compared to 41 years for those at low risk. Tondi et al's research in Senegal also reported a significant association between age over 50 and OSA, as did Seck et al's study. (55,58,59)

In contrast, some studies in Iran, did not find a significant link between older age and OSA risk, with high-risk patients averaging 64.92 years and low-risk patients 58.54 years. A study from the USA also found no significant association between age and OSA. In Saudi Arabia, however, a study among 227 ESKD patients showed a significant correlation between older age (mean age 58.07 years) and higher OSA risk. (13,36,56)

While some studies, like Ginger Chu's and Wali et al's, found older age among OSA patients but no statistically significant association, others, such as a case-control study in Cameroon, suggested that patients over 40 had a higher likelihood of developing OSA without significant association. (31,54,57)

Lastly, Jivanji et al's research in Kenya found no link between age and OSA risk, with younger patients showing a higher risk compared to older patients. Overall, the relationship between age and OSA risk in ESKD patients on HD remains inconclusive across different studies.(19)

2.2.1.2 Gender

Males are two to three times as likely to develop OSA as females are, despite the risk appearing to level off after women reach peri- and postmenopausal stages. Androgenic patterns of fat distribution and sex hormones account for the high predisposition of men to OSA. (65) OSA is estimated to be present in approximately 20% of male and 10% of female patients with ESKD. (35)

Studies on the relationship between gender and obstructive sleep apnea (OSA) among end-stage kidney disease (ESKD) patients on hemodialysis reveal inconsistent results. While some studies, like those in Cameroon and Egypt, find a significant association between male gender and OSA, others, including those from Senegal, Saudi Arabia, and Morocco, report no significant association. (11,13,19,31,54,55,57,59)

Contrastingly, research from China indicates females are less likely to have a high risk of OSA compared to males, though not all studies support this, as evidenced by findings in Switzerland and other regions. (10,12) Overall, the variability suggests that gender's impact on OSA in ESKD patients remains unclear and warrants further investigation.

2.3 Clinical Parameters

2.3.1 Neck circumference

It has been proposed that an increased neck circumference (NC) is a better indicator of OSA than other clinical indicators. Fat deposition in the peri pharyngeal region, which increases the thickness of the neck, is associated with an increased tendency for the pharyngeal wall to collapse.(66) However, in dialysis patients, increased neck circumference is an indicator of fluid overload in the upper extremity of the body that would impair the regulation of ventilation.(58)

Neck circumference (NC) is a more specific and sensitive predictor of obstructive sleep apnea (OSA) severity compared to BMI. (66)

Several studies found that larger NCs were significantly associated with OSA in ESKD patients on hemodialysis. Studies in Senegal, Switzerland, and Saudi Arabia demonstrated that higher NCs correlated with moderate to severe OSA. (10,13,58) However, in one study from Senegal, a lower threshold of NC (≥25 cm) was also significantly associated

with OSA. (59) However, some studies, including one from Senegal, found no such association between NC and OSA in ESKD patients, indicating mixed evidence in the field. (19,31,55)Overall, larger NC is consistently linked to an increased risk of OSA across different regions.

2.3.2 BMI

Approximately 40–60% of cases of OSA are attributable to excess weight. Obese individuals are at a fourfold or greater risk for OSA than their normal-weight counterparts.(25)

Several cross-sectional studies examined the relationship between BMI and obstructive sleep apnea (OSA) in end-stage kidney disease (ESKD) patients on hemodialysis (HD). Studies in Saudi Arabia, Egypt, Morocco, and Iran consistently found a significant association between higher BMI and increased likelihood of OSA, with obese patients being up to 3.7 times more likely to have OSA. (54,56,60,67)

However, studies in Senegal and Saudi Arabia found no significant association between BMI and OSA, suggesting regional or methodological differences. (13,59)

2.3.3 EDS

Excessive daytime sleepiness is one of the clinical presentations of patients with OSA as assessed by the ESS. Numerous factors, falling into at least four major groups, contribute to EDS, including inadequate sleep, sleep-related disorders, physical and mental health issues, and medications. Obstructive sleep apnea (OSA), a sleep-related breathing disorder, circadian rhythm sleep-wake disorders, such as restless legs syndrome, and central disorders of hypersomnolence, such as narcolepsy, are among the sleep disorders that lead to EDS.(68)

Multiple studies have investigated the connection between excessive daytime sleepiness (EDS) and obstructive sleep apnea (OSA) in patients with end-stage kidney disease (ESKD) undergoing hemodialysis (HD), showing a broad range of EDS prevalence from 17% to 82.6%.(55) In many of these studies, including those from China, Morocco, Saudi

Arabia, Cameroon, Italy and Senegal, a significant link between EDS and OSA was found. EDS prevalence in these regions varied from 17.8% to 50.7%, with higher ESS scores associated with an increased risk of OSA. (12,52,54,57–59,67)

However, some studies, particularly from Egypt, Switzerland, and Iran, found no significant association between EDS and OSA, even with high EDS prevalence rates (up to 82.6%).(11,31,34,55,60)

This indicates that while many studies demonstrate a strong correlation between EDS and OSA in ESKD patients on HD, differences in methodology or regional factors may explain the inconsistent results. (13,53,69–72) Overall, the findings highlight the need for additional research to better understand the variability in EDS and OSA relationships across various populations and settings.

2.3.4 Comorbid

Numerous comorbidities have been linked to the development and progression of OSA in both the general community and ESKD patients. Research into the relationship between hypertension (HTN), diabetes mellitus (DM), and obstructive sleep apnea (OSA) among end-stage kidney disease (ESKD) patients on hemodialysis yields varied results. Studies from Egypt and Saudi Arabia generally found a significant link between HTN and OSA, with increased risk indicated by high odds ratios. (11,13,54,60) Similarly, research in Switzerland showed a notable association between HTN and OSA.(10)Conversely, studies from Senegal, Kenya, Iran, and Australia did not find a significant connection between HTN or DM and OSA, even though these conditions were prevalent among patients. (12,19,56,58,59)This discrepancy suggests that while HTN and DM are often associated with OSA in some regions, the strength of this association may vary depending on the population and location.

2.4 Hemodialysis

2.4.1 Dialysis adequacy

Dialysis adequacy, which measures how well toxins are removed from the blood, is crucial for improving the quality of life in end-stage kidney disease (ESKD) patients.(73). The

NKF-KDOQI guidelines recommend achieving specific targets for hemodialysis efficiency, such as a single pool Kt/V > 1.2 or URR > 65%.(2,3)

Studies have shown mixed results regarding the association between dialysis adequacy and obstructive sleep apnea (OSA). For instance, research from Iran and Egypt found that inadequate dialysis was significantly linked to a higher risk of OSA, with odds ratios suggesting a strong association. (55,60) Conversely, studies from Saudi Arabia, Morocco, Senegal, and Switzerland did not find a significant relationship between dialysis adequacy and OSA, despite high proportions of adequate dialysis among patients.(10,13,31,54,58,59,67,70)These findings indicate that while adequate dialysis is essential for reducing complications and enhancing patient well-being, its direct effect on OSA risk may be inconsistent across different studies and populations.

2.4.2 Dialysis vintage

Several cross-sectional studies have examined the link between hemodialysis (HD) duration and obstructive sleep apnea (OSA) in end-stage kidney disease (ESKD) patients. In Switzerland, a study found that patients with moderate to severe OSA had a longer mean duration of dialysis (3.8 years) compared to those with no or mild OSA (1.9 years), though this difference was not statistically significant.(10)

Conversely, a Senegalese study showed that patients with OSA had a shorter mean duration of dialysis (34.8 months) compared to those without OSA (37.5 months), but this also lacked statistical significance.(58) Similarly, research from Canada and Saudi Arabia found no significant association between dialysis duration and OSA risk, with median durations being nearly identical between high and low-risk groups. (13,53)

In contrast, an Iranian study reported that patients at high risk for OSA had a slightly shorter mean duration of dialysis (58 months) compared to those at low risk (59 months), showing a statistically significant association with OSA (OR=0.99, p=0.05). (55) Overall, while some studies suggest trends or differences in dialysis duration related to OSA risk, the findings are inconsistent and often not statistically significant across various populations.

2.6 Laboratory parameters

Studies on anemia and other biochemical factors in ESKD patients on hemodialysis with obstructive sleep apnea (OSA) have yielded mixed results. While some research, such as a study by Jehan et al. in Egypt, found a significant association between hyperphosphatemia and OSA (OR=4.4, p=0.002), anemia did not show a significant link (OR=5.2, p=0.6). (60)

Similarly, a study in Senegal and others have reported no significant association between hemoglobin levels and OSA.(58) Consistent findings were observed in large cohort studies in Switzerland, Iran, and Australia, which found no significant links between OSA and biochemical markers like serum calcium, phosphate levels, anemia, BUN, or creatinine. (19,31,53–56,59)

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design

Hospital-based cross-sectional study.

3.2 Study population

ESKD patients on maintenance hemodialysis (hemodialysis for a minimum of 3 months) were recruited to participate in the study.

3.3 Study Area

The study was conducted at MNH Hemodialysis Center in Dar es Salaam. MNH is Tanzania's national referral and teaching hospital, providing super specialty health care to outpatients and inpatients, as well as training and research.

The facility provides dialysis treatments on a daily basis and has a capacity of 42 dialysis machines, which can run four sessions per day. Each dialysis machine has a digital BP machine incorporated within it. Fresenius dialysis machine is the brand used at MNH.

Every month, approximately 300 patients are on HD, with new patients being admitted virtually every day.

3.4 Study Duration

Data were collected for 5 months from September 2023 to January 2024.

3.5 Study Sample

Patients aged 18 years and above with ESKD on maintenance hemodialysis attending the dialysis unit at MNH who will fulfill the inclusion criteria and consent.

3.6 Sample size

Keish and Leslie’s formula was used to calculate the minimum sample size necessary:

$n = Z^2 P (100 - P)/\varepsilon^2$

Where: n = minimum sample size

z = standard normal deviate (1.96) responding to a 95% confidence interval

ε = margin of error (5.2%)

p= 34.8% of ESKD patients on hemodialysis patient at Kenyatta Hospital in Kenya had a high risk of OSA based on validated BQ, a study done in 2016 by Jivanji et al(19)

$n = 1.96^2 \ X \ 34.8 \ (100 - 34.8) / 5.2^2$

n = 322

Taking a none response of 10%

$n' = \frac{322 \ X \ 100\%}{100\%-10\%}$

N= 350

3.6.1 Inclusion Criteria

- All ESKD patients aged 18 years and above
- Patients with ESKD on maintenance hemodialysis for at least 3 months

3.6.2 Exclusion Criteria

- Patients who will refuse or are not able to consent to the study
- Patients on sedatives

3.7 Study Variables

3.7.1 Independent Variables

Social demographic characteristics:

- Age, Sex, Marital status, Level of education, health Insurance status, alcohol ingestion, occupation and smoking,

Clinical characteristics:

- BMI, neck circumference, Comorbidities-HTN/DM, Number of HD sessions/week, dialysis vintage, hemodialysis adequacy (URR%), and laboratory parameters (hemoglobin, serum calcium, serum phosphates, albumin)

3.7.2 Dependent Variable

- Risk of OSA

3.7.3 Definition of variables

Risk of OSA defined as SBQ score ≥ 3 and ESS ≥ 10 (6)

Anemia is defined as hemoglobin <12g/dl in females and <13g/dl in males (74)

Body Mass Index: a measure of weight adjusted for height, calculated as weight in kilograms divided by the square of height in meters (kg/m^2).

Underweight <18.5kg/m^2, normal BMI (18.5kg/m^2-24.9kg/m^2), overweight (25kg/m^2-29.9kg/m^2), obesity ≥ 30kg/m^2 (75)

Serum calcium; hypocalcaemia if calcium< 2.1mmol/L[1]

Serum phosphate; hyperphosphatemia if phosphorus>1.52mmol/L[1]

Serum albumin; hypoalbuminemia if albumin< 35g/dl

[1]cut-off values as per MNH Central Pathology Laboratory (CPL)

Dialysis vintage : as delineated by the patient from the date of the first dialysis session to the current date (19)

3.8 Sampling techniques

A consecutive sampling technique was used where patients attending hemodialysis services at MNH-Upanga, who fulfilled inclusion criteria and consented were consecutively enrolled in the study until the sample size was reached.

Enrolment of study participants

All patients who fulfilled the inclusion criteria were identified through patient records in the dialysis unit. Upon arriving at the centre for a dialysis session, the objective of the study was explained to the patients who met the inclusion criteria. Those who consented

to participate were provided with informed consent for the study and recruited into the study. Face-to-face interview was used to provide an opportunity to collect as complete data as possible and to overcome non-responses by those who could not read. A trained interviewer administered to the participants a translated Swahili ESS questionnaire for daytime sleepiness during or after hemodialysis session based on the patient's convenience and when necessary, he would clarify the questions to the patients but not influence the patient's response. Patients were encouraged to reflect on their overall sleepiness in the previous month rather than on the day of completing the survey. The interview lasted for about 15 to 20 minutes and was done without causing hindrance to patient care. Clinical and laboratory data such as dialysis vintage, number of dialysis sessions per week, types of vascular access, hemoglobin, serum albumin, calcium, and phosphorus were also documented from patients' hospital records.

Blood was collected for pre and post-dialysis urea on the day of the interview and used for calculating dialysis adequacy by using URR with the cut-off of 65% considered as adequately dialyzed as recommended by KDIGO.(76) The samples were taken before injecting saline or other any potential diluents. In the end, the researcher's assistant thanked each participant, and assurance was given to the study participants on maintaining the confidentiality of the data.

3.9 Data collection tool

Data was collected using a questionnaire containing two sections.

Section A

Section A had three sub-sessions

I. Demographical variables

This consisted of demographic characteristics of patients with ESKD which includes age, gender, marital status, health insurance status, and educational level, obtained from the patient's medical record

II. Clinical profile

This consisted of the history of smoking, alcohol drinking, DM, HTN, BMI, neck circumference, dialysis vintage, number of HD sessions per week and type of vascular access. Participants were asked to report if they were known diabetic or hypertension patients. Those who claimed to be known hypertensive or diabetic were required to show evidence for their hypertension or diabetes by showing the drugs they were using.

III. Laboratory investigations

Hemoglobin, serum albumin**,** calcium, phosphorus, pre- and post-dialysis urea which was used to calculate for urea reduction ratio (URR %).

Section B

This was comprised of a validated questionnaire called the Epworth Sleepiness Scale (ESS) score and STOP-Bang Questionnaire (SBQ) that were utilized in the formulation of the outcome of risk of OSA.

The STOP-Bang questionnaire is a simple and effective screening tool for the risk assessment of suspected sleep-disordered breathing which includes eight indicators: snoring (S), tiredness (T), observed apnea during sleep (O), blood pressure (P), BMI, age, neck circumference and gender; scores 3 are 93% sensitive and 43% specific for moderate OSA, and 100% sensitive and 37% specific for severe OSA (6)

The STOP-Bang questionnaire has eight questions on snoring, tiredness, observed apnea, hypertension, body mass index >35 kg/m2, age >50, neck circumference >40 cm, and male that are answered with “yes” or “no.” It adds one point for “yes” and zero points for “no.” When the total points are ≥3, this indicates that the patient is at high risk for OSA.

To improve the specificity of SBQ, the Epworth sleepiness scale was used to assess individual daytime sleepiness for all participants who scored ≥3 points on SBQ. The Epworth Sleepiness Scale (ESS) is a simple self-administered questionnaire measuring the general level of daytime sleepiness in eight different situations and activities that are often part of everyday life. The 8 situations are sitting and reading, watching television,

sitting inactive in a public place (e.g., a cinema or meeting, being a passenger in a car for > 1 hour, lying down to rest in the afternoon when circumstances permit, sitting and talking to a companion, sitting quietly after an alcohol-free lunch or being in a car, while stopped briefly in heavy traffic. The questionnaire has a four-point Likert response format (0-3) for each situation (0=would never doze,1=slight chance of dozing,2=moderate chance of dozing,3=high chance of dozing). The total ESS score is a measure of the average sleep tendency and the probability of falling asleep in those situations. The highest score of ESS is 24 (the most excessive daytime sleepiness), with a threshold for daytime sleepiness of 10 points or more.(21,39,62,71)

Participants were then classified as having the risk of OSA or no risk for OSA following a two-step screening method for OSA risk.

Patients with a risk of OSA were defined as those with a combined STOP-Bang score ≥ 3 points and ESS≥10 points and patients with no risk of OSA were those with STOP-Bang score <3 points and ESS <10 points. (6)

3.9.1 Physical examination

Patients' weight was measured using a well-calibrated digital weighing scale available at the dialysis unit in kilograms at the end of dialysis.

Height was measured to the nearest 0.5cm by using a metal measuring tape against the wall and a flat headboard at right angles to the wall.

Body mass index was calculated using the formula weight (kg)/ Height in meters squared. Based on WHO classification, the BMI was interpreted as follows: underweight <18.5 kg/m2; normal 18.5–24.9 kg/m2; overweight if 25.0–29.9 kg/m2; obesity if ≥30 kg/m2. (75) Neck circumference was measured with the flexible tape measure to the nearest 0.5centimeters at a level just below the laryngeal prominence (Adam's apple) and perpendicular to the long axis of the neck (19)

3.10 Data Analysis

Data obtained from questionnaires was entered into SPSS Version 23.0 for Windows which was used for data analysis. Data cleaning and reviewing the filled questionnaires were done to ensure quality control of data.

Categorical variables were presented as frequencies and percentages, continuous variables were presented as median and interquartile range. Association between categorical variables was explored using Chi-square. Variables with a p-value <0.2 on univariate analysis were further tested in the multivariable analysis using Robust Poisson Regression for factors associated with risk of OSA. A two-tailed p-value <0.05 was used as a cut-off level for statistical significance.

3.10.1 Data Storage:

The questionnaires used for data collection were stored in a secure place to access whenever necessary, ensuring confidentiality.

3.11 Ethical clearance

Ethical clearance was sought from the Research and Publications Committee of Muhimbili University of Health and Allied Sciences (MUHAS). Permission to conduct this study was sought from the authorities of MNH. A formal written informed consent, in Swahili, was sought from the participants. The patient's name and hospital registration number were accessible only to the principal investigator and research assistant as a means to follow up on the laboratory investigation results. No additional investigation was taken apart from routine monthly blood investigations for dialysis patients which is standard of care. Patient names were not used, and information collected on questionnaires was entered into the computer using identification numbers to maintain confidentiality.

The patients found at risk of OSA were counselled on the performance of confirmatory PSG test and initiated on individualized treatment modalities including lifestyle or behavioral change, and use of continuous positive airway pressure.

CHAPTER FOUR

4.0 RESULTS

4.1 Flow diagram of the study patients

This study was carried out from mid-September to the end of December 2023. Of 357 patients consecutively screened for eligibility, 7 did not meet the inclusion criteria. The remaining 350 were enrolled in the study and filled out the questionnaires.

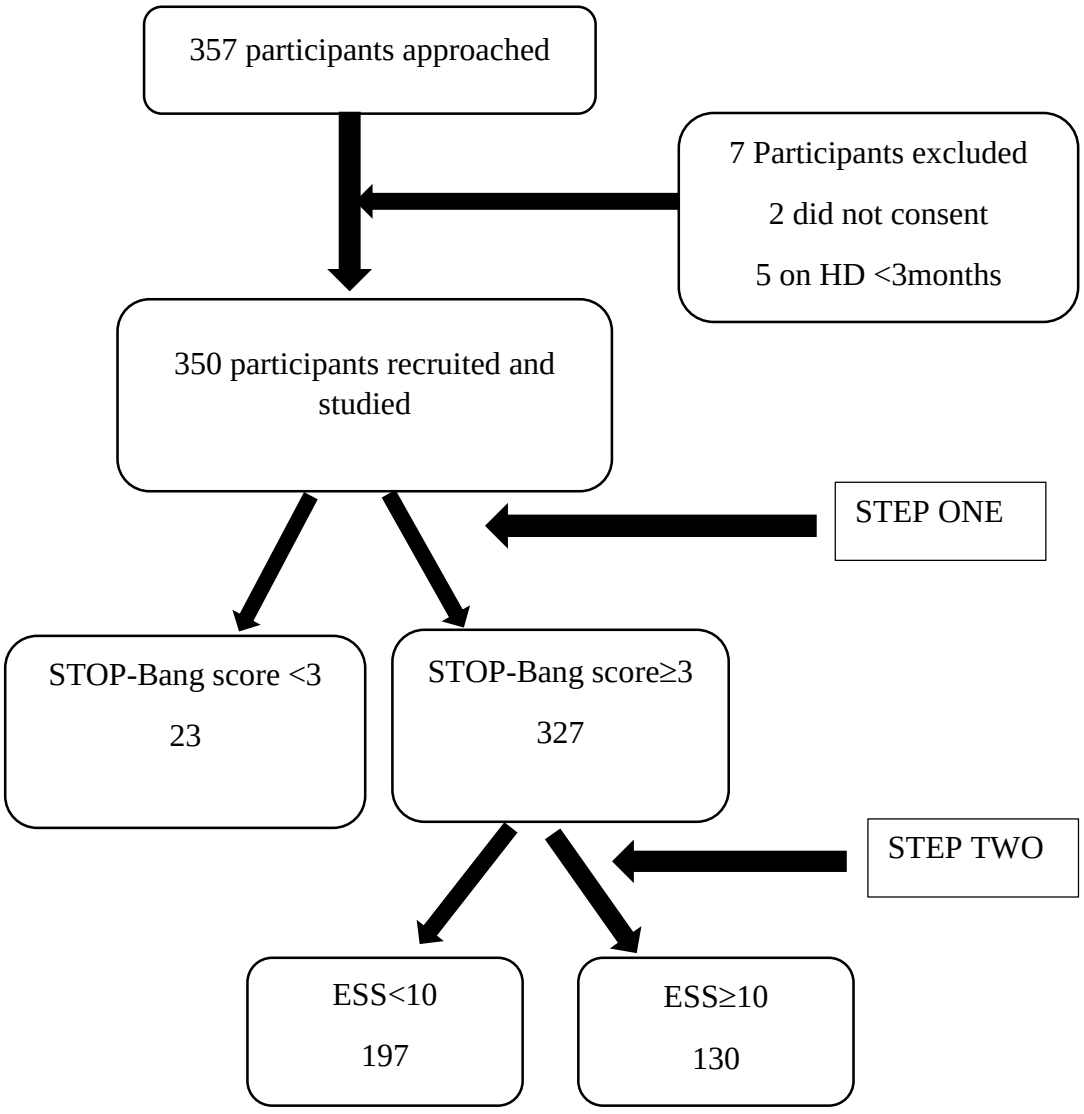


Figure 2: Flow chart showing the enrolment of the study participants

4.2 Sociodemographic characteristics of study participants

A total of 350 end-stage kidney disease patients on hemodialysis were studied, out of which 70.6% (247/350) were males. The median age of the study participants was 52.0 (43-59) years and 56.9 % (199/350) were above 50 years. There were 89.4% (313/350) married participants, 38.6% (135/350) with primary and below education level, 51.1% (179/350) employed participants, and 85.7% (300/350) insured participants.

Table 2: Social-demographic characteristics of study participants (ESKD patients) (n=350)

VARIABLE	FREQUENCY, N (%)	MEDIAN (IQR)
Age in years		52.0 (43.0-59.0)
≤50	151 (43.1)	
>50	199 (56.9)	
Sex		
Female	103 (29.4%)	
Male	247 (70.6%)	
Marital status		
Married	313 (89.4%)	
Unmarried	37 (10.6%)	
Education level		
Primary and below	135 (38.6%)	
Secondary	170 (48.6%)	
College/University	45 (12.8%)	
Occupation		
Unemployed	171 (48.9%)	
Employed	179 (51.1%)	
Health insurance status		
Uninsured	50 (14.3%)	
Insured	300 (85.7%)	

4.3 Clinical characteristics of study participants (ESKD patients) (n=350)

Hypertension was reported by 71.7% (251/300) participants followed by diabetes 21.2% (74/300). There were 4.0% (14/350) smokers, 11.1% (39/350) alcohol drinkers, median BMI was 25.0 (22.8-27.4) kg/m^2 while 40.9% of participants (143/350) were overweight, 8.2% (29/350) were obese respondents and median NC was 36.0 IQR (36-38) cm with 4.9% (17/350) of respondents having NC of above 40cm. The median dialysis vintage was 38 IQR (30-48) months, 82.3% (288/350) of the participants had 3 HD sessions per week. As far as vascular access of HD, 43.7% (153/350) of the participants had AVF access for HD and 36.3% (127/350) had permanent catheter. Adequate dialysis was present in 88.6% (310/350) of participants with median dialysis adequacy of 84.0 [72.7-90.0]. There were 97.7% (342/350) participants with anemia, 75.1% (263/350) participants with hypocalcemia, 53.1% (186/350) participants with hyperphosphatemia and 35.4% (124/350) participants with hypoalbuminemia. Table 2 below summarizes the results

AVF-Arteriovenous fistula, HD-Hemodialysis

Table 3: Clinical characteristics of study participants (ESKD patients) (n=350)

VARIABLE	FREQUENCY, N (%)	MEDIAN (IQR)
Comorbid		
Hypertension	251(71.7%)	
Diabetes Mellitus	74 (21.1%)	
Glomerulonephritis	13 (3.7%)	
Smoking		
No	336 (96.0%)	
Yes	14 (4.0%)	
Alcohol drinking		
No	311 (88.9%)	
Yes	39 (11.1%)	
BMI in Kg/m^2		25.0 (22.8-27.4)
<18.5	21 (6.0)	
18.5-24.9	157 (44.9)	
25.0-29.9	143 (40.9)	
≥30	29 (8.2)	
Neck circumference(cm)		36.0 (36.0-38.0)
≤40	333 (95.1)	
>40	17 (4.9)	
Dialysis vintage (Months)		38.0 (30.0-48.0)
<12	7 (2.0)	
12-48	264 (75.4)	
49-84	78 (22.3)	
>84	1 (0.3)	
Number of HD session/week		3.0 (3.0-3.0)
<3	62 (17.7)	
=3	288 (82.3)	
Vascular access		
AVF	153 (43.7)	
Temporary catheter	70 (20.0)	
Permanent catheter	127 (36.3)	
Dialysis adequacy (URR%)		84.0(72.7-90.0)
≥65	310 (88.6)	
<65	40 (11.4)	
Anemia (g/dl)		9.7 (8.5-10.5)
No	8 (2.3)	
Yes	342 (97.7)	
Hypocalcemia (mmol/L)		1.9 (1.4-2.1)
No	87 (24.9)	
Yes	263(75.1)	
Hyperphosphatemia(mmol/L)		1.6 (1.0-7.1)
No	164 (46.9)	
Yes	186 (53.1)	

Hypoalbuminemia (g/L)		36.0 (33.0-39.0)
No	226 (64.6)	
Yes	124 (35.4)	

4.4 Prevalence of risk of obstructive sleep apnea among ESKD patients on hemodialysis at MNH

The study revealed that the prevalence of risk of obstructive sleep apnea in ESKD patients was 37.1 % as displayed in Figure 3 below.

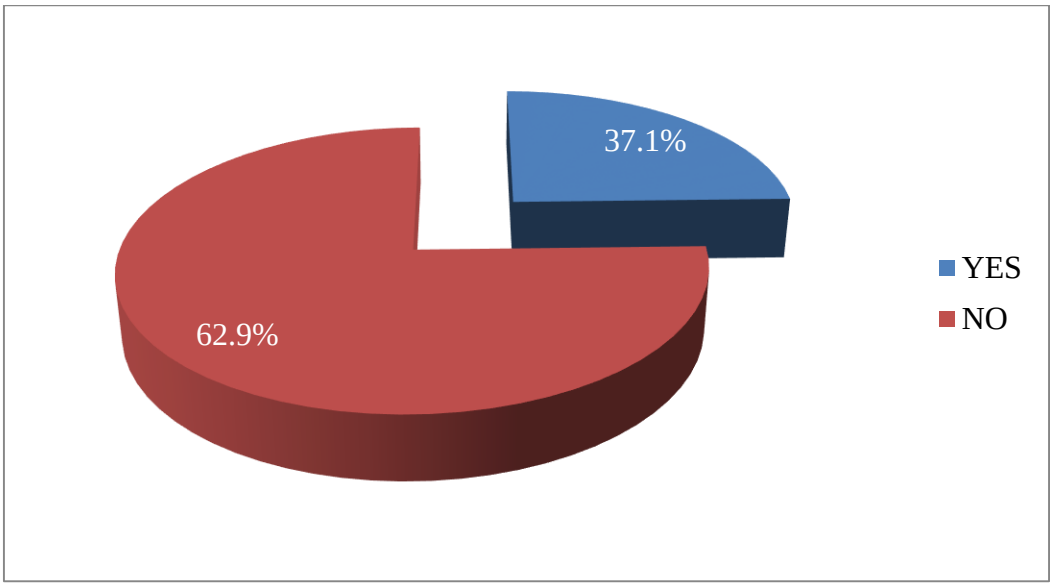


Figure 3: Prevalence of risk of OSA among ESKD patients on hemodialysis

4.5 OSA by social-demographic and clinical characteristics of study participants

Generally, in this study, 37.1% (130/350) of individuals were considered to have the risk of OSA. A significantly high prevalence of OSA was seen among hypertensive respondents (42.4%, 107/251) (p=0.001) and among diabetics (62.2%, 46/74) (p<0.0001). Glomerulonephritis**,** dialysis vintage, number of HD sessions per week, dialysis adequacy, and laboratory profile were not significantly associated with OSA.Table 3 below summarizes the results

Table 4: Risk of OSA by social-demographic and clinical characteristics of study participants (ESKD patients) (N=350)

VARIABLE	TOTAL NUMBER(N=350)	Risk of OSA		*p*-value
		No (n=220)	Yes (n=130)	
Hypertension				0.001
No	99	76 (76.8)	23 (23.2)	
Yes	251	144 (57.4)	107 (42.6)	
Diabetes				<0.0001
No	276	192 (69.6)	84 (30.4)	
Yes	74	28 (37.8)	46 (62.2)	
Glomerulonephritis				0.386
No	337	210 (62.3)	127 (37.7)	
Yes	13	10 (76.9)	3 (23.1)	
Dialysis vintage (Months)				<0.0001
<12	7	5 (71.4)	2 (28.6)	
12-48	263	185 (70.3)	78 (29.7)	
49-84	78	29 (37.2)	49 (62.8)	
>84	2	1(50.0)	1 (50.0)	
Number of HD session/week				0.389
<3	62	36 (58.1)	26 (41.9)	
=3	288	184 (63.9)	104 (36.1)	
Dialysis adequacy (URR%)				0.766
≥65	310	194 (62.6)	116 (37.4)	
<65	40	26 (65.0)	14 (35.0)	
Anemia (g/dl)				0.983
No	8	5 (62.5)	3 (37.5)	
Yes	342	215 (62.9)	127 (37.1)	
Hypocalcemia (mmol/L)				0.666
No	87	53 (60.9)	34 (39.1)	
Yes	263	167 (63.5)	96 (36.5)	
Hyperphosphatemia(mmol/L)				0.365
No	164	99 (60.4)	65 (39.6)	
Yes	186	121 (65.1)	65 (34.9)	
Hypoalbuminemia (g/L)				0.989
No	226	142 (62.8)	84 (37.2)	
Yes	124	78 (62.9)	46 (37.1)	

NB: Age, sex, neck circumference, BMI and Excessive daytime sleepiness (EDS) were excluded due to collinearity as they were involved in achieving the outcome (risk of OSA)

4.6 Bivariable and Multivariable robust Poisson Regression analysis for factors associated with risk of Obstructive Sleep Apnea in patients with ESKD

A multivariable analysis was done involving variables with p<0.2 in bivariable analysis and after adjusting for cofounders. Hypertensive patients had a prevalence of OSA that was 2.91 times greater than normotensive, aPR(95%CI) =2.91, (2.09-4.06), p<0.0001. Participants with diabetes had a prevalence of OSA that was 3.37 times greater than the participants with no diabetes, aPR(95%CI) =3.37 (2.68-4.23), p<0.0001. The dialysis vintage was not independently associated with OSA. Table 4 below summarizes the results

Table 5: Bivariable and Multivariable robust Poisson regression for the factors associated with OSA

VARIABLE	YES n (%)	BIVARIABLE cPR (95%CI)	p-value	MULTIVARIABLE aPR(95%CI)	P-value
Hypertension					
No	23 (23.2)	Ref		Ref	
Yes	107 (42.6)	1.83 (1.25-2.70)	0.002	2.91 (2.09-4.06)	<0.0001
Diabetes					
No	84 (30.4)	Ref		Ref	
Yes	46 (62.2)	2.04 (1.59-2.63)	<0.0001	3.37 (2.68-4.23)	<0.0001
Dialysis vintage (Months)					
<12	2 (28.6)	Ref		Ref	
12-48	78 (29.7)	1.04 (0.32-3.40)	0.951	1.11 (0.45-2.73)	0.828
49-84	49 (62.8)	2.20 (0.67-7.19)	0.193	2.33 (0.94-5.82)	0.069
>84	1 (50.0)	1.75 (0.62-10.77)	0.546	2.74 (0.27-28.05)	0.369

cPR =crude Prevalence Ratio, aPR =adjusted Prevalence Ratio,

CHAPTER FIVE

5.0 DISCUSSION

5.1 Discussion

Understanding the magnitude and associated factors of OSA among patients with ESKD on hemodialysis is critical in efforts to control the burden of OSA. In the present study, the prevalence of risk of OSA among ESKD patients on maintenance HD attending at MNH-Upanga dialysis center was 37.1% (32.0% and 39.3% for females and males respectively). Hypertension and Diabetes were significantly associated with the risk of OSA

The prevalence of risk of OSA among ESKD patients on maintenance HD found in our study was higher than the prevalence of 11.4% in the general population, although this prevalence still lies within a wide range of prevalence of OSA from 20% to a higher prevalence of 80% among ESKD patients on hemodialysis as reported from different studies.(10,62) Volume overload and night-time rostral fluid shift have been suggested as the pathogenic mechanisms for the high prevalence of OSA in HD patients.(59) The prevalence of OSA in this study is similar to other studies from Kenya (37.1% vs 34.8%) and Brazil (37.1% vs 36%).(19,58)

A higher prevalence of OSA than our study was found in studies done in Senegal (37.1% vs 49.1%), Spain (37.1% vs 44%), Japan (37.1% vs 42%) and Saudi Arabia (37.1% vs 44.2%).(19,58,63) However, a lower prevalence of OSA than in our study was found in other studies including in the USA (37.1% vs 12%), China (37.1% vs 20%), Germany (37.1% vs 16.4%), Egypt (37.1% vs 21.6%), Italy (37.1% vs 23.6%).(12,52,58,60)

The main reasons that explain the variability of prevalence in these studies include the differences in definitions of OSA, the study sample size, participant characteristics, and methods used for diagnosis of OSA.(43) Notably, variations in sample size, definitions of OSA, screening tools, and diagnostic methods have been found across different studies contributing to a wide range of prevalence of OSA.

Multiple studies defined high risk of OSA based STOP-Bang questionnaire with the cut-off points of at least 3 or more out of 8 in the questionnaire, studies utilized BQ to define OSA placed the individuals at high risk of OSA if a positive score is at least 2 out of 3 symptom domains (categories) (43). In contrast, the cohort study done in China and Egypt defined high risk of OSA based on BQ with a score of 1 and no risk with a score of 0. (12,60) Moreover, the definitions of OSA also varied among those studies that used objective methods like PSG. Some studies defined OSA based on the AHI cut-off value of >5(10,20,31,34,63), others based on the AHI cut-off value of >10 (77–79) and others confirmed the diagnosis based on the AHI cut-off value of >15 (18,29,80–82) and few studies defined OSA based on the AHI cut-off value of 20.(83,84) This has partly influenced the heterogeneity of the prevalence of OSA across different studies

In the present study, diabetes mellitus and hypertension were found to be significantly associated with the risk of OSA. This conformity with the findings in other studies done in the same population in Saudi Arabia, Switzerland, and Egypt.(10,13,54,60) In diabetic patients, this can be attributed to additional possible causes of upper-airway dilator muscle dysfunction like neuropathy associated with diabetes mellitus. (20,33,38) Significant association between hypertension and OSA can be attributed partly as the result of particularly intermittent hypoxia that triggers sympathetic nerve activity, systemic inflammation, and oxidative stress, causing endothelial cell dysfunction and arteriosclerosis commonly occurring in patients with OSA (20,21). However, this cannot explain fully this finding as the existence of hypertension could be present before the onset of OSA in a particular patient. In contrast, some studies found that DM was not significantly associated with OSA. (19,31,58,59,67,85)

Nevertheless, in our patients, there has been no discernible correlation found between risk of OSA and factors including, dialysis vintage, dialysis adequacy, number of HD sessions/week, anemia, hypocalcemia, hyperphosphatemia, and hypoalbuminemia.

5.2 Strengths and limitations of the study

To the best of our knowledge, this is the first study to be done in our setting that evaluated the prevalence of risk of OSA and associated factors among ESKD patients on hemodialysis. Therefore, it can later be used as a reference for other studies.

Despite the importance of these results, a few limitations of our study were noticed including; recall bias during administration of the questionnaires was, exclusion of known patients with OSA and heart failure would underestimate the prevalence of risk of OSA and being a cross sectional study couldn’t assess the temporal association between associated factors and risk of OSA (outcome of interest).

CHAPTER FIVE

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

In this study, we found that the risk of OSA is considerably common in dialysis patients at MNH. Hypertension and diabetes were independently associated with the risk of OSA among patients with ESKD on maintenance hemodialysis.

6.2 Recommendations

Based on our study findings and conclusions, the following recommendations are suggested:

- Regular screening programs be designed and implemented for the early detection of this disorder, especially clinicians should therefore actively look for the risk of OSA in hypertensive and diabetic patients on maintenance HD.
- Larger cohort studies with polysomnographic exploration are needed to better describe the epidemiology of OSA among Tanzanian dialysis patients

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APPENDICES

Annex I: Informed Consent Form-English Version

CONSENT TO PARTICIPATE IN THE STUDY ON PREVALENCE OF RISK OF OBSTRUCTIVE SLEEP APNEA AND ASSOCIATED FACTORS AMONG PATIENTS WITH END-STAGE KIDNEY DISEASE ATTENDING HEMODIALYSIS AT MUHIMBILI NATIONAL HOSPITAL

Identification number.....

Age.....

Dear Sir/Madam,

My Name is Dr Frank Peter, a resident doctor in Internal Medicine at Muhimbili University of Health and Allied Sciences (MUHAS). I am conducting a research study on prevalence of obstructive sleep apnea and associated factors among patients with end-stage kidney disease attending hemodialysis at Muhimbili national hospital, Dar es Salaam. Tanzania.

I would like to conduct this study as a requirement for the fulfillment of my postgraduate studies.

Purpose of the study: This study aims to determine prevalence of risk of obstructive sleep apnea and associated factors among patients with end-stage kidney disease attending hemodialysis at Muhimbili national hospital

How to participate: Participants who are willing to participate in this study will have to sign a consent form.

A short interview and physical examination will be done.

Confidentiality: All findings obtained will not be disclosed to anybody except the attending investigator and participant him/herself.

The information from this study will be beneficial by creating awareness on prevalence of obstructive sleep apnea and associated factors among patients with end-stage kidney disease attending hemodialysis at Muhimbili National Hospital, Dar es salaam. Tanzania. It will eventually help in optimizing care among this group of individuals at our hospital and nation at large.

Costs: You will not be required to pay any amount for your participation in this study.

Voluntary participation and the right to withdraw from the study: Your participation is voluntary, and you have the right to withdraw from participating in this study at any time. Whatever your decision may be, it will not affect in any way to your rights to care and treatment.

Risks: There are no risks associated with your participation in the study.

Benefits: Your participation in this study will help you know about whether you have OSA and the possible associated factors. You will as well get advice on the proper measures of treatment of OSA.

It is our hope that the information from this research will help improve the standard of care of OSA among patients with ESRD.

I will be grateful if you willingly agree to participate in this study.

Investigator's statement: I, the investigator, have educated the research participant on the purpose and applications of this
Study.
Signed…… Date…….
Participant's Statement: I am willing to participate in this study on prevalence of obstructive sleep apnea and associated factors among patients with end-stage kidney

disease attending hemodialysis at Muhimbili National Hospital, Dar es salaam. Tanzania. I do this with a full understanding of the purposes of the study and the procedures involved, which include filling out a study questionnaire and undergoing physical examination all of which have been explained to me by Dr. Frank Peter

Signature of Participant----------

Date----------

If you have questions during the course of the study, you may contact the following:

Dr. Frank Peter

Principal Investigator
Muhimbili University of Health and Allied Sciences (MUHAS)
Department of Internal Medicine
P.O. Box 65001, Dar es Salaam.
Mobile phone: 0694086845

OR

Dr Reuben Mutagaywa (MD, MMed, MSc Cardiology, PhD)
Supervisor for this research.
Muhimbili University of Health and Allied Sciences (MUHAS)
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P.O. Box 65001, Dar es Salaam.
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OR

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Annex II: Fomu ya kuomba ridhaa- nakala ya Kiswahili

RIDHAA YA KUSHIRIKI KWENYE UTAFITI KUHUSU UHATARI WA UGONJWA WA KUKOROMA USINGIZINI KWA WAGONJWA WENYE UGONJWA WA FIGO WA MUDA MREFU WANAOPATA MATIBABU KATIKA HOSPITALI YA TAIFA MUHIMBILI, DAR ES SALAAM. TANZANIA. UTAFITI HUU UNAANGALIA KIWANGO NA VIASHIRIA VINAVOAMBATANA NA UGONJWA WA KUKOROMA USINGIZINI.

Namba ya utambulisho.....

Umri.....

Kwa Bibi/Bwana,

Jina langu Frank Peter, mwanafunzi wa Shahada ya Uzamili katika Chuo cha Afya na Sayansi Shirikishi, Muhimbili, Idara ya Magonjwa ya Ndani nafanya utafiti kuangalia kiwango na viashiria vinavoambatana na uhatari wa ugonjwa wa kukoroma usingizini kwa wagonjwa wenye ugonjwa wa figo wa muda mrefu wanaopata matibabu katika hospitali ya taifa Muhimbili, Dar es salaam. Naomba ushiriki wako katika utafiti huu.

Jinsi ya kushiriki katika utafiti huu: Unaweza kushiriki katika utafiti kwa kujaza kwa hiyari yako fomu ya kuridhia kushiriki.

Utafiti huu utakuwa na mahojiano kwa kutumia dodoso na kufanyiwa uchunguzi wa mwili ikiwemo urefu, uzito, uzunguko wa shingo na shinikizo la damu.

Utunzaji wa siri: Taarifa zote zitakazochukuliwa katika utafiti huu zitakuwa ni siri na zitatunzwa kwa usiri na zitatumika katika utafiti huu ili ziweze kusaidia katika kuboresha huduma. Taarifa hizi za matokeo ya uchunguzi zitasaidia jamii kujua kiwango na viashiria vinavoambatana na ugonjwa wa kukoroma usingizini miongoni mwa wagonjwa wenye

ugonjwa wa figo wa muda mrefu wanaopata matibabu katika hospitali ya taifa Muhimbili, Dar es salaam

Gharama za Ushiriki: Ushiriki katika utafiti huu ni bure yaani hakuna gharama yeyote kwa mshiriki.

Hiyari ya kushiriki na kujitoa katika utafiti huu: Ushiriki katika utafiti huu ni wa hiyari na pia ni haki yako kujitoa katika utafiti huu muda wowote unapohisi kufanya hivyo. Maamuzi yako ya kuamua kutoshiriki au kujitoa katika utafiti huu hayataathiri haki yako ya kupata huduma na matibabu.

Madhara ya kushiriki utafiti: Hakuna madhara yeyote yatakayompata mshiriki wa utafiti huu.

Manufaa ya kushiriki utafiti huu: Ushiriki wako katika utafiti huu utakuwa na faida kwako kwa kuweza kujua kama una tatizo la kukoroma usingizini na kutambua viashiria vinavoambatana na ugonjwa wa huu ili basi maboresho ya huduma za afya kwa wagonjwa hawa yaweze kufanyika.

Pia, matokeo ya utafiti huu yatasaidia kushauri katika matibabu sahihi ya ugonjwa wa kukoroma usingizini kwa wagonjwa wenye ugonjwa wa figo wa muda mrefu.

Nitashukuru sana kama kwa hiyari yako utaamua kushiriki katika utafiti huu.

Kauli ya Mtafiti: Mimi mtafiti, nakiri nimemuelewesha mshiriki wa utafiti huu kuhusu huu utafiti.

Sahihi……

Tarehe…….

Kauli ya Mshiriki: Natoa idhini mwenyewe bila aina yoyote ya kushurutishwa au kulazimishwa kushiriki katika

utafiti uliotajwa hapa kuhusu utafiti wa kuangalia kiwango na viashiria vinavoambatana na ugonjwa wa kukoroma usingizini miongoni mwa wagonjwa wenye ugonjwa wa figo wa muda mrefu wanaopata matibabu katika hospitali ya taifa Muhimbili, Dar es salaam. Nafanya hivi baada ya kuelewa taarifa zote nilizoelezwa na mtafiti, Dr Frank Peter, na pia amenijibu na kunielewesha zaidi maswali niliyomuuliza.

Nimeelezewa kikamilifu kuhusu madhumuni na lengo lake na naelewa kuwa nitaulizwa maswali kadhaa na kufanyiwa uchunguzi wa mwili.

Pia naelewa kuwa naweza kujiondoa wakati wowote iwapo nitabadilisha mawazo.

Sahihi ya mshiriki……

Tarehe…….

Mawasiliano kwa wahusika:

Kwa maswali au maoni kuhusiana na utafiti huu tafadhali wasiliana na wafuatao:

Dr. Frank Peter

Mtafiti mkuu

Chuo kikuu cha afya na tiba shirikishi Muhimbili

Idara ya Magonjwa ya ndani

S.L.P 65001 Dar es Salaam

Nambari ya simu: 0694086845

AU

Dr Reuben Mutagaywa (MD,MMED,MSc Cardiology)

Msimamizi wa utafiti huu.

Chuo kikuu cha afya na tiba shirikishi Muhimbili

Idara ya Magonjwa ya ndani

S.L.P 65001 Dar es Salaam**.**

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AU

Dr Nahya Salim Masoud

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Annex III: Questionnaire-English version

STUDY QUESTIONNAIRE ON PREVALENCE OF OBSTRUCTIVE SLEEP APNEA AND ASSOCIATED FACTORS AMONG PATIENTS WITH END-STAGE KIDNEY DISEASE ATTENDING HEMODIALYSIS AT MUHIMBILI NATIONAL HOSPITAL

PATIENT'S IDENTIFICATION

Questionnaire No. .....
Date of study enrollment.....
MRN.....
Physical address(ward/district) .....
Telephone Number.....
Next of kin (mobile number) .....

Anthropometric and vital measurement

Weight(kg).....
Height(cm).....

Part 1: Socio-Demographic characteristic of respondent

1. Age..... Date.....Month.....Year……

2. Sex
a) Male
b) Female

3. Marital Status
a) Single
b) Married
c) Divorce
d) Separated
e) Widow

4. Education Level
a) No formal education
b) Completed Primary school education
c) Completed Secondary school education
d) College/University education

5. Occupation
a) Unemployed
b) Employed
c) Self-employed
d) Retired

6. Health insurance status
a) Insured
b) Non-insured

7. Habits
a) Do you smoke?
i. Yes ii. No
b) If YES, how many pack-years (mention and calculate) .....

c) Do you take alcohol?
i. Yes (calculate units) …….
ii. No

8. Medical history
a) Hypertension
b) Diabetes mellitus
c) Glomerulonephritis

9. Data regarding ESRD and hemodialysis:
a) Dialysis vintage ……. (in months)
b) Number of HD session per week……(Mention)
c) Hours on dialysis .....(hours)

10. Vascular access for Hemodialysis
a) AVF
b) AV graft
c) IJV catheter
d) Femoral catheter
e) Subclavian catheter
f) Permanent catheter

11. Erythropoietin use
a) Yes
b) No

12. BMI …….
a) underweight
b) Normal
c) Overweight
d) Obesity

Part 2: Laboratory Investigations

13. Pre-dialysis BUN (mmol/L) ..... and Post-dialysis BUN……. URR%.....
14. Serum Calcium.....
15. Serum phosphorus.....
16. Seru albumin…….
17. Haemoglobin level.....

Part 3:

A. STOP-BANG QUESTIONNAIRE (SBQ)

ITEM	0 POINT	1 POINT
Do you snore loudly?	No	Yes
Do you often feel tired, fatigue or sleepy during the day time?	No	Yes
Has anyone observed you stop breathing during sleep?	No	Yes
Do you have (or are you being treated for) high blood pressure	No	Yes
BMI	≤35kg/m^2	>35kg/m^2
Age	≤50years	>50years
Neck circumference*	≤40cm	>40cm
Gender	Female	Male

* Neck circumference is measured by principal investigator/research assistant

High risk of OSA*:* answering yes to three or more items

Low risk of OSA: answering yes to less than three items

B. EPIWORTH SLEEPINESS SCALE (ESS)

Annex IV: Dodoso kwa nakala ya Kiswahili

UTAFITI KUHUSU UGONJWA WA KUKOROMA USINGIZINI NA VIASHIRIA

QN	Situation	Responses	Score
1.	Sitting and reading	0 = would never doze 1 = slight chance of dozing 2 = moderate chance of dozing 3 = high chance of dozing	
2.	Watching television	0 = would never doze 1 = slight chance of dozing 2 = moderate chance of dozing 3 = high chance of dozing	
3.	Sitting inactive in a public place for example in a theatreor a meeting	0 = would never doze 1 = slight chance of dozing 2 = moderate chance of dozing 3 = high chance of dozing	
4.	As a passenger in a car for an hour without a break	0 = would never doze 1 = slight chance of dozing 2 = moderate chance of dozing 3 = high chance of dozing	
5.	Lying down to rest in the afternoon	0 = would never doze 1 = slight chance of dozing 2 = moderate chance of dozing 3 = high chance of dozing	
6.	Sitting and talking tosomeone	0 = would never doze 1 = slight chance of dozing 2 = moderate chance of dozing 3 = high chance of dozing	
7.	Sitting quietly after lunchwhen you have had no alcohol	0 = would never doze 1 = slight chance of dozing 2 = moderate chance of dozing 3 = high chance of dozing	
8.	In a car while stopped in traffic	0 = would never doze 1 = slight chance of dozing 2 = moderate chance of dozing 3 = high chance of dozing	
		TOTAL POINTS	

VINAVYOAMBATANA NA UGONJWA HUU MIONGONI MWA WAGONJWA WANAOHUDHURIA USAFISHAJI WA DAMU KUTOKANA NA FIGO KUSHINDWA KUFANYA KAZI KATIKA HOSPITALI YA MUHIMBILI

TAARIFA ZA AWALI ZA MSHIRIKI

Namba ya dodoso_____
Tarehe ya tafiti _____
Namba ya usajili hospitali _____
Makazi: (Wilaya/ Kata) _____
Namba ya simu: _____
Ndugu wa karibu (namba ya simu)_____

Vipimo vya awali
Uzito (kilo)_____
Urefu (sm)_____

Sehemu ya Kwanza: Taarifa binafsi na za kijamii za mshiriki

1. Umri……..

Tarehe……..Mwezi……..Mwaka

2. Jinsia

a) Kiume

b) Kike

3. Hali ya ndoa

a) Mpweke

b) Nipo kwenye ndoa

c)Nimeacha/Kuachika

d)Tumetengana

e) Mwenza alifariki

4. Kiwango cha elimu

a) Sina elimu rasmi

b) Shule ya msingi

c) Shule ya sekondari

d) Chuo

5. Kazi ya awali:

a) Sina kazi

b) Nimeajiriwa

c) Nimejiajiri

d) Nimestaafu

6. Chanzo cha gharama za usafishaji figo

a) Kutoka mfuko wa bima

b) Najigharamia

7. Mtindo wa Maisha

a) Unavuta sigara?

i. Ndio ii. Hapana,

Kama ndio, je unavuta kwa kiasi gani? (pakti-mwaka) …….

c) Unatumia pombe?

ii. Ndio (uniti ngapi) …….

iii. Hapana,

8. Historia ya

a) Shinikizo kubwa la damu

b) Ugonjwa wa kisukari

c) Glumerulonephritisi

10. Kuhusu figo kushindwa kufanya kazi na usafishaji wa damu

a. Muda gani sasa upo kwenye huduma ya kusafisha figo tangu ulipoanza?.....(miezi)

b. Unafanya huduma ya kusafisha damu mara ngapi kwa wiki? .....(miezi)

c. Je unatumia muda gani katika kila kipindi kimoja cha kusafisha damu?.....(masaa)

12. Unatumia njia gani/katheta ipi katika usafishaji wa damu

a) AVF

b) AV grafti

c) IJV katheta

d) Katheta ya kwenye mshipa wa femoral

e) Katheta ya kwenye mshipa wa subklaviani

f) Katheta ya kudumu

13. Unatumia sindano ya erythropoietini

a) Ndio

b) Hapana

14. Uwiano wa uzito na kimo (kg/m^2) .....

a) Uzito wa chini

b) Kawaida

c) Uzito uliopitiliza

d) Unene

Sehemu ya pili: Vipimo vya maabara

15. Pre-dialysis BUN..... Post-dialysis BUN……. URR%.....

16. Serum calcium.....

17. Serum phosphorus.....

18. Serum albumin…….

19. Kiwango cha Hemoglobini.....

Sehemu ya tatu:

A. DODOSO LA STOP-BANG

KIPENGELE	POINTI 0	POINTI 1
Unakoroma ?	Hapana	Ndio
Huwa unajisikia mwenye uchovu sana au kuhisi usingizi wakati wa siku nzima (mchana)	Hapana	Ndio
Kuna yeyote amekushuhudia ukishindwa kuhema nyakati za usiku?	Hapana	Ndio
Je una shinikizo la juu la damu au umeshawahi kutumia dawa za shinikizo la juu la damu?	Hapana	Ndio
Uwiano wa uzito na kimo	≤ kg/$m^2$35	> kg/$m^2$35
Umri	≤ miaka 50	> miaka50
Mzunguko wa shingo	≤ sm 40	>sm 40
Jinsi	Ke	Me

*Mzunguko wa shingo utapimwa na mtafiti mkuu au mtafiti msaidizi

Uhatari mkubwa wa kuwa na OSA: Majibu matatu au zaidi ya ndio

Uhatari mdogo wa kuwa na OSA: Majibu ya ndio yasiyofika matatu

B. ESS

Swali	Hali	Majibu	Pointi
1	Kuketi na kusoma	0= sipitiwi na usingizi kabisa 1=Uwezekeno mdogo wa kupitiwa na usingizi 2= Uwezekano mkubwa wa kupitiwa na usingizi 3= Uwezekano mkubwa wa kupitiwa na usingizi	
2	Kutazama televisheni	0= sipitiwi na usingizi kabisa 1=Uwezekeno mdogo wa kupitiwa na usingizi 2= Uwezekano mkubwa wa kupitiwa na usingizi 3= Uwezekano mkubwa wa kupitiwa na usingizi	
3	Kuketi katika eneo la wazi kama vile kwenye sehemu ya sinema au kikao	0= sipitiwi na usingizi kabisa 1=Uwezekeno mdogo wa kupitiwa na usingizi 2= Uwezekano mkubwa wa kupitiwa na usingizi 3= Uwezekano mkubwa wa kupitiwa na usingizi	
4	Ukiwa kama abiria katika chombo cha usafiri kwa muda was saa 1 bila kusimama sehemu	0= sipitiwi na usingizi kabisa 1=Uwezekeno mdogo wa kupitiwa na usingizi 2= Uwezekano mkubwa wa kupitiwa na usingizi 3= Uwezekano mkubwa wa kupitiwa na usingizi	
5	Ukitulia kupumzika wakati wa mchana	0= sipitiwi na usingizi kabisa 1=Uwezekeno mdogo wa kupitiwa na usingizi 2= Uwezekano mkubwa wa kupitiwa na usingizi 3= Uwezekano mkubwa wa kupitiwa na usingizi	
6	Kuketi na kuongea na mtu	0= sipitiwi na usingizi kabisa 1=Uwezekeno mdogo wa kupitiwa na usingizi 2= Uwezekano mkubwa wa kupitiwa na usingizi 3= Uwezekano mkubwa wa kupitiwa na usingizi	

7	Kuketi baada ya chakula cha mchana bila ya kutumia kilevi	0= sipitiwi na usingizi kabisa 1=Uwezekeno mdogo wa kupitiwa na usingizi 2= Uwezekano mkubwa wa kupitiwa na usingizi 3= Uwezekano mkubwa wa kupitiwa na usingizi	
8	Ndani ya gari huku gari ikiwa imesima katika foleni	0= sipitiwi na usingizi kabisa 1=Uwezekeno mdogo wa kupitiwa na usingizi 2= Uwezekano mkubwa wa kupitiwa na usingizi 3= Uwezekano mkubwa wa kupitiwa na usingizi	
		Jumla ya pointi	