



ST. PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE

**PREVALENCE AND PATTERN OF CHRONIC KIDNEY
DISEASE-MINERAL AND BONE DISORDER AMONG
PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS
AT ST. PAUL'S HOSPITAL MILLENNIUM MEDICAL
COLLEGE, ADDIS ABABA, ETHIOPIA.**

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A THESIS PAPER SUBMITTED TO THE DEPARTMENT OF INTERNAL
MEDICINE AND PUBLIC HEALTH, ST. PAUL'S HOSPITAL MILLENNIUM
MEDICAL COLLEGE IN PARTIAL FULFILLMENT OF THE REQUIREMENT
FOR SPECIALITY CERTIFICATE IN INTERNAL MEDICINE.

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ADDIS ABABA, ETHIOPIA

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AT ST. PAUL’S HOSPITAL MILLENNIUM MEDICAL COLLEGE,
ADDISABABA, ETHIOPIA FROM OCTOBER 1, 2023 TO
DECEMBER 31, 2023 G.C.**

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Contents

Acknowledgments.....	iii
Table of contents.....	vi
List of Figures.....	vi
Abbreviations and acronyms.....	vii
Abstract.....	viii
1. Introduction.....	1
1.1 Background.....	1
1.2 Statement of the problem.....	2
1.3 Significance of the study.....	2
2. Literature Review	3
3. Objectives	8
3.1 General Objectives.....	8
3.2. Specific Objectives.....	8
4. Methods and Materials.....	9
4.1. Study setting.....	9
4.2 Study design and period.....	9
4.3 Population.....	9
4.3.1. Source population.....	9
4.3.2. Study population.....	9
4.4. Inclusion and Exclusion Criteria.....	9
4.4.1 Inclusion criteria.....	9
4.4.2 Exclusion Criteria.....	9
4.5. Sample Size determination and sampling technique.....	10
4.5.1. Sample size determination.....	10
4.5.2. Sampling techniques.....	10
4.7. Study Variables.....	11
4.7.1. Dependent variables	11
4.7.2. Independent Variables	11
4.8. Operational Definitions.....	11
4.9. Data Collection Instruments and Techniques.....	12
4.10. Data Analysis.....	12

4.11 Data Quality	13
4.12. Ethical Consideration	13
4.13. Dissemination Plan	13
5. Results.....	14
5.1 Demographic characteristics	14
5.2 Behavioural and clinical details of the studied patients	15
5.3 Biochemical characteristics of the patients	18
5.4 Factors associated with turnover	19
6. Discussion	21
7. Strength and Limitations.....	24
7.1 Strength	24
7.2 Limitations	24
8. Conclusion and Recommendations.....	25
8.1 Conclusion	25
8.2 Recommendations	25
9. References.....	26
7. Annexes.....	30
8.1 Annex 1- The written consent form	30
1. Socio demographic characteristics	31
2. Clinical profile of CKD patient	31
CHECKLIST (FOR CHART REVIEW).....	32
3. Laboratory profile.....	32

Table of contents

Table 1. Background characteristics of patients undergoing maintenance hemodialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from October 1 to December 31, 2023.....	15
Table 2. Clinical characteristics of patients undergoing maintenance hemodialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from October 1 to December 31, 2023.....	17
Table 3. Markers of calcium homeostasis and bone metabolism in patients on maintenance hemodialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from October 1 to December 31, 2023.	20

List of Figures

Figure 1: Proposed conceptual framework of pattern of CKD-MBD and associated factors among dialysis patients	7
Figure 2. Pattern of mineral bone disorders in patients on maintenance hemodialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from October 1 to December 31, 2023.....	18
Figure 3. Bone turnover of patients on maintenance hemodialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from October 1 to December 31, 2023. ..	19

Abbreviations and acronyms

ALP - Alkaline phosphates

BUN: Blood Urea Nitrogen

BP: Blood Pressure

BMD: Bone and Mineral Disorder

Ca - Calcium

CI - Confidence interval

CKD: Chronic Kidney Disease

ESRD: End stage renal disease

ETB: Ethiopian Birr

FGF - Fibroblast growth factor

GFR: Glomerular Filtration Rate

HD – Hemodialysis

iPTH- Intact parathyroid hormone

KDIGO - kidney disease: Improving Global Outcomes

OR – Odds Ratio

SD - Standard Deviation

SBP: systolic blood pressure

SHPT – Secondary Hyperparathyroidism

SPHMMC: St Paul's Hospital Millennium Medical College

Abstract

Background: Mineral bone disorders in chronic kidney disease (CKD) patients is associated with high morbidity and mortality, and it has been reported to start early in the course of the disease and worsen as the kidney damage progresses and almost universally present among dialyzed patients. However, the prevalence and pattern of mineral bone disease in chronic kidney disease patients on maintenance Hemodialysis in our setting and in our country generally has not been established as to our knowledge

Objective: Assessment of prevalence and pattern chronic kidney disease mineral bone disorders in patients on hemodialysis in St Paul's Hospital Millennium Medical College.

Methods: A cross-sectional single center study was carried from all CKD patients established on maintenance hemodialysis and have follow up for at SPHMMC. All consecutive patients with CKD undergoing maintenance hemodialysis during the study period were recruited. A structured checklist that contained serum biochemical parameters was used to extract data from patient records. Data were entered and analyzed using SPSS version 26. Descriptive analysis was used to produce frequencies, median and interquartile range, mean and standard deviations for statistical analysis. Pearson's chi square test was used to identify associations between independent variables and bone turnover status. A p-value <0.05 was considered significant. Texts, tables and figures were used to present the results.

Results: Forty patients on maintenance hemodialysis were recruited for the study. Majority (n=26; 65%) were males Patients' age ranged from 23 years to 67 years with a mean of 41.7 years and standard deviation of 11.1. Diabetes mellitus was the predominant cause of CKD (20%). In total, all (100%) of the patients had CKD-MBD. Secondary hyperparathyroidism was observed in all (100%) of the patients, whereas 31 (77.5%) had hyperphosphatemia. Overall pattern of MBD turnover abnormality was 40%, Of these, 14 (35%) had high bone turnover, while only two (5%) had low turnover pattern. 60% of the patient had target PTH range in accordance with the KIDIGO recommendation. The chi square analysis showed that there was no significant relationship between serum calcium levels, serum phosphate level, serum vitamin D level and the bone turnover status.

Conclusion: CKD-MBD is highly prevalent among patients on hemodialysis in our center. Screening for CKD-MBD and appropriate treatment with phosphate binders and Vitamin D when indicated are highly recommended.

Keywords: Hemodialysis, MBD, SPHMMC

1. Introduction

1.1 Background

Chronic kidney disease (CKD) is a worldwide health problem affecting 5–10% of the world's population (1,2), and the majority of these patients are at an increased risk of developing disturbances of bone and mineral metabolism. These disturbances lead to a constellation of bone lesions which was previously referred to as renal osteodystrophy (ROD), with affected patients manifesting with symptoms such as bone pain, muscle-tendon rupture, pruritus and high incidence of fractures (2,3). Subsequently, evidence has shown that patients with ROD are also predisposed to cardiovascular calcification with associated high morbidity and mortality rates (4,5).

Unfortunately, the term ROD does not encompass this important extra skeletal manifestation. Therefore, to address these drawbacks and accommodate the extra skeletal manifestations, the kidney disease-Improving Global Outcomes (KDIGO) Foundation initiated a controversies conference with the aim of providing a globally acceptable definition and classification system for renal osteodystrophy. The KDIGO workgroup recommended a broader term, CKD–mineral and bone disorder (CKD-MBD) for the systemic disorder of mineral and bone metabolism due to CKD and that the term renal osteodystrophy should exclusively be used to describe disorders in bone morphology associated with CKD (6).

In clinical settings, although a bone biopsy is the gold diagnostic test, it is less frequently utilized because it is an invasive and cumbersome procedure and requires highly skilled personnel to interpret the tissue samples. Furthermore, KDIGO recently suggests to perform a bone biopsy only if knowledge of the type of renal osteodystrophy will impact treatment decisions and to do BMD testing to assess fracture risk patients only in patients with evidence of CKD-MBD and/or risk factors for osteoporosis (7). For these reasons, clinicians largely depend on trends in the levels of parathyroid hormone in conjunction with levels of serum phosphate, calcium and alkaline phosphatase as markers of bone turnover to guide in the treatment of mineral bone disorder (3).

1.2 Statement of the problem

Chronic kidney disease–mineral and bone disorders (CKD-MBD) are current complications of CKD patients undergoing dialysis. Despite the great advances in the knowledge of the pathogenesis of these disorders and the availability of new drugs, the control of CKD–MBD is still inadequate and it has been associated with increased morbidity and mortality (8–12).

In Ethiopia, there is limited study done on patients with CKD and on dialysis. A recent Cross-sectional Study that evaluated the magnitude and factors associated with biochemical CKD-MBD abnormalities among pre-dialysis CKD from July 1 – September 30, 2020 in the renal clinic of TASH showed high prevalence of biochemical abnormalities of CKD MBD. The study revealed that 31% of the participants had hyperphosphatemia, 36% hypocalcemia, and 89% had hyperparathyroidism (13). However, there is no study done on CKD-MBD in patients established on hemodialysis as to our knowledge.

St Paul's Hospital Millennium Medical College which is a referral Hospital in Addis Ababa is providing dialysis service to the public and the adult renal dialysis unit is giving the service for about 20-30 patients per day as of 2020. This study aims to evaluate the prevalence and pattern of mineral bone disorders in CKD patients established on hemodialysis

1.3 Significance of the study

Despite the high prevalence of Mineral bone disorders in CKD patients on dialysis, there is no published data on CKD-MBD in patients on hemodialysis from Ethiopia as to our knowledge. In addition, the practice of CKD MBD is from guidelines which are based on developed countries and expert suggestions.

Because of the paucity of established data in Ethiopia, a study in this area is needed to fill the existing knowledge gap and improve patient management. Therefore, a study to describe the prevalence and pattern of MBD in CKD patients on HD will be done.

2. Literature Review

Chronic kidney disease (CKD) constitutes a public health problem and is a leading cause of morbidity and mortality in both developed and developing countries, with an estimated 10% of the population worldwide having CKD (1).

The overall prevalence of CKD in adult African population was found to be 15.8% in a systematic metanalysis involving 98 studies (14). In Ethiopia, there is limited data on CKD but a hospital based cross-sectional study conducted at Jimma University Medical Center showed the prevalence of CKD is 26% and the predictors of CKD were uncontrolled blood pressure, fasting blood sugar > 150mg/dl, long duration of hypertension, ACEIs nonusers, and poor knowledge about CKD (15).

CKD is defined according to KDIGO as structural or functional abnormalities of the kidney that persist for at least 3 months and is manifested by either kidney damage (most frequently detected as persistent albuminuria or proteinuria (> 30 mg/ 24h or > 1 on specific dipstick); or a decreased glomerular filtration rate (GFR), (< 60 mL/min per 1.73 m²) (2).

KDIGO defined CKD-MBD as a systemic disorder of mineral and bone metabolism due to CKD, manifested by either one or a combination of the following three components: Abnormalities of calcium, phosphorus, PTH, or vitamin D metabolism, Abnormalities in bone turnover, mineralization volume linear growth, or strength or Extra skeletal (Vascular or other soft tissue) calcification (3).

The bone mineral metabolism abnormalities start during first stages of CKD as renal function decreases, long before the need for renal replacement therapy. Classically, prior to the discovery of fibroblast growth factor 23 (FGF23), phosphate retention due to a decline in renal function had been considered as the main trigger of secondary hyperparathyroidism (16). The retained phosphate leads to a triad of hyperphosphatemia, low 1,25(OH)₂D₃ and hypocalcemia which are well-known stimuli for PTH secretion that in turn enhances phosphate excretion and development of secondary hyperparathyroidism in advanced CKD. However, what mitigates this process in the early stages of CKD continued to be a point of discussion.

However, the pathophysiology of secondary hyperparathyroidism has evolved with new discoveries (17). For example, the emergence of FGF23 has revolutionized the understanding of the mechanisms underlying the development of secondary hyperparathyroidism, leading to an updated trade-off hypothesis. Plasma FGF23 levels become elevated with progressively worsening renal function, likely to occur before observed changes in the levels of phosphate and PTH (18). Fibroblast growth factor 23 (FGF23) is derived from osteocytes and plays a vital role in vitamin D and phosphate metabolism. It requires klotho (a transmembrane protein) to enable it to bind to the FGF receptor (FGFR) in classic target organs such as kidneys and parathyroid glands (10). Plasma FGF23 enhances phosphate excretion in the proximal renal tubule by decreasing the expression of luminal sodium dependent phosphate transporters and may also decrease intestinal phosphate absorption by inhibiting NaPi cotransporter activity (11). In addition, it reduces the synthesis of 1,25- dihydroxy vitamin D [1,25(OH)2D3] by down-regulating the activity of 1 α -hydroxylase and accentuating the activity of 24-hydroxylase (12,19).

In the early stages of CKD, high levels of FGF23 attenuate hyperphosphatemia at the expense of 1,25(OH)2 vitamin D suppression, thus initiating the development of secondary hyperparathyroidism (19). The decrease in serum 1, 25(OH) 2D3 leads to decreased intestinal calcium absorption. The triad of low levels of calcium, calcitriol and hyperphosphatemia further enhances excessive PTH secretion. This excess PTH leads to mobilization of calcium from the bone and osteitis fibrosa (20).

According to DOPPS which is a large multinational study and most representative observational studies carried out on CKD patients on dialysis described the state of MB disorders and their management in five European countries, the US and Japan, between 1996 - 2001 and 2002 and 2004 (DOPPS I, DOPPS II) (21,22). This study showed that, depending on the country studied, there were differences in the prevalence of different BMM disorders. Thus, the percentages of patients with low or high PTH were 58.6% and 19.0% for Japan, 50.1% and 26.9% for European countries and 48.2% and 30.3% for the United States, respectively (6). The factors related to the probability of having hyperparathyroidism were young age, being female, having lower hemoglobin and Kt/V, absence of diabetes, human immunodeficiency virus and receiving dialysis treatment in Japan. The percentage of patients outside the range suggested for serum phosphorus (3.5 to 5.5mg/dl) was 51.6% and 7.6% for hyper and hypophosphatemia, respectively, whereas for

suggested levels of calcaemia (8.4 to 9.5mg/dl) it was 50.2% and 9.3% for hyper and hypocalcemia, respectively (6).

In Iran, a cross sectional study was done among 128 ESRD patients (52 men and 76 women) with a mean age of 59.3 years undergoing maintenance hemodialysis at Imam Reza Referral Hospital. Renal osteodystrophy was diagnosed in 93 (72.7%) out of 128 patients studied. Of them, 53 (41.4%) patients had PTH levels above 300 pg/mL (high bone turnover) and 40 patients (31.3%) had PTH levels below 150 pg/mL (low bone turnover). No statistically significant difference was detected in terms of renal osteodystrophy-related clinical findings ($p = 0.110$), age at the time of ESRD diagnosis ($p = 0.200$), and the number of hemodialysis sessions per week ($p = 0.200$). Hyperphosphatemia was more prevalent in the ROD group ($n = 52$, 57.1%) compared with 11 patients (31.4%) included in the group without ROD ($p = 0.004$) (23).

In Pakistan, Rizvi et al. conducted a cross sectional with the objective to finding out the prevalence of bone mineral disease in sixty dialysis patients. The prevalence of CKD-MBD among dialysis patients is 83.33%. The study also reported that 41 (68.33%) had high bone turnover, 10 (16.6%) were normal bone turnover whereas 9 (15%) had low bone turnover (24).

Data about the burden of CKD-MBD in African dialysis populations are very scarce. A recent Cross-sectional Study done in Tanzania from May to December 2019 which evaluated a total of 300 participants with chronic kidney disease stage 3 and above found the prevalence of mineral bone disease to be 75.0%. The most common form of mineral bone disease was hyperparathyroidism 196 (87.1%), followed by hypocalcemia 174 (77.3%) and hyperphosphatemia 82 (36.4%), was the least common. In this study, Factors found to be significantly associated with CKD-MBD were the use of calcium supplements, use of phosphate binders, being on dialysis, a calcium rich diet and a low phosphate diet (13).

Another cross-sectional study on prevalence of CKD-MBD among patients on maintenance hemodialysis in Northwestern Nigeria between December 2011 and June 2012 found the total prevalence of CKD-MBD to be 58%. The study revealed the predominant form of CKD-MBD to be SHPTH (12), this was in agreement with a study in Senegal, in which SHPTH was found in 57 of 118 (48%) patients on hemodialysis (25).

A similar cross-sectional descriptive study done from June 2009 to April 2016, evaluated biochemical markers of mineral bone disorder in South African patients on maintenance hemodialysis and revealed a high prevalence of derangements of biochemical markers of mineral bone disorder. Based on the cut-off values utilized by the study, hyperparathyroidism (PTH>150) was present in 73.4% of the patients and 37% with a stricter cut-off value of 585 ng/ml (9 times the upper normal of the laboratory assay) (26), this was in agreement with previous studies from Africa and developed countries (25,27).

Another cross-sectional study was carried out on 186 regular hemodialysis patients from five hemodialysis centers in the west of Tripoli-Libya District. According to the Kidney Disease Outcomes Quality (KDOQ) iPTH level guideline, 88.10% of the studied patients had metabolic bone disorders, and 39.80% showed low bone turnover. About 48.40% were high bone turnover; only 11.80% of studied patients were within the target range according to the KDOQ Initiative guidelines. About 40.36% of studied patients had low calcium levels (below 8.5 mg%), and 35.48% had high phosphorus levels (more than 5.5 mg%). About 61.10% of high bone turnover patients complain of bone pain and 50.50% complain of muscle weakness. Among low bone turnover patients, 36.48% had no symptoms, and 28.38% were complaining of both muscle weakness and bone pain (28).

In Ethiopia, a Cross-sectional Study that evaluated the magnitude and factors associated with biochemical CKD-MBD abnormalities among pre-dialysis CKD patients from July 1 – September 30, 2020 in the renal clinic of TASH showed high prevalence of biochemical abnormalities of CKD MBD. The study revealed 31% of the participants had hyperphosphatemia, 36% hypocalcemia, and 89% had hyperparathyroidism. Patients with stages 3a, 3b, 4 and 5 CKD contributed to 23%, 29%, 26% and 22% of the total respectively and the main causes of CKD identified were diabetes and hypertension (7).

However, despite high prevalence of MBDs in CKD patients, there are no data on CKD MBD from Ethiopia. Even the practice of CKD MBD is from guidelines which are based on Western data and expert suggestions, due to paucity of data from the country. Hence, there is an urgent need to study in this area and investigate the prevalence of MBD in CKD patients on HD.

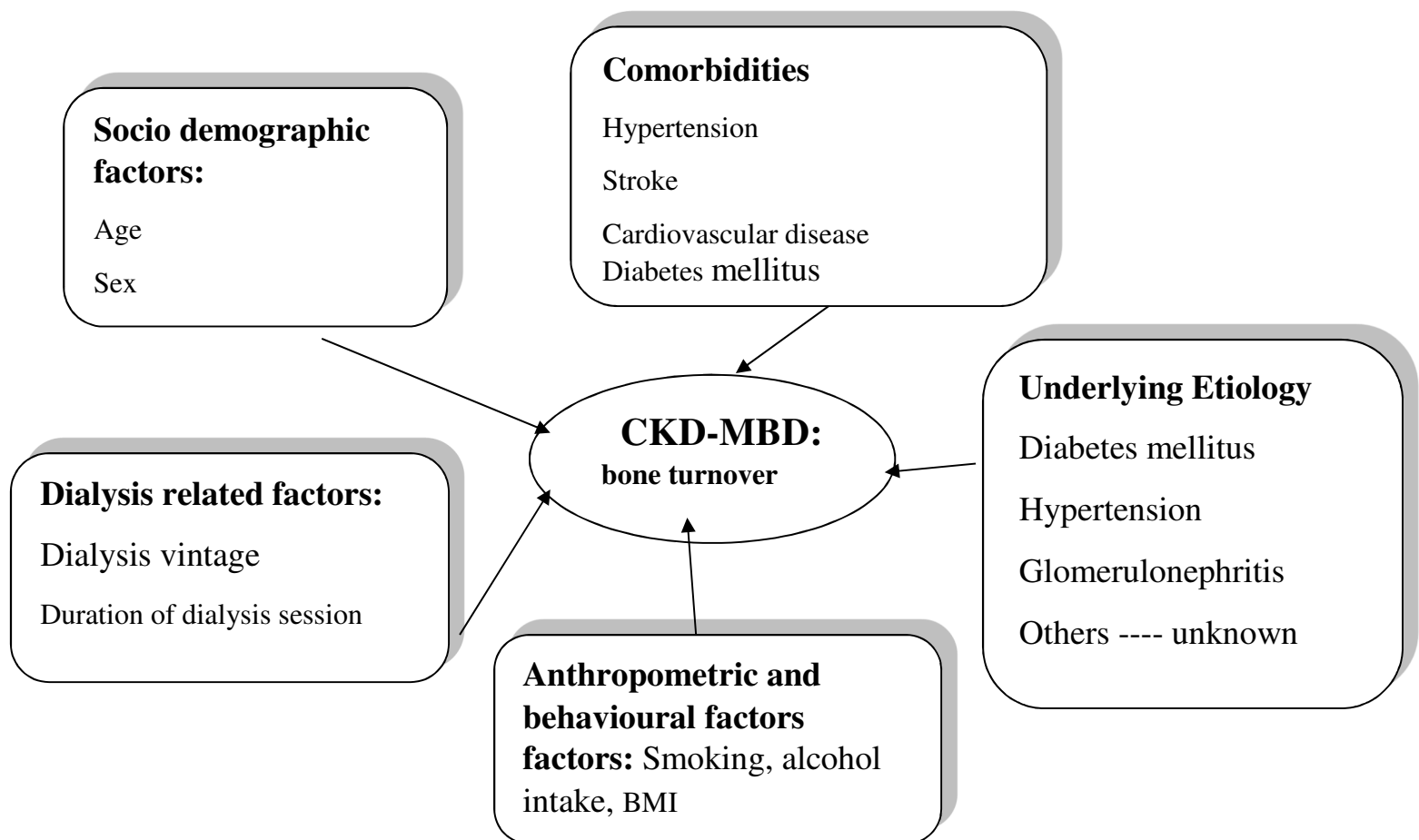


Figure 1: Proposed conceptual framework of pattern of CKD-MBD and associated factors among dialysis patients

3. Objectives

3.1 General Objectives

- To assess prevalence of chronic kidney disease and Mineral bone disorder in hemodialysis patients in St Paul's Hospital Millennium Medical College from October 1, 2023 to December 31, 2023 G.C.

3.2. Specific Objectives

- ✓ Determine the Prevalence and pattern of mineral bone disorders in chronic kidney disease patients on maintenance hemodialysis from October 1,2023 to December 31, 2023 G.C.
- ✓ To identify risk factors associated with chronic kidney disease and mineral bone disorders in hemodialysis patients from October 1, 2023 to December 31, 2023 GC.

4. Methods and Materials

4.1. Study setting

This study was conducted in SPHMMC, Renal unit. St Paul hospital millennium medical college is one of the two biggest specialized referral hospitals in Addis Ababa and in the country. It was established in 1968. It is a rapidly expanding hospital especially after it started working as a medical college since 2000 E.C/2007G.C. Currently it runs residency and subspecialty programs in many fields. It is a center of excellence in medical services for renal center providing a dialysis and also the first hospital in the country with renal transplantation center. The renal unit established in 2012, started dialysis service a year later limited to AKI and has the only transplant center in the country with the first transplant done in 2015. The renal unit has around 20 dialysis machines in the dialysis unit currently with capability of dialyzing 18-20 patients daily.

4.2 Study design and period

A hospital-based, cross-sectional study was conducted on patients established on maintenance HD in St Paul hospital millennium medical college renal unit from October 1, 2023 to December 31, 2023 GC.

4.3 Population

4.3.1. Source population

The source population for this study was all patients labelled CKD and established on maintenance HD in St Paul hospital millennium medical college renal unit.

4.3.2. Study population

CKD patients on maintenance hemodialysis and fulfilling inclusion criteria. were included in the sample during data collection period

4.4. Inclusion and Exclusion Criteria

4.4.1 Inclusion criteria

- Age >18
- Complete data parameters

4.4.2 Exclusion Criteria

Patients documented to have

- Active malignancy,
- Active liver disease

- Primary hyperthyroidism

4.5. Sample Size determination and sampling technique

4.5.1. Sample size determination

Sample size is calculated by using the single population proportion formula

$$n = Z^2 p(1-p) / d^2$$

n= required sample size

Z= confidence level at 95% (standard value of 1.96)

d= margin of error = 5%

P=estimated prevalence of MBD in CKD patient on dialysis from previous study was 58%[21]

- So, when we substitute the values in the formula, it gives us a sample size of 374.

$$n = (1.96)^2 * 0.58 * 0.42 / (0.05)^2$$

$$n = 374$$

- Since the study population is <10,000, there is a need to use population correction formula which is $n = n_i * N / N + n_i$

Where n_i = initial sample size is 374

N= study population (CKD patients at follow up in dialysis centre in 2 months) is 120

- Because the source population is <10,000, the final sample size is determined as follows:

n_i

$$n_f = \frac{n_i}{1 + \frac{n_i}{N}}$$

$$[1 + \frac{n_i}{N}]$$

$$n_f = 374 / (1 + 374/120) = 90.99$$

This gives us a sample size of 91 patients.

When we add the 10% non-response rate, it gives us a final sample size of 100 patients

4.5.2. Sampling techniques

A consecutive sampling technique was used, all CKD patients undergoing regular hemodialysis at the dialysis center and meeting inclusion criteria were included.

4.7. Study Variables

4.7.1. Dependent variables

Bone turnover status

4.7.2. Independent Variables

Age, sex, Blood pressure, place of residence, educational status, marital status, occupation, medical comorbidity, smoking history, Cause of CKD, duration of dialysis, dialysis vintage, frequency of dialysis, dialysis access, Hemoglobin

4.8. Operational Definitions

CKD: serum creatinine level above laboratory baseline for sex for more than 03 months

Stage 5D CKD: Patients who have started dialysis

Hypertension: Blood pressure $\geq 140/90$ mmHg which is measured more than one time or participants with known hypertension.

Dialysis vintage: length on hemodialysis in months

Cause of CKD: As documented and decided by the treating physician

Mineral bone disorder will be defined in the presence of any of the following: in accordance with KIDIGO and K/DOQI

Hypocalcemia: Corrected Total calcium < 8.5 mg/dl

Hypercalcemia: Corrected TCa > 10 mg/dl

Hypophosphatemia: Phosphorus < 2.5 mg/dl

Hyperphosphatemia: Phosphorus > 4.5 mg/dl

Vitamin D deficiency: 25(OH)vitamin D < 20 ng/ml

Vitamin D insufficiency: 25(OH)vitamin D: 20 ng/ml - 29 ng/ml

Vitamin D sufficiency: 25(OH)vitamin D > 30 ng/ml

Hypoparathyroidism: iPTH < 15 pg/ml

Hyperparathyroidism: iPTH > 65 pg/ml

Low turnover MBD: serum iPTH < 130 pg/ml

High turnover MBD: serum iPTH > 585 pg/ml

Target treatment for MBD: serum iPTH between 2X and 9X of upper limit of normal for assay.
(iPTH between 130 pg/ml and 585 pg/ml)

4.9. Data Collection Instruments and Techniques

First, the aim of the study was clearly explained to the participants. And then, after oral consent was received, data was collected by an interview questionnaire and checklist adopted from similar studies.

The interview questionnaire consisted of information on the socio demographic factors (age and sex), education, religion, family history of kidney disease

In addition, checklist data extracted from patient chart included: clinical profile (underlying kidney disease and medical conditions), dialysis profile (access, duration, frequency).

Furthermore, laboratory values (serum iPTH, calcium, phosphorus, 25(OH) vitaminD, albumin, Hgb) was extracted from the physical as well as electronic charts and Blood pressure was measured by using a well-calibrated digital sphygmomanometer.

An hour-long training was given to 6 data collectors and 2 supervisors (internal medicine residents and GPs) on the components of the checklist, how to fill the data and the importance of the study. Data were assessed for completeness (presence of biochemical mineral bone disorder, namely PTH, calcium, phosphorus) before entry and the entered data were checked by the data supervisor on a daily basis for any incompleteness (when laboratory measurements for the dependent variables are not available) and/or inconsistency.

The principal investigator had a supervisory role.

Document review was done by data collectors and principal investigator.

The data collection was done from October 1, 2023 to November 30, 2023 G.C.

4.10. Data Analysis

Data were analyzed using the Statistical Package of Social Sciences (SPSS) version 26 for Microsoft Windows. The background and clinical characteristics of patients were computed using descriptive statistics such as mean $\pm$ standard deviation, percentage, frequencies, median +

interquartile range (IQR). Pearson's chi square test was used to extract factors associated with bone turnover status. A p value was considered significant at the level of <0.05 . Finally, the study findings were presented using texts, diagrams, tables and figures.

4.11 Data Quality

To ensure the quality of data, preceding data collection, training of the data collectors was carried out for one day by the principal investigator on the objective, relevance of the study and confidentiality of information.

Interview questionnaire was translated in to Amharic so that patients gave accurate answers with a better understanding and the checklist was prepared in English and is adopted from similar studies done in the past.

Pre-testing was done two weeks prior to data collection using 5% of the total sample size to check its variability and it was assessed for its clarity, length and completeness.

4.12. Ethical Consideration

Prior to conducting the research, permission was obtained from SPHMMC Research Ethics committee. Patients were informed about the aim and benefit of the study. The information obtained from the interview as well as from the charts of the patients was kept confidential and was used only for the purpose of this study.

4.13. Dissemination Plan

At the end of the research, the output of the study will be communicated to the department of Internal Medicine and Public Health, St. Paul's Hospital Millennium Medical College in partial fulfillment of the requirement for a specialty certificate in Internal Medicine. It will also be submitted to the hospital's Nephrology unit. Moreover, it will be presented in scientific conferences including SPHMMC. And all efforts will be made to publish the results on local or international journals.

5. Results

5.1 Demographic characteristics

This study included data derived from forty patients who were undergoing maintenance hemodialysis at SPHMMC during the study period. Majority (n=26; 65%) were males and the remaining 14 (35%) were females, with male-to-female ratio of 1.9 to 1. Patients' age ranged from 23 years to 67 years with a mean of 41.7 years and standard deviation of 11.1. Most (n=37;92.5%) of the patients were from Addis Ababa city (Table 1).

On the other hand, majority (n=23;57.5%) of the patients included in this study stated to have attended up to secondary school. While twelve patients (30%) were self-employed, twelve (n=12; 30%) were unemployed. In addition, with regard to religious affiliation, close to two-thirds (n=25;62.5%) were Orthodox Christians (Table 1).

Table 1. Background characteristics of patients undergoing maintenance hemodialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from Oct 1 to December 31, 2023

Variable	Frequency	Percent (%)
Age group		
18–35 years	15	37.5
36–55 years	19	47.5
>55 years	6	15.0
Sex		
Male	26	65.0
Female	14	35.0
Residence		
Addis Ababa	37	92.5
Out of Addis Ababa	3	7.5
Marital status		
Single	15	37.5
Married	23	57.5
Divorced	2	5.0
Educational level		
Unable to read and write	2	5.0
Able to read and write	1	2.5
Primary education	5	12.5
Secondary education	23	57.5
Tertiary and above	9	22.5
Occupational category		
Public servant	6	15.0
Housewife	10	25.0
Self-employed	12	30.0
Unemployed	12	30.0
Religious affiliation		
Orthodox Christian	25	62.5
Protestant Christian	7	17.5
Muslim	8	20.0

5.2 Behavioural and clinical details of the studied patients

Most (n=37;92.5%) claimed not to have ever smoked cigarette. More one-third (n=14;35%) reported to be consume alcoholic beverages prior to their illness. With regard to anthropometric data, more than two-thirds (27;67.5%) were overweight, with BMI ranging from 25 to 29.9, and ten (25%) had normal BMI (Table 2).

Only two (5%) had a positive first-degree family history of CKD. Majority (n=28;70%) had a coexisting medical condition. Of these, all (28;100%) had hypertension, with 4 (14.3%) had hypertensive heart disease. The predominant presumed cause of end-stage renal disease was diabetes mellitus (25%), followed by chronic glomerulonephritis (20%), hypertension (15%), and autosomal dominant polycystic kidney disease (5%). In 14 (35%) of patients, the etiology was unknown (of note 80% of these patients had hypertension as comorbidity) (Table 2).

The median (IQR) serum albumin level 3.2 (3.1–3.5) gm/dL. Patients' median hemoglobin level was 9, with a range of 7–11.6 gm/dL. The median (IQR) of systolic blood pressure was 140 (130–150) mm of Hg while that of diastolic blood pressure was 80 (80–90) mm of Hg. While 37 (92.5%) of the patients had 3 times a week session, the dialysis time duration per session was 4 hours for most (n=36;90%) of the patients. The median (IQR) hemodialysis vintage was 48 (24–67.5) months (Table 2).

Table 2. Clinical characteristics of patients undergoing maintenance hemodialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from Oct 1 to December 31, 2023

Variable	Frequency	Percent (%)
Smoking status		
Never	37	92.5
Former smoker	3	7.5
Alcohol history		
Never	26	65.0
Former smoker	14	35.0
Body mass index		
Normal (18.5–24.9)	10	25.0
Overweight (25–29.9)	27	67.5
Obese (≥ 30)	3	7.5
Positive family history of CKD		
No	38	95.0
Yes	2	5.0
Presence of comorbidity		
No	12	30.0
Yes	28	70.0
Type of comorbidity (n=28)		
Hypertension	28	100.0
Hypertensive heart disease	4	14.3
Cerebrovascular disease	1	3.8
Hepatitis B virus infection	1	3.8
Presumed etiology		
Diabetes mellitus	10	25.0
Chronic glomerulonephritis	8	20.0
Hypertension	6	15.0
Polycystic kidney disease	2	5.0
Unknown	14	35.0
Serum albumin level (gm/dL) (median + IQR)	3.2	3.1–3.5
Hemoglobin level (gm/dL) (range)	9	7–11.6
Systolic blood pressure	140	130–150
Diastolic blood pressure	80	80–90
Duration of dialysis		
3 hours	4	10.0
4 hours	36	90.0
Frequency of dialysis per week		
2	3	7.5
3	37	92.5
Dialysis vintage (months) (median + IQR)	48	24–67.5

CKD: Chronic Kidney Disease, IQR: Inter Quartile Range

5.3 Biochemical characteristics of the patients

In this study, secondary hyperparathyroidism was the commonest mineral bone abnormality, occurring in all (100%) of the patients. This is followed by hyperphosphatemia, hypocalcemia and vitamin D insufficiency, which were documented in 31 (77.5%), 26 (65%) and 23 (57.5%) of the cases, respectively (Figure 2).

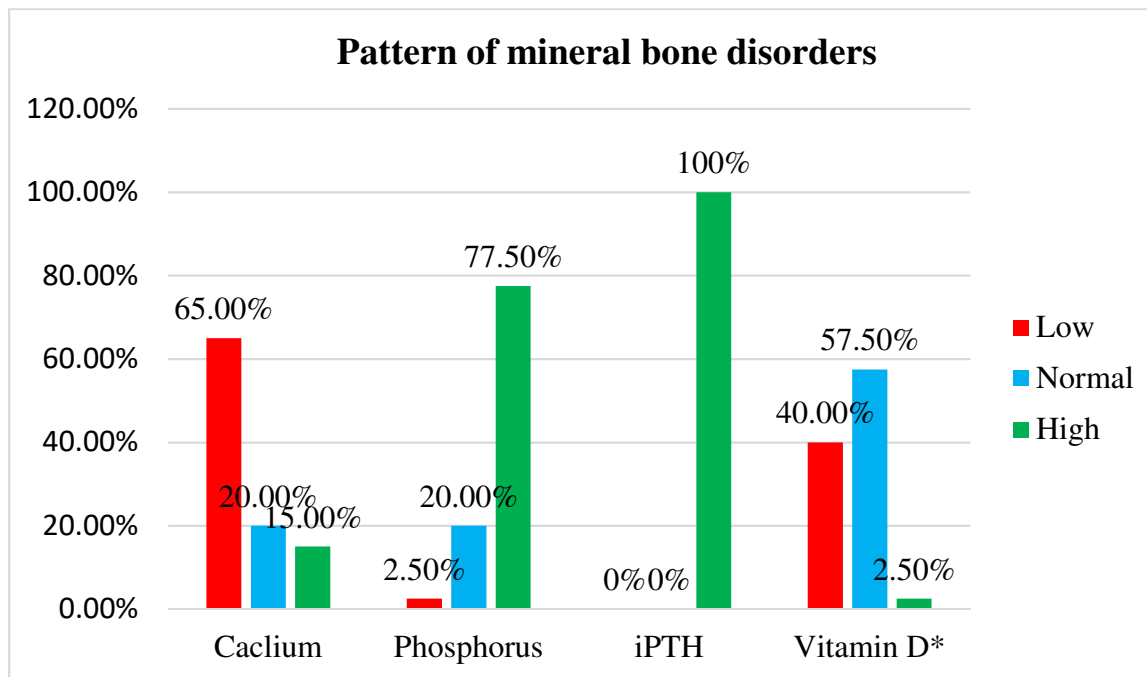


Figure 2. Pattern of mineral bone disorders in patients on maintenance hemodialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from October 1 to December 31, 2023.

*Vitamin D level was categorized into deficiency, insufficiency and sufficiency, respectively.

Moreover, while majority (n=24;60%) of the patients had within normal range of target level (iPTH), fourteen (35%) had showed high bone turnover, with serum iPTH level of greater than 585 pg/mL. On the other hand, only two (5%) had low bone turnover according to iPTH values. Altogether, this study showed that 16 (40%) had abnormal BMDs turnover (Figure 3).

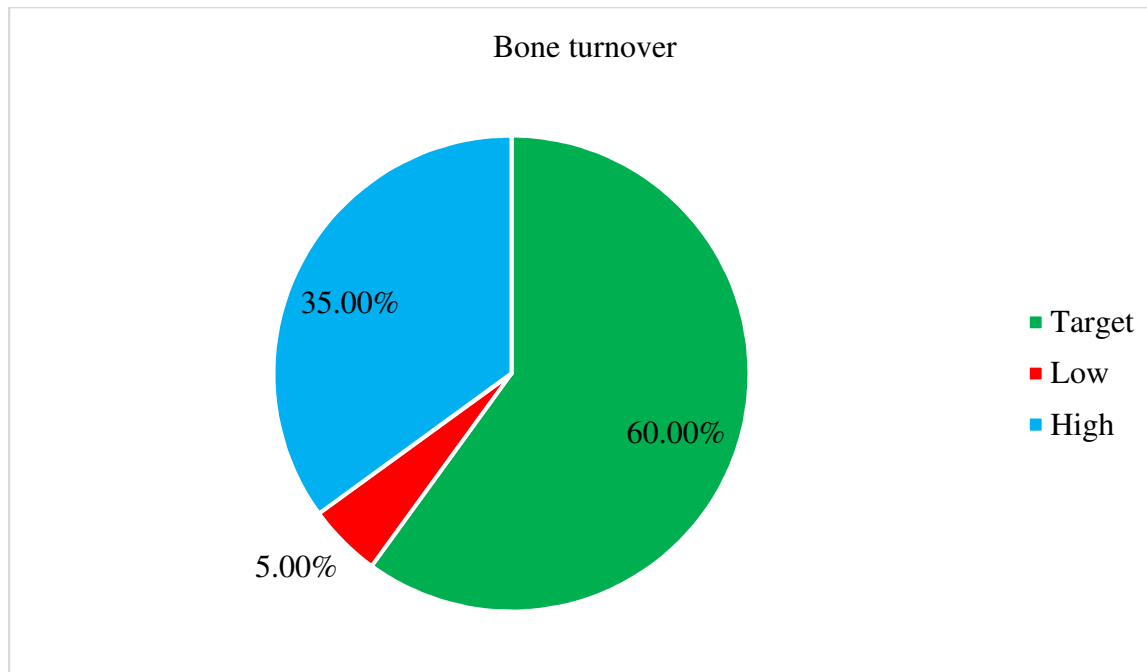


Figure 3. Bone turnover of patients on maintenance hemodialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from December 1, 2023 to January 31, 2024

5.4 Factors associated with turnover

The chi square analysis showed that there was no significant relationship between serum calcium levels, serum phosphate level, serum vitamin D level and the bone turnover status (Table 3).

Table 3. Markers of calcium homeostasis and bone metabolism in patients on maintenance hemodialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia from June 1 to July 31, 2023

Variable		High bone turnover (n=14)	Low bone turnover (n=2)	X ² value	P value
Age category	18–35 years	6(85.7%)	1(14.3%)	0.749	0.945
	36–55 years	6(85.7%)	1(14.3%)		
	>55 years	2(100%)	0(0%)		
Serum calcium (mg/dl) *	<8.5	8(88.9%)	1(11.1%)	1.78	0.411
	8.5–10	4(100.0%)	0(0%)		
	>10	2(66.7%)	1(33.3%)		
Serum phosphate (mg/dl)	<2.5	0(0%)	0(0%)	0.51	0.468
	2.5–4.5	3(100%)	0(0%)		
	>4.5	11(84.6%)	2(15.4)		
Serum vitamin D level (ng/ml)	<20	8(80.0%)	2(20.0%)	1.37	0.504
	20–29	5(100%)	0(0%)		
	≥30	1(100%)	0(0%)		

*Corrected to serum albumin level

6. Discussion

This study aimed to assess prevalence and pattern of mineral bone disorder among CKD patients undergoing maintenance hemodialysis at St Paul's Hospital Millennium Medical College, a tertiary hospital in Addis Ababa, Ethiopia. As a result, it showed that all of the patients had at least one form of disturbance in bone and mineral metabolism, with hyperparathyroidism and hyperphosphatemia being the predominant features. The prevalence of pattern MBDs among the studied patients according to abnormal PTH levels was 40% (5% had low bone turnover and 35% had high bone turnover).

The prevalence rate of MBDs (100%) obtained in this study was relatively comparable to the high prevalence of bone mineral disorder observed in Pakistan and Libya, in which 88.1% and 87.5% of hemodialysis patients had biochemical evidence for MBDs (28,29). The present prevalence was slightly higher than the rates obtained in Iran and Senegal, where the corresponding prevalence rates were 72.7% and 66.9%, respectively (25,23). Furthermore, it was higher than the prevalence (68% and 58%) of dialysis patients with biochemical abnormalities in Pakistani and Nigerian studies (22,30). The prevalence of CKD-MBD in this study was different from the observation in Singapore, where 86.0% and 54.7% had these disorders based on KDOQI and KDIGO guidelines, respectively (31).

The high frequency of CKD-MBD in this study can be partly justified by the fact that there prevails a suboptimal control of phosphate balance as a result of limited access to hemodialysis and expensive drugs therapies in resource-challenged settings like ours. In fact, systemic dysregulation of minerals homeostasis manifesting as disruption of serum and tissue concentrations of phosphorus, calcium (Ca), and parathyroid hormone (PTH) is expected among patients with advanced CKD. However, the extremely high prevalence of MBD observed in this study is a reflection of previous reports that show that biochemical monitoring is not done as per the standard recommendations even in a tertiary care center in developing settings (32).

The possible explanations for discrepancy can be the differences in medical care level, dialysis quality (adequacy of dialysis, types of dialysis membrane, dialysis water) differences in cutoff points used to define abnormalities. Of note, the majority of our patients were dialyzed less than 12 hours a week. Apart from this, the socio-economic characteristics and health literacy of patients may account for the apparent variations as previous studies have indicated that adherence to

medication and dietary modifications were more likely to occur in population with more awareness among CKD patients (33).

Moreover, it is to be noted that majority of the study population were individuals who had cost-free access to hemodialysis and medications via the available health insurance system although access to high-cost medications such as phosphate binders is commonly limited, and patients are required to afford costly medications (especially newer agents such as sevelamer, lanthanum carbonate, and calcimimetics) which are only available in private facilities.

Regarding the pattern of CKD-MBD, secondary hyperparathyroidism was the most frequent biochemical disorder observed in this study. This is in agreement with the aforementioned Senegalese study (25). The observation that secondary hyperparathyroidism is a predominant form of CKD-MBD is also in agreement with a study in Nigeria (22) and India (34). However, this finding was contrasting the Pakistani report, which observed that more than one-third (35.4%) of patients had adynamic bone disease while one-fourth (25.6%) had hyperparathyroidism (35). It was quite different from the pattern in China, in which the proportion of patients with hyperphosphatemia 58.6% and that for high iPTH was 45.4% (36).

The preponderance of hyperparathyroidism can be attributed to ethno-racial differences, since earlier reports indicated that African individuals have comparatively higher parathyroid glands mass and circulating PTH level than their Caucasian counterparts (37,38). In this regard, a substantial proportion of Black American patients with low bone turnover had very high serum PTH levels (38).

Based on serum iPTH level, 35% of the studied patients had high turnover renal while only 5% evidence for low turnover BMDs. This finding is similar to the observation noticed in Pakistan, where 68.33% had high bone turnover 15% showed low bone turnover (24). A consistent finding was obtained in Senegal, where high turnover hyperparathyroidism was more common (72.2% patients) than adynamic bone disease (27.8%) (25). Also, in agreement with the Senegalese (25), Pakistani (30) and Iranian (23) reports, low turn-over osteodystrophy in this study was less frequent than high turn-over osteodystrophy. Similarly, it is different from what was obtained in Libya, where 48.40% had high turnover hyperparathyroidism bone disease while 39.80%% of patients had low turnover BMDs (28). Of note ,60% of patients had target range PTH in accordance with the recommendations of KIDIGO.

Finally, in Keeping with the Senegalese study (25), this study showed that there was no significant relationship between serum calcium levels, serum phosphate level, serum vitamin D level and the bone turnover status. This is different from the Libyan and Pakistani studies, in which the mean calcium level in low turnover bone disease was higher than the hyperparathyroidism bone group (28,24). This discrepancy can be attributed to the sample size of the study population and the cutoff used to classify categories. For example, this study included only 40 patients while the Libyan study included 186 patients (28).

7. Strength and Limitations

7.1 Strength

- ✓ This study used both primary and secondary data, which is believed to improve the accuracy of the data gathered.

7.2 Limitations

- This study is subject to the typical limitations of any cross-sectional design, including the inability to determine causation alternative explanation apart from association.
- The study was a single center study with a small study population; hence results should only be generalized with caution.
- Laboratory tests were not performed in one central laboratory, some of the biochemical parameters were not done at the same time and the same laboratory; therefore, variations between laboratories may exist. In addition, laboratory tests were done at early times with no recent update which may not tell current status.
- The study also did not take into account dietary factors and habits as this was a cross-sectional study as these needs prospective follow up of dietary habits of patients with subsequent biochemical monitoring to correlate.
- MBD treatment/compliance status with vitamin D analogues and phosphate binders was not studied also as there was no documentation of MBD treatment in the patient physical as well as electronic charts up on extensive search. Of note, most of the patients had follow up elsewhere and might have been treated for MBD, but at our hospital charts there was no documentation.
- Patient's relevant information was not documented properly and were missing electronically, in the history sheets (e.g. Information like possible underlying etiology for the CKD), and the significant proportion of biochemical laboratory values that were done in different times can potentially affect the results and produce biased estimates, leading to invalid conclusions.

8. Conclusion and Recommendations

8.1 Conclusion

This study demonstrated that MBD is a highly common condition among CKD patients on maintenance haemodialysis. It showed that secondary hyperparathyroidism was the most dominant feature, followed by hyperphosphatemia, hypocalcemia and vitamin D insufficiency. It is dominated by high turn-over MBDs, with majority (60%) also having target PTH. with no association with clinic-demographic factors.

8.2 Recommendations

On the basis of the findings obtained in the study, the following recommendations can be forwarded.

To health care professionals,

Clinicians should measure biochemical parameters such as serum phosphate, calcium, vitamin D levels and most importantly i-PTH levels initially when initiating dialysis and subsequently serial measurement according to recommended guidelines in order to treat and prevent the potentially dire consequences of CKD-MBD.

To local health policy makers,

Concerned stakeholders including local policy makers should consider availing necessary medications and optimize dialysis care to maintain mineral-bone homeostasis in these patients.

To researchers,

Further studies should be carried out to validate the current findings, and they should be multi-center with larger sample size to better characterize the pattern of CKD-MBD.

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7. Annexes

8.1 Annex 1- The written consent form

Title: PREVALENCE CKD-MBD BIOCHEMICAL ABNORMALITIES IN PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS AT ST. PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE, ADDIS ABABA, ETHIOPIA, A CROSS SECTIONAL STUDY.

Investigator: Ahmednasir Abdi, M.D., Internal medicine department, SPHMMC

Phone: 0913838726

Introduction:

Greetings, you are being asked to participate in a study of hemodialysis in the SPMMC renal unit. You were selected because you are on hemodialysis on the selected time frame of the study and you have received a required diagnosis.

Please listen carefully and feel free to ask any questions you may have to the investigator.

Purpose of the study: to evaluate the prevalence and pattern of CKD MBD patients on hemodialysis.

Procedure: If you agree to this study, you will be asked questions including basic things about you and will be followed during the selected session of hemodialysis for the complications that may occur.

Risks: there is no anticipated risk of participation and acceptance or refusal will not affect any further care.

Benefits: It will help us to know the burden of acute complications of hemodialysis and will guide us to treat accordingly.

Confidentiality: The study will be anonymous, findings will be strictly confidential, and your identification will not be mentioned. All information will be kept in a password protected computer.

Payment: You will not receive any payment for your participation except gratitude.

Right to refuse or withdraw: You may refuse any time to participate in the study and can withdraw your consent for the data gathered to be used.

Subject's Signature:

Date:

Investigator's signature:

Annex 1: QUESTIONNAIRE (Patient interview)

Date: _____ MRN/ICARE NUMBER: _____ Study ID: _____

1. Socio demographic characteristics

1.1. Age: _____

1.2. Sex: A) Male B) Female

1.3. Address: A) Addis Ababa B) Oromia C) Amhara D) SNPPR E) Others (specify)

1.4. Marital status: A) Single B) Married C) Divorced D) Widowed

1.5. Occupation: A) Civil servant B) Merchant C) Farmer D) Housewife E) self-employed
F) Daily laborer G) Student H) Others (retired, no job) specify

1.6. Education: A) Unable to read and write B) Able to read and write C) Primary education
D) Secondary education E) College and above

1.7. Religion: A. Orthodox Christian B. Catholic Christian Protestant Christian D. Muslim

2. Clinical profile of CKD patient

2.1. Smoking status: A) Never B) former C) Current D) unknown

2.2. How often do you drink alcohol? A) Never B) former C) Current D) unknown

2.3. Do you have a sibling, parent or offspring who has chronic kidney disease?

A) Yes B) No

CHECKLIST (FOR CHART REVIEW)

2.5. Co morbidities (other than cause of CKD): A) Yes B) No /

If yes: (A) coronary artery disease (CAD) ;(B) Heart Failure; (C) Cerebrovascular disease
(D)Peripheral arterial disease (E) Diabetes

(F) Others (specify) _____

2.7. Presumed etiology of CKD

A). Hypertension B) Diabetes C) Chronic glomerulonephritis D) HIV

E) Polycystic kidney disease F) Obstructive uropathy. G) Unknown

H) others (specify) -----

2.8. vital sign; Blood Pressure: SBP: _____ DBP: _____

Dry Weight(kg): ----- height(m)----- BMI(kg/m2)-----

3. Laboratory profile

3.1. hemoglobin----- 3.2. Albumin -----

3.3. CKD Mineral bone disease panel

	available	Not available
Corrected Calcium		
Phosphorus		
iPTH		
25-(OH) vitamin D		

3.4. **HIV serology:** A) reactive B) non-reactive C) unknown

4. Dialysis profile

A) Type of dialysis access -----B) dialysis vintage (months)

C) frequency of hemodialysis per week-----D) duration of hemodialysis session-----

Assurance of Investigator

I the undersigned resident agree to accept all responsibilities for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the Research and Publication Directorate and /or Department of Public Health of St. Paul's Hospital Millennium Medical College.

Name of the Resident: _____

Signature: _____

Date: _____

Approval of Advisors

Name of Public Health Advisor: _____

Signature: _____

Date: _____

Name of Clinical Advisor: _____

Signature: _____

Date: _____