SUBOPTIMAL VITAMIN D LEVELS IN CHILDREN WITH CHRONIC KIDNEY DISEASE AT KENYATTA NATIONAL HOSPITAL

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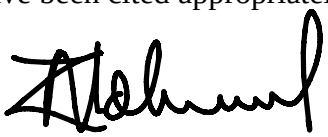
DECLARATION

This proposal is my original work, drafted under the guidance of my supervisors, and has not been presented for the award of a degree in any other university. References for work done by others have been cited appropriately.

Signature  Date 10-11-2021

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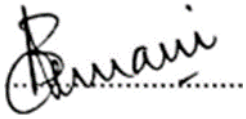

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OPERATIONAL DEFINITIONS

- **Pediatric age group**: Children aged 1-18 years as per WHO guidelines (1).
- **Pediatric CKD**: Chronic kidney disease diagnosis as found in the hospital records of study subjects which included either and/or
    1. Markers of renal damage, histological, or radiological diagnosis of CKD.
    2. Estimated glomerular filtration rate (eGFR) of <60 mL/ min/1.73 m^2 for at least 3 months.
- **Measured vitamin D was Calcidiol and categorized based on KDOQI guidelines.**
    1. Deficiency :5-15ng/ml.:
    2. Insufficiency: 16-30ng/ml.
    3. Adequate: 30ng/ml.
- **Stages of Chronic kidney disease as per KDIGO categories based on glomerular filtration rate.**
    1. Stage 2: 60- 89 (ml/min/1.73m2)- mildly decreased.
    2. Stage 3a: 45-59 9 (ml/min/1.73m2)- mild to moderately decrease.
    3. Stage 3b: 30-44 (ml/min/1.73m2)- moderately to severely decreased.
    4. Stage 4: 15-29 (ml/min/1.73m2)- severely decreased.
    5. Stage 5: < 15 (ml/min?1.73m2)- end stage disease

ABBREVIATIONS ACRONYMS

CKD-	Chronic Kidney Disease
CA $^{2+}$-	Calcium
CKD-MDB-	Chronic Kidney Disease-Mineral Bone Disease
FGF 23-	Fibroblast Growth Factor 23
GFR-	Glomerular Filtration Rate
HD-	Hemodialysis Dialysis
KDIGO-	Kidney Disease Improving Global Outcome.
KDOQI-	Kidney Disease Outcomes Quality Initiative
ND-	Non-Dialysis
PD-	Peritoneal Dialysis
PTH-	Parathyroid Hormone
SD-	Standard Deviation
VD-	Vitamin D
VITAMIN D2-	Ergocalciferol
VITAMIN D3-	Cholecalciferol
VDR-	Vitamin D Receptor
[25(OH) D]-	Calcidiol
1,25 (OH) D-	Cholecalciferol

ABSTRACT

Background: Pediatric chronic kidney disease remains a challenging and relatively understudied area of pediatric nephrology, which affects several children globally. Patients with chronic kidney disease are more susceptible to developing suboptimal vitamin D than the general population. . In children particularly, Vitamin D deficiency has been associated with hyperparathyroidism leading to defective bone mineralization. Currently, the prevalence of suboptimal vitamin D is unknown in Kenya.

Objectives: The primary objective was to determine the prevalence of suboptimal vitamin D in chronic kidney disease children. The secondary objective was to correlate the levels of vitamin D with the stage of CKD, Parathyroid hormone, Calcium, phosphate and to determine factors associated with vitamin D deficiency.

Methodology: A cross-sectional study design that recruited participants aged less than 18 years from KNH renal units with recorded CKD diagnoses in their hospital records. Data was collected using a structured interviewer-based questionnaire, physical examination was conducted and 4mls of blood was drawn for determination of vitamin D (calcidiol), parathyroid hormone, calcium, and phosphate.

Data Analysis: Data was entered into the Microsoft access database for coding and cleaning then exported to STATA 13.0. Categorical and continuous data were summarized as frequencies & their respective percentages as mean or median, respectively. Calcidiol was categorized as adequate, deficiency, and insufficiency which were reported as percentages with binomial exact 95% confidence intervals. Logistic regression with crudes odds ratio reported as measures of effect was used to determine the association between D levels with CKD stage, PTH, Ca2+, phosphate levels, and factors associated with vitamin D deficiency.

Results: Eighty patients with chronic kidney disease were recruited into the study. The majority were in Stage 3 (58%) and stage 4 (40%). Those with adequate and insufficient vitamin D levels were 36% and 54% respectively. The odds of having hypocalcemia with suboptimal vitamin D was 8 times more (CAR 8.87, P=0.01).

Conclusions: The study findings revealed a higher prevalence of 90% suboptimal vitamin D levels.

1.0 CHAPTER ONE: INTRODUCTION

1.1 Background

Extensive research done in the past decade has revealed numerous regulatory processes controlled in the body controlled by vitamin D. The significance of this statement, is underestimated by the epidemic of suboptimal vitamin D in the general population and disproportionately increased incidence in high-risk group patients such as Chronic kidney disease (2)

Emerging science has established the role of vitamin D to be beyond its principle classical function in maintaining calcium and phosphorous homeostasis (2). It plays an extensive role (non-classical) as a cell differentiate and antiproliferative factor with numerous functions in a variety of tissue notably renal, cardiovascular, and immune systems (2). This evidence, therefore, suggests that traditional supplementation of 1,25- vitamin D to CKD patients, assessing and repleting 25-(OH) vitamin D deficiency, physicians will adequately fuel both the renal and extra-renal pathways of calcitriol synthesis maintaining both the functions of vitamin D that ultimately influence clinical outcomes in this high-risk group of patients (2–4). KDIGO guidelines define CKD as abnormalities of function or structure of the kidney present for three months, with health implications(5). It further classified into three categories; that is based on the cause, GFR, and albuminuria(5). Refer to appendices 1 for table1,2,3, on the classification of CKD.

1.2 Physiology

The metabolism of vitamin D involves various steps (6). Please refer to appendices 2 for a summarized figure. Absorption of calcium in the intestines, bone resorption, and excretion of phosphate and calcium in the kidneys are regulated by the active form of vitamin D, Calcitriol(7). Calcitriol production is reduced in CKD as a result of altered renal function(8), leading to hypocalcemia and hyperphosphatemia(7). Both hypocalcemia and hypophosphatemia lead to PTH secretion with the resultant increase in tubular reabsorption of calcium, secretion of phosphate as well as calcitriol secretion (7). In normal individuals, PTH secretion is inhibited by the presence of a phosphaturic hormone (FGF-23). Production of calcitriol is limited by inhibition of 1-alpha hydroxylation by FGF-23.(7). Secondary hyperphosphatemia ensues, leading to bone disease, termed CKD-MBD(7).

1.3 Forms of Vitamin D

Calcitriol and calcidiol are the main forms of vitamin D.

Calcidiol is the main circulating form in the body. The mentioned reasons below make calcidiol a good marker of assessment of vitamin D status in the body(10–15);

- Mainly found in the circulation hence its assessment of its levels is easy (4,17,20–23)
- A long half-life of approximately 2-3weeks. (4,17,20–23)

1.4 Consequences of Vitamin D Deficiency in CKD

- **Progression of CKD** whose etiology is multifactorial including the NF-KB pathway that modulates genes involved in the immune response, inflammation, and fibrosis in the pathogenesis of CKD. Tissue injury therefore in CKD occurs through activation of this pathway through a cascade of events, yielding cytokines and other inflammatory mediators. Studies done, have shown that vitamin D inhibits the NF-KB pathway activation and therefore altering tissue injury and progression of the disease. (14,16,17).
- **Effect on the cardiovascular and renal system**- involves the Renin-angiotensin system, which activates angiotensin II which is responsible for vasodilation of the vasculature that ultimately leads to renal parenchymal damage(14,17,18). Studies done on animal models (mice) that do not have vitamin d receptors (VDR) have demonstrated high blood pressure, cardiac enlargement, and higher consumption of water as a result of increased production and expression of both renin and angiotensin. Upon supplementation with vitamin D analogs, there was the suppression of RAS activity along with concurrent stoppage of glomerular and tubulointerstitial damage with improvement in blood pressure(17,18). Both vitamin D deficiency and hyperglycemia appear to be activators of RAS. Research done in diabetics has demonstrated higher levels of intrarenal interstitial angiotensin II than in healthy individuals. The usage of vitamin D analogs therefore to prevent activation of RAS in experimental diabetic models has proven to be therapeutic. Treatment with active vitamin D has been shown to halt myocardial hypertrophy, preventing the development of heart failure and myocardial hypertrophy from experimental models ((4). Vascular calcification, atherosclerosis, and arterial stiffness are other effects of the deficiency(14,18,19).

- **Secondary hyperparathyroidism** leads to low bone mineral density (4,6,14,18,20).
- **Falls and fractures** from muscle weakness.

1.5 Etiology of vitamin D deficiency in Chronic Kidney Disease

- **Reduced food intake** resulting from decreased appetite, uremia-related GIT symptoms, and dietary restrictions such as phosphate (13–15,21).
- **Sunlight**- CKD patients, especially those on dialysis, are less likely to have reduced sunlight exposure and physical activity. Insufficient sunlight exposure was revealed by Del Valle *et al* in 80% of the patients with VDD (21). Ultraviolet rays are blunted by uremia deposition on the skin (13–15,21)
- **The proteinuric renal disease** leads to the loss of vitamin d binding protein (VDBP) and vitamin metabolites through urine. More than 85% of circulating calcidiol is carried by VDBP (7).

1.6 Causes of Vitamin D Deficiency Generally

- **Malabsorption** resulting from a variety of diseases causes decreased bioavailability of vitamin D by impairing absorption in the body (22).
- **Obesity -** leads to reduced availability of vitamin D by causing fat sequestration(22).
- **Medications** such as anticonvulsants, for example, is phenytoin, phenobarbitone, and antituberculosis cause increased catabolism by binding to the steroid receptors which in turn activates the destruction of calcidiol and calcitriol into inactive compounds (22).
- **Liver failure**-malabsorption of vitamin D occurs with minimal dysfunction however with severe (90%)dysfunction, the ability to make enough 25-hydroxyvitamin D is altered as the second hydroxylation step occurs here (22).
- **Skin pigment (melanin)** reduces the absorption of ultraviolet radiation thereby reducing vitamin D3 synthesis by approximately 99% (22).
- **Breast feeding** - due to poor vitamin D content in breast milk, the risk of vitamin D deficiency increases in an infant when it's the only source of nutrition. (22)

1.7 Current Guidelines On The Treatment of Vitamin D Deficiency /Insufficiency In CKD

The current recommendation by kidney diseases outcome quality initiative and kidney disease initiative global outcome involves measuring and replenishing low plasma 25(OH)-VD levels in(5,23,24). Measuring starts from CKD stage 2a-5 and is repeated according to the baseline value(25). Either ergocalciferol or cholecalciferol can be used for supplementation however, the optimal treatment is still unknown(23,25).

1.8 Evaluation of Vitamin D, PTH, Calcium and Phosphorous for Pediatric CKD-(KDIGO-KDOQI guidelines)

Table 1: Evaluation of Vitamin D, PTH, calcium, and Phosphorous for CKD

Parameter	Stage	Recommendations
Calcium, phosphate, ALP, PTH	2	Begin initial monitoring(26)
Calcium and phosphate	3a-3b	Six to twelve months(26)
	4	Three to six months(26)
	5-5D(HD/PD)	One to three months(26)
PTH	3a-3b	Based on CKD progression and baseline levels(26)
	4	Six to twelve months(26)
	5-5D	Three to six months(26)
Calcidiol	3a-5d	If PTH is within the range, do calcidiol at first encounter then annually(26)

2.0 CHAPTER TWO : LITERATURE REVIEW

2.1 Prevalence of Vitamin D Deficiency and Insufficiency in Pediatric CKD and Its Association With the Stage of the Disease, Parathyroid Hormone, Calcium, and Phosphate

An increased prevalence of suboptimal levels of vitamin D is seen in patients with chronic kidney disease than in the general population(14).

In retrospective research, Solarian et al in Cape town found the prevalence of vitamin D deficiency and insufficiency was at 43.5% and 30.4% respectively. In those with suboptimal levels, 58.8% had increased PTH levels. Additionally, the mean values of PTH also increased with the advanced CKD stage. (4)

Ki Wuk Lee et al retrospective research, carried out in Korea on children aged up to 18 years, vitamin D deficiency and insufficiency prevalence rate, was at 54.9% and 22.9% respectively. Furthermore, the deficiency was more prevalent in those with advanced stages of CKD. Those with deficiency and insufficiency were found to have increased PTH levels as compared to those with sufficient, but there was no significant difference. Parathyroid hormone levels were negatively correlated with serum vitamin D, (p=0.0386)(27).

He Yeon Cho *et al* in Korea's retrospective study on 59 children with CKD who were on dialysis found the prevalence to be at is 32.2% and 50.8% respectively. Besides, he found that these groups had higher PTH levels (p=0.001). He found no correlation between serum vitamin D levels and PTH (P=0.238), calcium (p=0.415), or phosphorous((28). He concluded that the prevalence was high and another study was needed to look at the consequences and impact of therapeutic interventions in those who were found to be deficient(28).

Zahra Mirzaei *et al* in 2016 at Mofied hospital Tehran, Iran did a comparative study for two years on 68 children. In CKD and healthy children, vitamin D deficiency was recorded as 69.1% and 42.5% while insufficiency was 20.6% and 38.4% respectively, and normal as 10.3% and 19.1% respectively. The prevalence was noted to increase as the CKD stage advanced in these patients. She also found a direct association between the CKD stage and serum levels of PTH. Those found to have deficiency had increased levels of PTH(16).

V Belostoky *et al* carried out a study on 143 pediatric CKD patients in 2008 at Manchester. He found, Vitamin D deficiency and insufficiency prevalence rate to be at 22% and 36% respectively. Advanced CKD and increased levels of PTH were seen with those with insufficiency levels than those with normal levels (90%vs 50%, p=0.013). Additionally, no

correlation was found between serum vitamin D, PTH, and calcium. No correlation between decreased levels of vitamin D deficiency (p=0.04) and insufficiency (p=0.001) was noted He recommended early measurements of vitamin d levels and supplementation(29).

Farah N Ali *et al* in the year 2010 carried out a study in Pediatric CKD patients in Chicago. He aimed to determine Vitamin D deficiency prevalence and the impact of KDOQI guidelines. Therefore, this study had two arms of participants. The first group (1074 patients) who were evaluated over 10 years (1987-1998) which was before the implementation of KDOQI guidelines, and the second group (88 patients) evaluated between 2005-2006 was a group that was being evaluated after the implementation of the guidelines. The first group had a higher prevalence of vitamin D deficiency of 20-75% while the second group was at 39%. Hyperparathyroidism was noted in those with deficiency. The recommendation was the implementation of KDOQI guidelines(6).

Paula et al in 2013-2015 did a comparative study in children aged 1-19 years. The prevalence of vitamin D deficiency among the healthy and CKD group was at 12.5% and 32% respectively. High parathyroid, high phosphate, and advanced CKD stage were noted in those with a deficiency(30).

2.2 Factors Associated With Vitamin D Deficiency in Chronic Kidney Disease.

2.2.1 Clinical Factors

2.2.1.1 Advanced Chronic Kidney Stage

There is a decreasing renal mass with advancing CKD stage with a resultant decline in the enzyme responsible for the synthesis of 1,25-dihydroxy(14).

Solarian *et al* found increased vitamin D deficiency among those with advanced CKD (stage 4-5D) at 65% as compared to those in moderate (stage 3) at 35%. Insufficiency levels were noted in the moderate stage(14).

The percentage of vitamin D deficiency percentage was found to be higher in advanced CKD (stage 3-5D) than those in moderate or early-stage i.e. (42% vs 26%; $p < 0.5$)by Seeherunveng *et al*(31).

Zahra *et al* found an inverse association of serum vitamin D levels with the stage and severity of disease ($p<0.001$)(16).

2.2.1.2 Dialysis

Hee Yeon Cho *et al* study on 59 children with CKD on chronic dialysis revealed that 32.2% and 50.8% of the patients had vitamin D deficiency and insufficiency, respectively. Patients on peritoneal dialysis were found to have a lower mean serum vitamin D concentration as compared to those on hemodialysis. (28).

Warady *et al* study on 51 CKD patients on hemodialysis or peritoneal dialysis, found 40 (78.4%) patients with reduced serum vitamin D concentrations. Of these 40 patients, 2% had severe vitamin D deficiency, 41.2% mild deficiency, and 35.3% insufficiency(32).

A retrospective cross-sectional study by Seeherunvong *et al* recruited 258 pediatric patients with CKD. Twenty-six were on maintenance dialysis (5 peritoneal,21 hemodialyses). He found that 60 % has suboptimal vitamin D levels (32% insufficiency, 28% deficiency). Additionally. patients receiving maintenance dialysis, serum vitamin D levels were similar in those on peritoneal and hemodialysis (38±15 vs 28±15ng/ml ; p, NS)(31).

Solarian *et al* study in South Africa on 46 children with CKD stage 3-5, observed low levels of vitamin D in patients on peritoneal dialysis. Out of the 10 patients on PD, 8(80%), 2(20%) had vitamin D deficiency and insufficiency respectively. T(14).

An observational study carried out on 152 adult CKD patients(108 HD) by Gonzalez et al, demonstrated a 97% prevalence of suboptimal vitamin D in the HD group (80% deficiency and 17% insufficiency)(33).

2.2.2 Demographic Factors

2.2.2.1 Age And Sex.

Warady *et al* in a single-center study of 51 CKD patients observed that older children (> 12 years) had low serum vitamin D levels. Vitamin D deficiency was found in 91.2% (31/34) patients >12 years vs 52.9% (9/17) in <12 years old ($p<0.006$). Furthermore, no relationship was detected between gender and low serum vitamin D levels(32).

In yet another cross-sectional study done by Holmund *et al* on 1351 children with CKD, serum vitamin D mean levels differed significantly in different age groups (Kruskal Wallis; $p<0.01$). High and low serum concentrations were seen in infants and adolescents, respectively(11).

Seeherunveng et al, observed that gender did not affect vitamin D serum levels. However, the deficiency was higher in older children ($p< 0.01$)(31).

2.2.2.2 Skin Color

Holick *et al* described that absorption of ultraviolet radiation is interfered upon by melanin responsible for skin pigment. This causes a reduction of vitamin D3 synthesis from the skin by approximately 99%(22).

Solarian *et al* in South Africa, Cape Town, found that race had an impact on serum vitamin D levels. Suboptimal levels were high in 12(80%) black patients and 19(73.1%) mixed races(14). Contrary to this, Raga *et al* cross-sectional study on vitamin D levels, Johannesburg, observed a lower trend of serum vitamin D levels in blacks as compared to other races(34).

2.3 Summary of Studies

Table 2: Summary of Studies

Study Title and Author	Study Design and population	Conclusion
Vitamin D status of children with moderate to severe chronic kidney disease at a tertiary pediatric center in cape town(14)**.** Adaobi Uzoamaka Solarin, Peter Nourse, Priya Gajjarf (2014)	A retrospective cohort study. 46 children with moderate to severe CKD.	Prevalence of suboptimal [25(OH)D levels were (43.5% and 30.4% had vitamin d deficiency and insufficiency, respectively. The majority with suboptimal levels had a high serum PTH (58.8%).
Vitamin D Deficiency in Children with Chronic Kidney Disease: Uncovering an Epidemic(6)**.** Farah N. Ali, Lester M. Arguelles, Craig B. Langman (1987-1996, 2005-2006)	A single observational prospective study. Two groups of patients followed up before and after the publication of KDIQO guidelines. 1074 CKD children followed for a decade and a contemporary group of 88 for a year,	Both groups had extensive suboptimal [25(OH)D levels. Group followed up over a decade (20% and 75% for deficiency and insufficiency respectively). Contemporary group (39% and 72% deficiency and insufficiently respectively).
Vitamin D deficiency in children with renal disease(29)**.** V Belostotsky, M.Z Mughal, J.L Berry (2008)	Cross-sectional study. 143 children aged 1-18 years.	The prevalence of vitamin d deficiency [25(OH)D] was at 22% while that of insufficiency was 36%.
Optimal Vitamin D levels in Children with Chronic Kidney Disease(27)**.** Ki Wuk Lee, Sang Taek Lee and Heeyeon Cho De (2012)	Retrospective study. 113 children aged 1-18 years.	Prevalence of [25(OH)D] deficiency and insufficiency were 54.9% and 22.9% respectively. PTH was noted to be high in this group but with not much statistical difference (p= 0.218).
Vitamin D deficiency in children with chronic kidney disease(16)**.** Nasrin Esfandiar, Marjan Shakiba, Zahra Mirzaei (2016)	Comparative study. 68 children with CKD 73 healthy children	Vitamin d deficiency was recorded as 69.1% and 42.5% while insufficiency was 20.6% and 38.4% respectively in CKD and healthy children.
Prevalence of [25(OH)D] deficiency/insufficiency in pediatric patients on chronic dialysis(28)**.** Hee Yeon Cho, Hye Sun Hyun, Hee Gyung Kang, *et al*, (2011).	Cross-sectional study Pediatric patients with CKD on dialysis	Prevalence of vitamin d deficiency and insufficiency (32.2%,50.8% respectively) with higher PTH levels (p=0.001) but no correlation with calcium or phosphate.

2.4 Study Justification and Objectives

2.4.1 Study Justification and Utility

Children suffering from chronic kidney disease are at increased risk from vitamin D deficiency and insufficiency compared to their healthy counterparts. The classical core function of vitamin D is the maintenance of calcium and phosphorus homeostasis. Vitamin D deficiency alters levels of Parathyroid hormone which leads to defective bone mineralization that eventually interferes with somatic growth of children and risk of fractures(14). Furthermore, suboptimal vitamin D levels have been associated with the progression, morbidity, and mortality of chronic kidney disease. (14,18,35).

There is a paucity of research in determining what the prevalence of suboptimal vitamin D levels is in patients with CKD in East Africa and its factors. Filling this knowledge gap would serve as benchmark statistics of the magnitude of this problem.

This information will aid in identifying the high-risk population for suboptimal vitamin D levels and managing appropriately. Additionally, this will be a great step forward for further studies looking at vitamin D and CKD in East Africa.

Kenyatta National hospital is an appropriate site for the study because it is a regional referral hospital, and it receives a significant percentage of children with CKD in the region for specialized treatment.

2.5 Research Question

What is the prevalence of suboptimal vitamin D levels (deficiency/insufficiency) in children with chronic kidney disease as seen at Kenyatta National Hospital?

2.6 Primary Objectives

To determine the prevalence of suboptimal vitamin D (deficiency/insufficiency) in children with kidney disease as seen at Kenyatta National Hospital.

2.7 Secondary Objectives

To determine the association between vitamin D levels with the stage of CKD, Parathyroid and biochemical parameters (calcium, and phosphate) in children with chronic kidney disease. To determine factors associated with vitamin D deficiency in children with chronic kidney disease.

3.0 CHAPTER THREE : METHODOLOGY

3.1 Study Design

Analytical cross-sectional study.

3.2 Study Site

The settings of the study were both adult and pediatric renal units at Kenyatta National Hospital (KNH), the largest and oldest public main referral hospital for East and Central Africa. At KNH, nephrology services are provided at the outpatient renal clinics, inpatient general wards, dialysis units, and specialized pediatric renal wards. These units are headed and run by consultant nephrologists with assistance from adult and pediatric nephrology fellows and senior House Officers. In addition, there are nurses with diverse experience and qualifications in nephrology.

The outpatient renal clinic (both adult and pediatric) runs every Friday from 8.00 am to 12.30 pm. Attendance to the clinic is by appointment. The adult and pediatrics sections run side by side. The clinic is located at unit no 24 in the outpatient department of KNH. On average, 9 pediatric patients aged 0-18 years of age are attended to at each clinic. These patients have a variety of renal diseases ranging from acute illnesses to chronic kidney diseases.

The KNH dialysis unit was also another study site. The dialysis unit runs every day and provides both in and outpatient hemodialysis services to both adult and pediatric patients with CKD.

The inpatient wards were another set of study sites in this study. In practice, pediatric patients with CKD are admitted for inpatient care in any of the admitting pediatric general wards. While in the general wards, these patients have access to care from the hospital's nephrologists and the dialysis unit.

At KNH, patients under the age of 13 years are considered pediatric and they are admitted in any of the pediatric general wards (namely 3A, 3B,3C & 3D). They may also be admitted to the specialized pediatric renal ward, located on the hospital's 2^{nd} floor, depending on the availability of bed space. This unit provides peritoneal dialysis services to pediatric patients. Chronic kidney disease patients between ages 13 & 18 years of age are usually admitted to the adult ward on the hospital's 7^{th} & 8^{th} floors.

3.3 Study Population

The study population was pediatric patients aged 1-18 years at KNH with a recorded diagnosis of CKD in their hospital records and on follow-up at the KNH renal unit. The inclusion of children aged above 13 years in this study was based on WHO definitions of children as persons below the age of 19 years(1). Thus, in this study, the subjects were drawn from both adult and pediatric units that provide care to CKD patients up to the age of 18 years.

3.3.1 Inclusion Criteria

- Pediatric patients whose guardians/parents gave consent to participate.
- Pediatric patients are known to have CKD and are on follow-up at the KNH renal for at least 3 months.

3.3.2 Exclusion Criteria

- Pediatric patient with known liver disease, malabsorption syndrome, malignancy (as was diagnosed and documented by the clinician in the file)
- A pediatric patient who had undergone parathyroidectomy.
- Pediatrics patients on these medications; isoniazid, rifampicin, theophylline, phenobarbitone, phenytoin.

3.4. Case Definitions

A) Suboptimal Vitamin D Level.

- Was defined as vitamin D Deficiency and Insufficiency.

B) Vitamin D[25(OH)D]

- Vitamin D deficiency defined: 5-15ng/ml (36).
- Insufficiency:16-30 ng/ml(36).
- Adequate: above 30 ng/ml (36).

3.5 Sample Size Calculation

Fisher's formula with a population correction factor will be used to calculate the sample size. An estimated target population of 90 was used for the calculation based on the estimate of 30 to 34 patients seen every month based on statistics from the hospital medical records.

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

- ✓ N = estimated target population= 90
- ✓ P= estimated prevalence of outcome of interest= 74% (0.74% (Solarin et al 2014)
- ✓ Z= level of confidence (1.96 for 95%)
- ✓ d= desired level of precision (0.05)
- ✓ n= 69 participants

For the sample size calculation, the estimated prevalence of suboptimal vitamin D levels shall be set at 74% based on the study by Solarin et *al*, 2014 (43.5% and 30.4% had vitamin D deficiency and insufficiency respectively). From the above calculations, the sample size for the study was 69 participants. To allow for a 10% non-response rate, the sample size was estimated at 80 participants.

3.6 Study Period

The study was carried out over four months (November- December 2020 and January – February 2021).

3.7 Study Outcomes

The prevalence of patients with suboptimal vitamin D in children with chronic kidney diseases at Kenyatta National Hospital. Associations of vitamin D levels with the stage of diseases, parathyroid hormone, and biochemical parameters which included calcium and phosphate. Factors associated with vitamin D deficiency in children with chronic kidney disease.

3.8 Sampling Procedure

3.8.1 Sampling Method

All patients who gave assent (for above 6 years)/ consent (for above 6 years) were recruited through continuous sampling until the desired sample size was achieved.

3.8.2 Study Procedure

The research assistant was recruited to assist in data collection and entry. He was an individual who was a registered clinical officer and was working/studying within the hospital and therefore he was familiar with the day-to-day running of the hospital. The principal investigator took him through a training session that covered topics on the study's aim, study participant recruitment, who measurement techniques, questionnaire administration, standard precautions, and techniques of blood sampling to ensure patient safety during sample collection. He was stationed at the renal unit but would help the principal investigator recruit the patients from other areas mentioned on a day-to-day basis with exception of weekends and nights as the university laboratory was nonoperational during these times.

The estimated glomerular filtration rate used to stage the chronic kidney disease was based on when the diagnosis of disease was initially made as recorded in the patient's file. For the new patients and those whose gfr was not indicated, we calculated it using the schwartz formula to assess it and stage the disease.

3.8.3 Clinical Methods

The principal investigator/ research assistant administered the questionnaire that was used to collect data from the patients. The questionnaire captured details on age, gender, date of diagnosis, residence, whether on hemodialysis or peritoneal dialysis was recorded, as well as the number of sessions per week. Other information on the etiology of chronic kidney disease, use of vitamin d supplements, any other medication was recorded. A detailed general examination was carried out. Vital signs (heart rate, blood pressure, respiratory rate, temperature) and anthropometric measurements (weight, height, muac) were taken.

Blood pressure was measured using an electronic bp machine with an appropriate cuff size. Classification into hypertension or normal was done using blood pressure by gender, age, and height percentile. Measurement of height and weight was done using a calibrated stadiometer and a stand weight scale in kilograms respectively. The basal metabolic index was then calculated in kilograms per meter squared. The recorded anthropometric measurements were then plotted in the respective who anthropometric charts to determine nutritional status in terms of waz, haz, whz for age. Lastly, 4 mls of blood was taken for the measurement of calcidiol, pth, calcium, and phosphate.

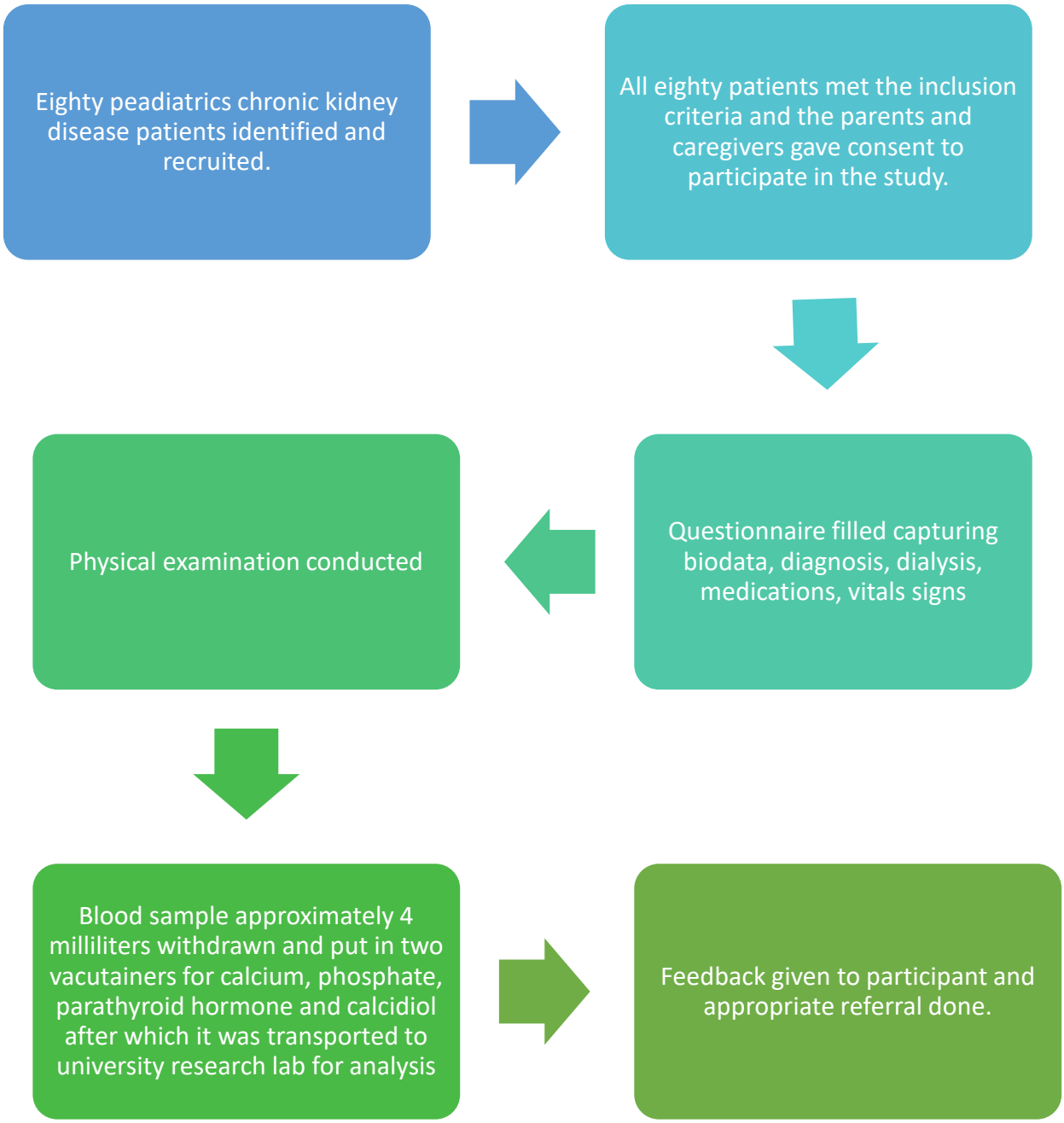

Figure 1: Flow diagram of participant recruitment into the study.

3.8.4 Laboratory Methods

3.8.4.1 Sample Collection and Processing

Once the participant was recruited, blood samples for serum vitamin d levels, parathyroid hormone, calcium, and phosphate were collected. The principal investigator drew blood using an aseptic technique from the antecubital vein of the participants. Safety and hygiene were always maintained. Four mls of blood were collected and put in two tubes with ethylenediaminetetraacetic acid (edta, purple top) for pth and vitamin d, and one plain tube (red tube) for calcium and phosphate in aliquots of 2ml that was already labeled with a study number.

The samples were then safely transported in a cool box to the department of pediatrics, university of nairobi research laboratory within 1-2 hours.The sample collected was centrifuged for 2 minutes at 3000 revolutions per minute (rpm) to extract serum which was stored at negative 20 degrees celsius and batched.

3.8.4.2 Sample Analysis

Both calcium and phosphate levels were assayed using the photometric method with humastar 600 machine and were reported in mmol/l. The principle used for phosphate is that it reacts with molybdate in a strongly acidic medium to form a complex. The absorbance of this complex in the near-ultraviolet (uv) is directly proportional to the phosphate concentration. Calcium ions react with o-cresolphthalein - complexone in an alkaline medium to form a purple-colored complex of which its absorbance is proportional to the calcium concentration in the sample.

Serum vitamin d was determined by liason ® 25-oh vitamin d assay technique, which adopts a “flash” chemiluminescence technology (clia) with a pragmatic microparticle solid phase (mp). This method is rapid, accurate, and precise. It is also validated according to the national committee for clinical laboratory standards (nccls) protocols(37). Additionally, it is comparable to the gold standard liquid chromatography isotope dilution tandem mass spectrometry (lc-idm/ms)(38) and well correlated with the radioimmunoassay technique(39). The measuring range is between 4.0 and 150ng/ml with the lowest reportable value as 4.0ng/ml which is based on an inter-assay precision that approximates 20% cv (functional sensitivity).

Serum pth was determined by the liaison® in-tact® pth gen ii assay that is intended for the quantitative determination of intact human pth. It is a modified 2-step, 2 sites sandwich assay that uses 2 polyclonal antibodies for capture and detection of intact pth. The measuring range is between 3.0 and 1900pg/ml, with the lowest value reported as < 3.0pg/ml. Normal reference ranges for pth will be between 35-70pg/ml and any value above 70ng/ml will be considered high.

3.9 Quality Assurance.

3.9.1 Pre-Analytical Errors

- Samples were collected according to the laid down standard operating procedure in the proper vacutainers and transported in a cool box.
- monitoring reagents and refrigerator temperatures were done twice daily during the week.

3.9.2 Analytical Errors

- The manufactures laid down standard operating procedures that were used to run all the tests.
- The different tests were interpreted based on the manufacturer's insert.
- Controls were run when a new bottle of reagent is used.
- If control was out of its specified range, the associated test results were considered invalid, and samples retested.

3.10 Measures That Were Undertaken to Minimize the Risk of Covid-19 Transmission

The following infection prevention control measures were taken per the kenyan ministry of health / who guidelines and protocols.

- Alcohol-based sanitizers and hand washing were used before and after contact with the participants.
- Disposable gloves were used as an additional measure to the above, before contact with the participants and hands cleaned. It was disposed of as per health care waste disposal guidelines.
- Scrubs or dust coats were worn when in contact with participants.
- Surgical masks were always worn. N95 masks were used in participants suspected to have respiratory illnesses.

- Goggles were worn for eye protection when collecting blood samples.
- there was minimal time with participants (not more than 15 minutes) to avoid the risk of being exposed.
- Disinfection of commonly shared clinical equipment (tape-measure, stethoscopes, thermometers) before and after use on each of the participants.
- All participants had their temperatures taken using a non – contact thermometer. Those who were found to have fevers (38 degrees celsius and above) were asked for additional history including that of cough, difficulty in breathing, and exposure. Those with suspected symptoms were directed for covid -19 screening at knh.
- Alcohol-based sanitizers/hand washing was availed to the participants to be used before and after encountering them.
- Participants above 5 years old with their guardians were advised to put on a 3-ply surgical face mask provided by the principal investigator during the face-to-face interactions.
- Participants were advised to maintain social distancing at least 1.5 meters in the clinic.

3.11 Ethical Considerations

The proposal and all data collection tools were submitted to KNH/UON Ethics and Review Committee for evaluation. The study commenced only after formal authorization from the committee and the KNH administration. Belmont principles were used to ensure justice to participants and respect for their autonomy(40).

Autonomy- Study participants were explained fully the risks and benefits involved in the study in addition to the study procedures. They were then be asked to voluntarily choose whether to participate. Those who agreed were given an informed consent/assent form to sign. It was free of coercion.

Confidentiality of gathered information- Personal identifiers such as names of children or parents were not captured on data collection tools. Instead, serial study numbers were used to identify study participants. Beneficence- Insight into suboptimal vitamin D levels in this high-risk population provided information on timely intervention and management improving their overall outcome. Additionally, patients were assured of continued care whether they participated in the study.

Justice- Each participant had a fair chance of selection into the study. It was free of coercion. Patients were also be informed that they were not incurring any cost because of participating in the study. Non-maleficence- Caution was taken not to cause physical or psychological harm to subjects during the study.

3.12 Data Storage and Security

Each questionnaire was checked to ensure that there were no personal identifiers to maintain the confidentiality of the patients. Any personal identifier found was discarded. The principal investigator was responsible for the storage of all questionnaires and was only accessible to the principal investigator and research assistants. These measures ensured that patient confidentiality is always maintained.

3.13 Data Management and Analysis

The collected study data were entered into a customized password-protected MS Access database. After completion of data entry, the data was exported to R statistical software for cleaning, verification, and analysis.

3.14 Study Characteristics

The first step in the data analysis involved describing the study's participants' characteristics. This included demographic, clinical, biochemical, and anthropometric measurements. Categorical demographic and biochemical variables were summarized as frequencies and their respective percentages. Continuous anthropometric and biochemical variables were presented as mean (standard deviation) or median (interquartile range) depending on their distribution.

Vitamin D deficiency, insufficiency, and adequate were reported as percentages with binomial exact 95% confidence intervals. Medians (IQR) were reported for each category too. Vitamin D deficiency and insufficiency were collapsed into one category and referred to us as Suboptimal levels.

Height for age z-score (HAZ) and Basal metabolic index (BMI) was calculated using WHO 2006 references for children < 60 months old and WHO 2007 for those ≥ 60 months. BMI z - the score was classified as; not wasted (BMI z-score ≥-2) and wasted (BMI z-score < -2). HAZ was categorized into two groups; not stunted (HAZ ≥-2) and stunted (HAZ <-2).

3.15 Association Between Vitamin D Levels With CKD Stage, PTH, Ca2+, and Phosphate

To determine the above, **a** logistic regression analysis was conducted. Vitamin D levels were classified into a binary variable: adequate and suboptimal (insufficient or deficiency) levels and was the dependent variable in the regression analysis. Parathyroid hormone, calcium, and phosphate variables were categorized into three levels: normal, hyper (above normal levels), and hypo (below normal) using specificized cut-offs. Univariate analysis was conducted with each independent variable separately and crudes odds ratio (CRO) was reported as a measure of effect with 95% CIs. For the multivariable logistic regression models, all univariable models were adjusted by *prior* confounders (age, sex, etiology of CKD).

3.16 Factors associated with Vitamin D Deficiency

To determine the above, logistic regression analysis was used. The dependent variable was the binary Suboptimal vitamin D as defined previously. Univariate analysis was conducted with each independent variable separately and crudes odds ratio (COR) was reported as measures of effect with their 95%CIs. For the multivariable logistic regression models, all univariate models were adjusted by prior confounders (age, sex, etiology of CKD). Statistical significance was evaluated using a 95% confidence interval and a two-tailed p-value <0.05. Statistical analyses were conducted using STATA version 15.1 (College Station, TX, USA).

3.17 Dissemination of Study Findings

The study findings were presented to the UON Department of Paediatrics and Child Health as part of the MMED program in both hard and soft copies. Hard copies will be sent to the UON repository for storage. The findings shall also be shared with the office of the head of department pediatrics in KNH with the view of dissemination of the new knowledge that has been generated to improve patient care. The findings shall also be submitted for publication in peer-reviewed scientific journals.

4.0 CHAPTER FOUR: RESULTS

4.1 Participant's Characteristics

The study recruited 80 chronic kidney disease patients, with age in median (IQR) 132 (91 to 168) months old. Half (n=40, 50%) were male. Approximately one-third (n=26, 33%) of the household head, had tertiary education, while 34 (42%) and 20 (25%) had secondary and primary/no education, respectively. Forty-three (54%) were employed. The household average monthly income for majority (n=33, 41%) of the participants was KSHS 10000 to 50000, while 18 (23%) and 12 (15%) was KSHS <5000 and >50,000, respectively.

The most frequent CKD etiology was nephrotic nephritic disorder (n=23, 29%), Lupus nephritis 16 (20%), posterior urethral valve 10 (13%), diabetic nephropathy 8 (10%), HIV nephropathy 8 (10%) and polycystic kidney disease 8 (10%). Seven (8.8%) children had other CKD etiology, which were: 2 with unknown etiology, 2with hypertension, 1 with obstructive uropathy, 1 with bilateral pelvic- ureteric junction obstruction, and 1 with left renal calculi.

Majority (n=46, 58%) had CKD stage 3 disease, while 1 (1.3%), 32 (40%) and 1 (1.3%) had CKD stage 2, 4 and 5, respectively. The median (IQR) follow-up for the CKD patients was 3 (2 to 5) months. A total of 33 (41%) had ever been on dialysis. All 33 CKD patients were on hemodialysis.

The mean (Sd) body temperature at admission was 36.9 ±1.1 0C, BMI z-score and height-for-age z-score were -0.11 ±0.6 and -0.56 ±1.0, respectively. All children had normal BMI (BMI z-score ≥-2). Only 3 (3.8%) children were stunted (HAZ- score ≤ -2). The median (IQR) heart rate and respiratory rates were 88 (79 to 101) and 22 (20 to 26) respectively. No child had uremic frost, widening of wrists, bowlegs, or worn-out enamel. Twenty-one (26%) had edema.

The most frequent treatment for Vitamin D deficiency was calcitriol (n=20, 25%). Twenty (25%) CKD patients were treated with vitamin D supplements and 8 (10%) with calcium supplements. In total, 53 (66%) CKD patients were not on any Vitamin D deficiency treatment while, 8 (10%), 17 (21%), and 2 (2.5%) were on one, two, and three medications respectively (Table 3).

Table 3: Participant characteristics (N =80).

Table 3: Participant's characteristics(N=80)		
	Frequency	**Percentage (%)**
Sex		
Male	40	50
Female	40	50
Age in months: median (IQR)	132 (91–168)	
Household head education level		
None/Primary level	20	25
Secondary	34	42
Tertiary	26	33
Household head occupation		
Unemployed	6	7.5
Casual employment	31	39
Employed	43	54
Average household monthly income (KSH)		
<5000	18	23
5000 to 10000	17	21
10000 to 50000	33	41
>50000	12	15
Clinical signs		
CKD etiology		
Nephrotic nephritic disorder	23	29
Lupus nephritis	16	20
Posterior urethra valve	10	13
Diabetic nephropathy	8	10
HIV nephropathy	8 (10)	10
Polycystic kidney disease	8 (10)	10
Others*	7 (8.8)	8.8
CKD stage		
Stage 2	1	1.3
Stage 3	46	58
Stage 4	32	32
Stage 5	1	1.3
Patients on dialysis (Hemodialysis)	32	40
Patients ever on dialysis	33	41
Patients not on dialysis	15	18
Signs		
Oedema	21	26
Systolic Bp		115(108-120)
Diastolic Bp		74(71-78)
Treatment offered for vitamin D deficiency		
Calcitriol	20	25
Vitamin D supplement	20	25
Calcium supplement	8	10
No medication	32	40
Anthropometry		
BMI z-score, mean ±Sd		-0.11±0.6
Height for age z score, mean ±Sd		
Not stunted (HAZ≥-2)	77	96
Moderate stunted (-3to-2)	0	0
Severe stunted (HAZ<-3)	3	3.8
* Others: 2 hypertension, 1 obstructive uropathy, 1 bilateral pelvic ureteric junction obstruction, 1 bilateral renal calculi, 2 unknown etiology		

Table 4: Participant's characteristics categorized according to Vitamin D levels

	Vitamin D deficiency (N=43)	Insufficiency vitamin D (N=29)	Adequate vitamin D (N=8)	All participants (N=80)
Social demographics				
Sex				
Male	23 (53)	12 (41)	5 (63)	40 (50)
Female	20 (47)	17 (59)	3 (37)	40 (50)
Age in months: median (IQR)	120 (86–144)	144 (86–144)	186 (90–210)	132 (91–168)
Household head education level				
None/Primary level	12 (13)	7 (24)	1 (13)	20 (25)
Secondary	19 (44)	13 (45)	2 (25)	34 (42)
Tertiary	12 (28)	9 (31)	5 (63)	26 (33)
Household head occupation				
Unemployed	3 (7.0)	3 (10)	0	6 (7.5)
Casual employment	21 (49)	9 (31)	1 (13)	31 (39)
Employed	19 (44)	17 (59)	7 (87)	43 (54)
Average household monthly income (Ksh)				
<5000	12 (28)	5 (17)	1 (13)	18 (23)
5000 to 10000	9 (21)	7 (24)	1 (13)	17 (21)
10000 to 50000	18 (42)	14 (48)	1 (13)	33 (41)
>50000	4 (9.3)	3 (10)	5 (61)	12 (15)
Clinical signs				
Skin color				
Dark	32 (74)	22 (76)	5 (63)	59 (74)
Light	11 (26)	7 (24)	3 (37)	21 (26)
CKD etiology				
Nephrotic nephritic disorder	18 (42)	5 (17)	0	23 (29)
Lupus nephritis	8 (19)	6 (21)	2 (25)	16 (20)
Posterior urethra valve	5 (12)	3 (10)	2 (25)	10 (13)
Diabetic nephropathy	3 (7.0)	3 (10)	2 (25)	8 (10)
HIV nephropathy	3 (7.0)	4 (14)	1 (13)	8 (10)
Polycystic kidney disease	3 (7.0)	5 (17)	0	8 (10)
Others*	3 (7.0)	3 (10)	1 (13)	7 (8.8)

Table 5:Participant's characteristics categorized according to Vitamin D levels.

	Vitamin D deficiency (N=43)	**Insufficiency vitamin D (N=29)**	**Adequate vitamin D (N=8)**	**All participants (N=80)**
CKD stage				
Stage 2	0	1 (3.5)	0	1 (1.3)
Stage 3	17 (40)	22 (76)	7 (88)	46 (58)
Stage 4	25 (58)	6 (21)	1 (13)	32 (40)
Stage 5	1 (2.3)	0	0	1 (1.3)
Duration of diagnosis/follow-up: median (IQR) months	2 (2–4)	3 (2–5)	5 (3.5–9.5)	3 (2–5)
Patient currently on dialysis	19 (44)	10 (34)	3 (38)	32 (40)
Patient had ever been on dialysis	20 (47)	10 (34)	3 (38)	33 (41)
Signs				
Edema	13 (30)	7 (24)	1 (13)	21 (26)
Temperature ^{0}C	36.9 ±1.1	36.8 ±1.1	36.4 ±0.8	36.9 ±1.1
Heart rate$^{\$}$	94 (82–102)	87 (78–104)	83 (75–88)	88 (79–101)
Respiratory rate$^{\$}$	24 (20–28)	21 (20–26)	21.5 (19.5–24)	22 (20–26)
Systolic blood pressure (mmHg)$^{\$}$	114 (108–119)	117 (107–120)	120 (107–120)	115 (108–120)
Diastolic blood pressure (mmHg)$^{\$}$	73 (71–75)	75 (70–84)	78 (73–80)	74 (71–78)
Anthropometry				
BMI z-score, mean ±Sd$^{\#}$	-0.06 ±0.6	-0.27 ±0.5	0.20 ±1.1	-0.11 ±0.6
Height-for-age z-score, mean ±Sd	-0.42 ±0.7	-0.51 ±1.0	-1.48 ±1.6	-0.56 ±1.0
Not stunted (HAZ ≥-2)	43 (100)	28 (97)	6 (75)	77 (96)
Moderate stunted (-3 to -2)	0	0	0	0
Severe stunted (HAZ <-3)	0	1 (3.5)	2 (25)	3 (3.8)
Treatment offered for Vit D deficiency				
Calcitriol	11 (26)	7 (24)	2 (25)	20 (25)
Vitamin D supplement	13 (30)	5 (17)	2 (25)	20 (25)
Calcium supplement	6 (14)	2 (6.9)	0	8 (10)
Total medication provided for Vit D				
No medication	26 (60)	21 (72)	6 (75)	53 (66)
One	5 (12)	3 (10)	0	8 (10)
Two	11 (26)	4 (14)	2 (25)	17 (21)
Three	1 (2.3)	1 (3.5)	0	2 (2.5)

$results reported are median (IQR), all other reported results are N (%) unless were specified, *2 unknown etiology, 2 hypertension, 1 obstructive uropathy, 1 bilateral pelvic-ureteric junction obstruction, and 1 bilateral renal calculi, #All children had BMI z-scores ≥-2.

4.2 Prevalence of Vitamin D Deficiency /Insufficiency

The median (IQR) vitamin D of the 80 CKD patients was 14.6 (11.3–19.9) ng/ml. Only 8 (10%, 95%CI 4.4 to 19) CKD patients had adequate vitamin D levels with a median (IQR) of 33.1 (22.8–35.3) ng/ml. Twenty-nine (36%, 95%CI 26 to 48) had insufficient vitamin D with a median (IQR) of 19.9 (17.5–21.9) ng/ml, while 43 (54%, 95%CI 42 to 65) had deficient Vitamin D with a median (IQR) 11.8 (8.3–14.1) ng/ml as shown in figure 2 and 3. In figure 2, the Y-axis corresponds to vitamin D with 95%Cls as depicted by the red line while the bar graph depicts the levels.

Table 6: Proportion of CKD patients with suboptimal vitamin D levels.

Vitamin D levels	**N=80**	**Percentage (%)**	**95%CI**	**Vitamin D (calcidiol)ng/ml; median (IQR)**
Adequate	8	10	(4.4 to 19)	33.1 (22.8–35.3)
Insufficient	29	36	(26 to 48)	19.9 (17.5–21.9)
Deficiency	43	54	(42 to 65)	11.8 (8.3–14.1)
Suboptimal	72	90	(81 to 96)	14.1 (11.3–18.9)
Overall	80			14.6 (11.3–19.9)

The proportion of Vit D deficiency is reported as a percentage and their 95% confidence intervals, Vitamin D levels are reported as median (IQR) ng/mI, suboptimal are children with both Vitamin D deficiency and insufficient.

A total of 72 (90%) CKD patients had suboptimal vitamin D levels with median (IQR) 14.1 (95%CI 11.3–18.9) ng/mI (
Figure 3).

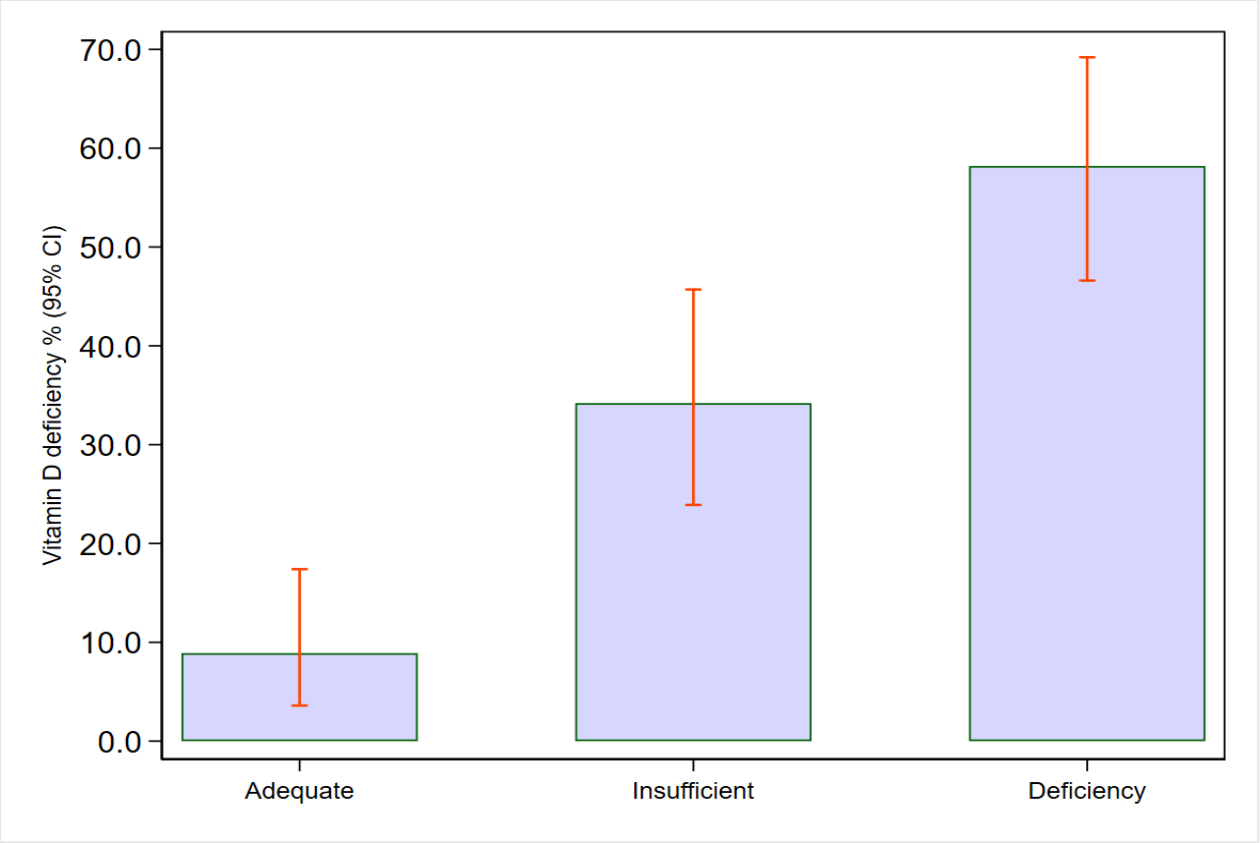

Figure 2: A bar graph illustrating the levels of vitamin D with IQR and CI

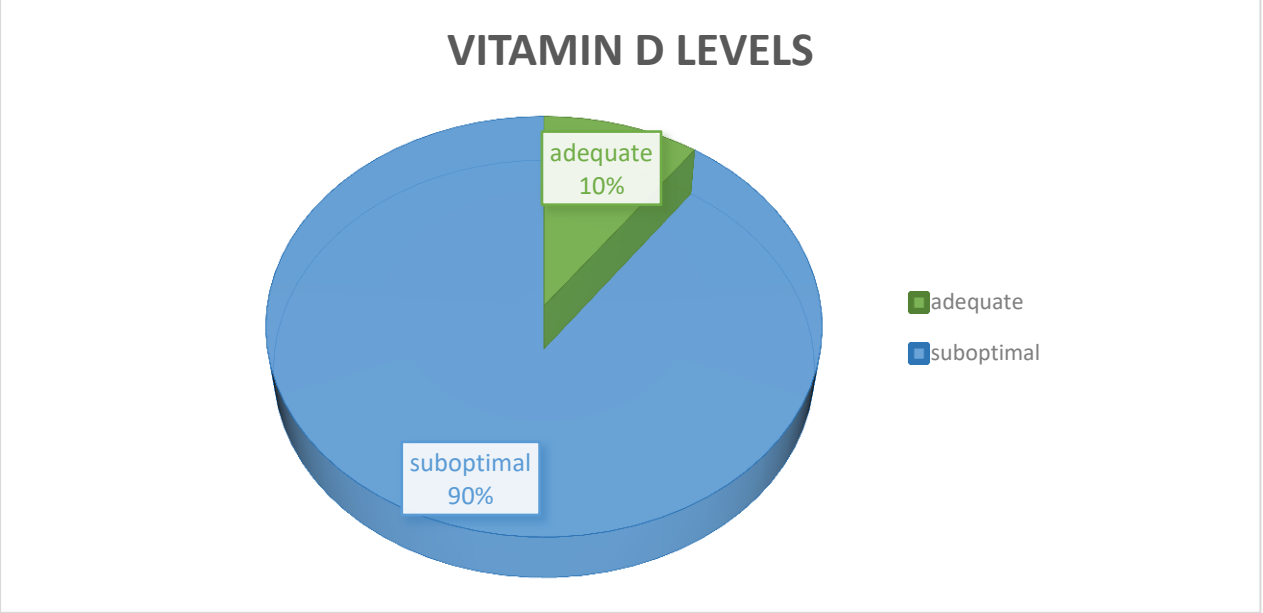

Figure 3: A pie chart of proportions of CKD patients with adequate and suboptimal (include insufficiency and deficiency) Vitamin D levels.

4.3 To Determine The Association Between Vitamin D Levels With The Stage Of CKD, PTH, Calcium, And Phosphate In Pediatric CKD Patients Aged Up To 18 Years As Seen At KNH.

In the univariate analysis, hypocalcemia (COR 8.37 (95%CI 1.55–45.1), p= 0.01)) was positively associated with odds of having suboptimal Vitamin D compared to those with normal levels of Calcium. In the multivariable analysis, the odds of having hypocalcemia (COR 8.33 (95%CI 1.11–62.4), p= 0.04) with suboptimal vitamin D levels was eight times more and statistically significant as the p-value is less than 0.05. All other factors examined in the analysis were not associated with odds of having suboptimal Vitamin D (

Table 7: Univariate and multivariable analysis of biochemical features associated with suboptimal Vitamin D levels.

	N (%)	Univariate analysis		Multivariable analysis	
		Crude Odds Ratio (95% CI)	P-value	**Adjusted Odds Ratio (95% CI) ***	**P-value***
Stage of CKD					
Stage2/3	47 (59)	Reference		Reference	
Stage 4/5	33 (41)	5.60 (0.65–47.9)	0.12	2.04 (0.17–24.2)	0.57
Calcium levels					
Normal levels	25 (31)	Reference		Reference	
Hypocalcemia	55 (69)	8.37 (1.55–45.1)	**0.01**	8.33 (1.11–62.4)	**0.04**
Hypercalcemia	0				
Phosphate levels					
Normal level	79 (99)	Reference		Reference	
Hypophosphatemia	0				
Hyperphosphatemia	1 (1.3)				
Alkaline phosphate levels					
Normal	55 (69)	Reference		Reference	
Hypo	0				
Hyper	25 (31)	3.50 (0.41–30.1)	0.25	2.72 (0.27–27.4)	0.40
Parathyroid hormones					
Normal	24 (30)	Reference		Reference	
Hypo	17 (21)	0.46 (0.09–2.42)	0.36	0.25 (0.03–1.99)	0.19
Hyper	39 (49)	5.43 (0.53-55.5_	0.15	3.79 (0.32–44.4)	0.29
Odds Ratio from logistic regression analysis, *adjusted for age, sex, and etiology of CKD, ¶; not enough numbers to be included in analysis.					

4.4 To Determine Factors Associated With Vitamin D Deficiency In Pediatric CKD Patients

In the univariate analysis, all factors examined in the analysis were not associated with of having suboptimal Vitamin D. (

Table 8).

Table 8: Univariate and multivariable logistic regression analysis of factors associated with suboptimal Vitamin D levels.

	N (%)	**Crude Odds Ratio (95% CI)**	P-value	**Adjusted Odds Ratio (95% CI) ***	**P-value**
Sex					
Male	40 (50)	Reference		Reference	
Female	40 (50)	1.76 (0.39–7.93)	0.46	1.20 (0.18–8.17)	0.85
Age in months					
<120 months	33 (41)	Reference		Reference	
≥ 120 months	47 (59)	0.84 (0.19–3.79)	0.82	0.87 (0.05–13.9)	0.92
Wasting status					
Not wasted	80 (100)	Reference			
Wasted	0	¶		¶	
Stage of CKD					
Stage2/3	47 (59)	Reference		Reference	
Stage 4/5	33 (41)	5.60 (0.65–47.9)	0.12	4.43 (0.46–42.3)	0.20
Duration of dialysis					
<12 months	71 (89)	Reference		Reference	
≥ 12 months	9 (11)	0.32 (0.05–1.92)	0.21	0.11 (0.01–1.46)	0.10
Vitamin D supplementation					
No	60 (75)	Reference		Reference	
Yes	20 (25)	1.00 (0.19–5.40)	0.98	0.44 (0.06–3.18)	0.42
Vitamin D or calcitriol supplementation					
No	57 (71)	Reference			
Yes	23 (29)	1.24 (0.23–6.62)	0.81		
CKD etiology					
Non Proteinuric	41 (51)	Reference		Reference	
Proteinuric	39 (49)	3.17 (0.60–16.8)	0.17	4.31 (0.72–25.8)	0.11
Odds Ratio from logistic regression analysis, *adjusted for age, sex, and etiology of CKD, ¶; not enough numbers to be included in analysis.					

5.0 CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

Suboptimal vitamin D levels are a significant problem, more so in the high-risk population, chronic kidney disease being one of them. A high prevalence (90%) of suboptimal vitamin D levels among these patients has been demonstrated in this study which is comparable with other hospital-based studies. In this study, the prevalence of suboptimal vitamin D was 90% which slightly higher than 73.9% previously reported in South Africa at 73.9% (14), China at 77.8% (27), Michigan at 77% but comparable to an Iranian study where the prevalence was at 89.7%(16). Numerous factors can account for the high prevalence: lack of sunlight exposure secondary to patient inactivity. Uremic frost on the skin, blunting the response to sunlight, though none of our participants had this clinical sign Additionally, poor nutritional and decreased consumption of vitamin D and calcium-rich foods (41) is a contributory factor. A high prevalence of suboptimal vitamin D in nephrotic-nephritic syndrome, attributed to loss of vitamin D binding protein along with 25(OH)D3(41) has been reported in various studies, and the bulk of our CKD etiology was (42%) for nephrotic -nephritic syndrome. We, however, did not assess the albumin range.

The most common etiology attributed to chronic kidney diseases is Nephrotic -nephritic syndrome (42%), this is comparable to global and regional figures. In the Nigerian study by Odetudende *et al,* where the participants had also glomerular disease accounting for the majority, nephrotic syndrome accounted for 70%(42). Fareen et al also demonstrated nephrotic -nephritic as the commonest etiology (31%) in her prevalence study of iron deficiency in CKD.

In our study, hypocalcemia (COR 8.33 (95%CI 1.11–62.4), p=0.04) was positively correlated with suboptimal vitamin D levels. However, other variables assessed which included the stage of CKD, and biochemical parameters (PTH, Phosphorous) had no significant correlation. In studies done by He Yoon Cho *et al*(28), and Ki Wuk Lee *et al*(27), they found that PTH was inversely correlated with vitamin D levels (p=0.038) but no significant correlation between vitamin D levels with calcium, phosphate, and stage of the disease. VBelostoky *et al*(29) on the other hand, found a significant correlation between low phosphate and suboptimal vitamin D levels although he failed to detect any correlation with calcium or parathyroid hormone. The different findings in these studies between vitamin D

levels and biochemical parameters could be because calcium, phosphate, and PTH levels may not become abnormal until a relatively late stage of vitamin D deficiency because of the endocrine system's tight control of calcium homeostasis(29). Additionally, in our study, we did not categorize vitamin D deficiency as either early, moderate, or severe.

Univariate and multivariable analysis of various variables including gender, age, stage of disease, duration of dialysis, vitamin D etiology, and vitamin D supplementation was done, and none was statistically significant These findings are contradictory to some studies but comparable to others. Solarian *et al* found that advanced CKD stage, chronic dialysis, peritoneal dialysis, older children (> 10 years), those on vitamin D supplements to be factors associated with vitamin D deficiency while gender was not(14). Similarly, Jameela *et al* found older age, peritoneal dialysis, and advanced CKD stage to be factors associated with Vitamin D deficiency(43). Juhi Kumar et al also demonstrated that older age and non -use of vitamin D supplements were factors associated with vitamin D deficiency while gender and stage of CKD were not (44). Elisa velle *et al* further found out that female gender, obesity(high BMI), older children, and hemodialysis were factors associated with vitamin D deficiency while the stage of CKD was not(45). All our participants had normal BMI. None of the variables analyzed in our study was associated with vitamin D deficiency. This could be attributed to the study not being powered to address this objective. This is one of the limitations of this study.

5.2 Study Strength

This study was conducted at the largest referral hospital that captures patients from all over the country. The renal units and clinics are supervised by pediatric nephrologists. All the caregivers and children approached for the study agreed to participate meaning there was minimal non -participation bias. Feedback was given to participants which enhanced their medical care.

5.3 Study Limitations

- The study was conducted in one single study site (tertiary) hence the results may not be generalizable to other pediatric CKD patients being attended in other hospitals.
- The sample size was small, thus limiting the power to detect factors associated with vitamin D deficiency and to find the correlation with the stage of disease, biochemical parameters, and parathyroid hormone.

- No data about behavioral or dietary factors such as daily activity or sunlight exposure was taken.
- The study is prone to selection bias due to the sampling technique used.
- Recall and information bias. The majority of patients could not remember vitamin D supplements or calcium prescribed the dosage or duration of these medications, and compliance. We could therefore not assess this statistically.
- To know the true picture/prevalence of suboptimal vitamin D, a comparative study would be ideal but due to lack of funding, it was not possible.

5.4 Conclusion

The prevalence of suboptimal vitamin D levels was high at 90% (54%, 36%, for deficiency and insufficiency respectively), and hypocalcemia a risk factor in patients with chronic kidney disease.

5.5 Recommendations

All pediatric chronic kidney disease patients require routine assessment of vitamin d levels as guided by the KDIGO/KDIQO guidelines and all with suboptimal levels should be supplemented. Further research on the factors associated with vitamin d deficiency in chronic kidney disease patients.

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APPENDICES

Appendix I: Diagnosis of CKD based on KDIGO Guidelines

Table 9 Diagnosis of Chronic Kidney Disease based KDIGO

KDIGO (2012) criteria based on kidney structure or function for diagnosis of CKD (Either of the following parameters that have present for 3 months)	
Indicators of renal damage (one or more of the following parameters)	Abnormalities in urine sediments
	Albuminuria (AER)of less than or equal to 30ml/24hours and urine albumin Creatinine ratio of more than or equal to 30mg/g
	Histological abnormalities of the kidney
	Any structural abnormalities detected using imaging
	Tubular disorders causing electrolyte abnormalities.
	History of renal transplant.
A decrease in Glomerular filtration rate	Glomerular filtration rate of less than 60 ml/min/1.73 m2 (GFR categories G3a–G5)

Table 10 KDIGO (2012) GFR Criteria for CKD

Category	**Glomerular filtration rate (GFR) ml/min/1.73m2**	**Description**
Category G1	More than 90	Normal or high
Category G2	60-89	Mildly decreased
Category G3a	45-59	Mildly to moderately decreased
Category G3b	30-44	Moderately to severely decreased
Category G4	15-39	Severely decreased
Category G5	Less than 15	Kidney failure

Table 11 KDIGO (2012) Albuminuria For CKD.

Category	**Albuminuria (mg/24hours)**	**Urine albumin Creatinine ratio**		**Terms**
		Mg/mmol	**Mg/g**	
A1	Less than 30	Less than 3	Less than 30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased
A3	Less than 300	Less than 30	Less than 300	Severely increased

Appendix II : Vitamin D Metabolism

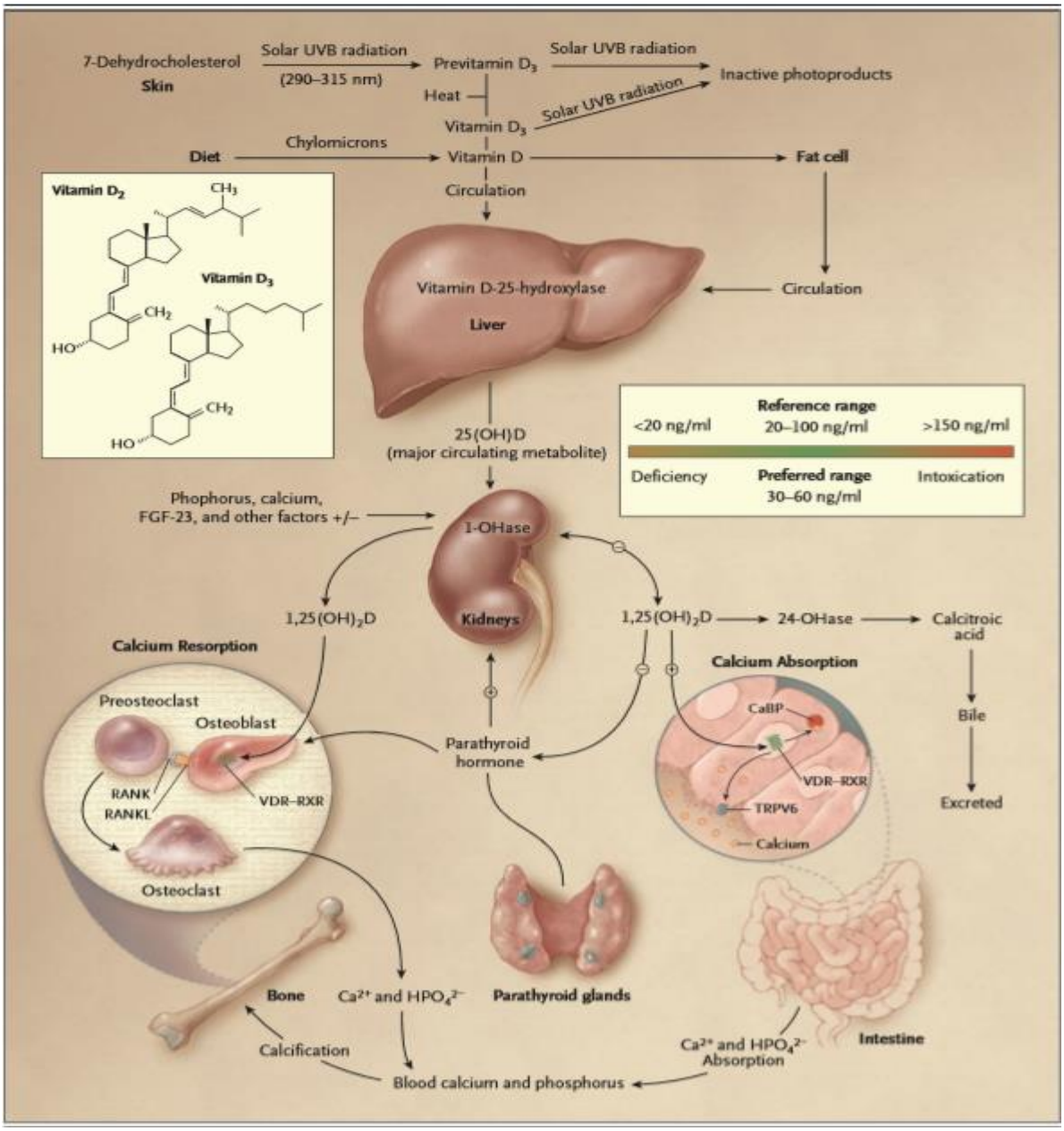


Figure 4 The figure above is a diagrammatic representation of the steps involved in Vitamin D metabolism. This diagram has been borrowed from an article on vitamin D deficiency(22) and can be accessed from the following link **N Engl J Med 2007; 357:266-281 DOI: 10.1056/NEJMra070553**(22)**.**

Appendix III: Time Frame

Activity	**Estimated time**
Development of Proposal and presentation	Dec 2019- Feb 2020
Proposal Submission for ethical approval	Feb 2020- July 2020
Data Collection	November 2020- February 2021.
Data Analysis	April 2021
Thesis Writing	April 2021- May 2021
Thesis Submission	May 2021

Appendix IV : BUDGET

The following was the budget for the study.

Category	Remark	Unit	Unit cost	Total (Kshs)
Proposal development	Printing drafts	1000	5	5000
	Proposal copies	1000	8	8000
Data collection	Stationary	400	10	4000
	Training research assistants	1	3000	3000
	Research assistant	20 weeks	1500	30000
Lab test		60		200000
Data entry	Data clerk	1	7000	7000
Data analysis	Statistician	1	30000	30000
Thesis write up	Printing drafts	1000	5	5000
	Printing thesis	10	1500	15000
Contingency fund				20000
Total				300000

Appendix V: Consent Form

a) Children below the age of 6 years the following consent forms will be issued to the guardian/parent(S)

b) This form shall also be issued to the parent(s)/guardians of children above the age of 6 years and below 18 years; in addition to the assent form to be filled by the child himself/herself

c) Swahili versions of both the consent and assent forms shall be issued

Consent Information Form (English Version)

- My name is Dr. Zanuba Chep'koech Mohammed a pediatrics registrar at Kenyatta National Hospital undertaking a master's degree in pediatrics and child health, in the school of Medicine, Department of Pediatrics and Child Health, University of Nairobi.
- This study is being conducted with the permission of Kenyatta National Hospital- the University of Nairobi and the Ethics and research committee (KNH-UON ERC Protocol no……).
- I am conducting a study on vitamin D, parathyroid hormone, calcium, and phosphate in children with chronic kidney disease aged 18 years and below, seen at Kenyatta National Hospital. Your son's/daughter's is being requested to participate in the study because he/she meets the conditions required to be included in the study (inclusion criteria).

Purpose

- The results of the study will help us get important information that will help in the care of children with chronic kidney disease seen at Kenyatta National Hospital.

Procedure

This interview will take 30-45 minutes, I will not write down his/her name, and all the information he/she provides will be kept SAFE and will not be shared with anyone else. His/ Her participation in this survey depends on you and him/her. If you consent to participate in this study, I will proceed to ask a series of questions and will subsequently note your responses in writing. I will conduct a physical examination of him/her. Six milliliters of blood will then be withdrawn for tests. The blood sample will be used to carry out the following tests: Vitamin D, Parathyroid hormone, Calcium, and Phosphate. I will inform you of the results of the tests and the test results remain confidential. The results will be availed to the primary physician within 72hours to improve the care of your child. The purpose of this consent is to ask you to permit me to do so. If you decline, it will not affect the quality of care that will be provided to him/her. If you agree to participate, I shall ask you to sign the consent

form. However, this form will not be linked to your answer. Your answers will only be seen by the researcher and will be stored safely, only accessible to the researcher.

The risks to you as a participant in the study

- Pain at the puncture site following specimen collection.
- Swelling may appear at the site of the venipuncture.
- Note: should any of the above occur, feel free to contact Dr. Zanuba Chep'koech Mohammed.

The benefits to you as a participant in the study.

- Free evaluation of vitamin D, parathyroid hormone, calcium, and phosphate.
- A copy of the results will be provided to the primary physician and yourself.
- The results will assist in improving management and follow-up of him/her.

Right to Withdraw/participate.

- Your son's/ daughter's participation in this research is voluntary and your choice to participate or not will affect the quality of care given to your child at any point.
- You have the right to refuse to participate or withdraw at any point.
- Do you have any questions?

The parent/ guardian has given consent.

- **Yes_____1**

  No_____2

Consent Form (Statement of Consent)

Participant's statement

I have read this consent or had the information read to me. I have the chance to discuss the research with the researcher/ researcher assistant. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw at any time. I understand that all efforts will be made to keep information regarding my identity confidential. I, agree to participate in the study on Vitamin D levels, Parathyroid, Calcium, and Phosphate in children with chronic kidney disease. I do this with a full understanding of the purpose of the study and the procedures involved. These procedures include filling in the study questionnaire and having 7 milliliters of blood withdrawn for laboratory tests, namely, serum vitamin D, serum parathyroid, serum calcium, and phosphate. These tests will enable knowing their levels in the body.

- Signature of the parent/guardian _____
- Signature of the witness _____
- Date _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's name: _____Signature :_____

Date:_____

What if you have questions/ concerns in the future?

If you have further questions or require further information or clarification about participation in this study, you may contact the following: Dr. Zanuba Chep'koech Mohammed(primary researcher)Mobile Number: 0722854703, chepzanuba@gmail.com Lead supervisors: Dr. Lucy Mungai Mobile Number and Email: 0724654135 dr.lmungai@gmail.com and Dr. Bashir Admani Mobile Number: 0721967818 Email: pedbashir@yahoo.com

Kenyatta National Hospital/University of Nairobi, Ethics and Research Committee, College of Health Sciences, P.O BOX 19676 00202, Nairobi. Telephone: (254-020) 2726300-9 Ext 44355.Email: uonknh-erc@uonbi.ac.ke

What are your other choices?

- Your decision to participate in research is voluntary.
- You are free to decline participation in the study and you can withdraw from the study at any time without injustice and loss of any benefit.

Assent Form (English Version)-for children above 6 years and below 18 year

My name is Dr. Zanuba Chep'koech Mohammed, a pediatric resident at Kenyatta National Hospital undertaking a master's degree in pediatrics and child health, in the school of Medicine, Department of Pediatrics and Child Health, University of Nairobi.

This study is being conducted with the permission of Kenyatta National Hospital – the University of Nairobi and the Ethics and research committee (KNH-UON ERC Protocol no…….

I am conducting a study on vitamin D levels, parathyroid, calcium, and phosphate in children with chronic kidney disease aged 18 years and below, seen at Kenyatta National Hospital. You are being requested to kindly participate in the study because you meet the conditions to be included in the study.

Benefit

You have chronic kidney disease. You also came to the hospital regularly for the doctor to check if you are doing well. To enable the doctor, know how well you are doing, it's important to know the levels of the above-mentioned tests.

Purpose

We want to find out if the levels of vitamin D, Parathyroid, calcium, and phosphate are good to allow your body to function well. Sometimes due to your chronic illness, the levels may be reduced.

Procedures

- If you accept, I will ask you some questions to enable me to know more about you and your illness.
- I will then examine you before taking some blood from your arm.
- We will take about three tablespoons of blood.
- We will send the blood to a lab for tests.
- These tests will help us know the levels of vitamin D, parathyroid, calcium, and phosphate in your body.
- We will provide these results to your doctor each time and then he will be able to take care of you in a better way

Risks, Stress, And Discomfort

- The needle we use to take the blood may hurt. You might get a bruise on your arm. Sometimes you may develop swelling at this site.
- In case this happens, please call us so that we may assist you.

Who Can You Call If You Need Help Or Have Any Questions?

If you have further questions or require further information or clarification about participation in this study, you might conduct the following: If you have further questions or require further information or clarification about participation in this study, you may contact the following: Dr. Zanuba Chep'koech Mohammed(primary researcher)Mobile Number: 0722854703, chepzanuba@gmail.com Lead supervisors: Dr. Lucy Mungai Mobile Number and Email: 0724654135 dr.lmungai@gmail.com and Dr. Bashir Admani Mobile Number: 0721967818 Email: pedbashir@yahoo.com

Kenyatta National Hospital/University of Nairobi, Ethics and Research Committee, College of Health Sciences, P.O BOX 19676 00202 Nairobi, Telephone: (254-020) 2726300-9 Ext 44355.Email: uonknh-erc@uonbi.ac.ke.

Other Information

- We will not tell anyone you took part in this study.
- Your name will not be on the sample of blood we take.
- You do not have to take part in this study if you do not want to. No one will be unhappy with you.

- We will give you a copy of this paper to keep.

_____ _____

Name and signature of the investigator Date

Subject's statement

- This research study has been explained to me. I agree to take part in this study. I have had a chance to ask questions. If I have more questions, I can ask the doctor.

_____ _____

Name and signature of the subject Date

_____ _____

Name and signature of parent / legal guardian Date

Swahili Consent Forms.

Fomu Ya Maelezo Ya Kiswahili.

- Jina langu ni Dk. Zanuba Che'pkoech Mohammed, mtaalamu wa Watoto was hospital ya Taifa ya Kenyatta akifanya shahada ya Ualimu katika afya na Watoto, katika shule ya Dawa, Idara ya Ma'abara yak Afya na Afya ya Watoto, chuo kikuu cha Nairobi.
- Utafiti huu unafanyika kwa idhini ya hospitali ya Taifa ya Kenyatta- Chuo Kikuu cha Nairobi na Kamati ya maadali na utafiti (Protocol ya KNH-UON ERC hakuna……)
- Ninafanya utafiti juu ya upungufu wa vitamini D, homoni ya paradundumio, kalisiumu, fosfati kwa Watoto wenye ugonjwa wa figo wenye umri wa miaka 18 na chini, ambao wanaonekana katika hospitali ya Taifa ya Kenyattta. Wana na binti yako wanaombwa kushiriki katika utafiti kwa sababu yeye hukutana na masharti yanayotakiwa kuingizwa katika utafiti (vigezo vya kuingizwa)

Kusudio

- Matokeo ya utafiti itatusaidia kupata maelezo muhimu ambayo itasaidia katika Huduma ya Watoto wenye ugonjwa wa figo sugu inayoonekana katika hospitali ya Taifa ya Kenyatta.

Utaratibu

- Mahojiano haya yatachukua dakika 30-45, sitaandika jina lake, na maelezo yote atakayotoa itahifadhiwa SALAMA na haitashirikiwa na mtu mwingine yeyote. Ushiriki wake katika utafiti huu kabisa unategemea wewe na yeye.
- Ikiwa unakubali kushiriki katika somo/utafiti hili, nitaendelea kuuliza maswahili mfufulizo na hatimaye kuandika majibu yako kwa maandishi.
- Nitafutalia kufanya uchunguzi wa kimwili.
- Mililita 6 ya damu yatatolewa kwa ajili ya vipimo. Sampuli ya damu itatumika kutekeleza vipimo vifuatavyo; viwangu vya vitamini D, homoni ya paradundumio, madini ya kalisiamu na ya fosfati. Uchunguzi huu unatusaidia kujua viwangu hivi katika mwili wa mtoto wako.
- Nitawajulisha matokeo ya vipimo na matokeo ya mtihani yanabaki Siri. Matokeo pia yatatolewa kwa daktarin ili kuboresha utunzanji wa mtoto wako.
- Kusudi la idhini hii ni kukuuliza uniruhusu nifanye hivyo.
- Ikiwa unapungua,hauathiri ubora wa utunzaji ambao utapewa

- .Ikiwa unakubaliana kushiriki,nitawaomba kusaini fomu ya kibali. Hata hivyo fomu hii haiwezi kuunganishwa na jibu lako. Majibu yako binafsi yataonekana tu na mtafiti na itahifadhiwa kwa usalama, inapatikana tu kwa mtafiti.

Hatari Kwako Kama Mshiriki Katika Utafiti

- Maumivu kwenye tovuti ya kufuatia mkusanyiko wa vipimo.
- Kuvimba huweza kuonekana kwenye tovuti ya kutengana (hematoma).
  Note: lazima yoyote ya hapo juu kutokea kujisikia huru kuwasiliana na DK. Zanuba Mohammed

Faida Kwako Kama Mshiriki Katika Utafiti

- Tathmini ya bure ya viwango vyo vitamini D, madini ya kalisiamu, fosfati na homoni ya paradundumio(parathyroid).
- Nakala ya matokeo yatatolewa kwa daktari na wewe.
- Matokeo yatasaidia kuboresha usimamizi wake.

Haki Ya Kujiondoa/ Kushiriki

- Ushiriki wa mtoto wako/ wa binti katika utafiti huu ni hiari na uchanguzi wako wa kushiriki au la hautaathiri ubora wa huduma aliyopewa mtoto wako wakati wowote.
- Una haki ya kukataa kushiriki au kujiondoa wakati wowote.
- Una maswali yoyote?

Mzazi / mlezi ametoa kibali

Ndiyo_____1

Hapana_____2

Fomu Ya Saha(Taarifa Ya Kusha)

Taarifa ya Mshiriki

- Nimeisoma kibali hiki au nilisoma habari. Nimekuwa na fursa ya kujadili utafiti na mtafiti/ msaidizi wa utafiti. Hatari na faida zimeelezwa kwangu. Ninaelewa kwamba ushiriki wangu katika utafiti huu ni hiari na kwamba nipate kuchagua wakati wowote. Ninaelewa kwamba jitihada zote zitafanywa kweka taarifa kuhusu utambulisho wangu binafsi.
- Mimi,_____ kukubali kushiriki katika utafiti juu ya upungufu wa vitamin D, madini ya kalisiamu, fosfati na homoni ya paradundumio kwa Watoto wenye ugonjwa wa figo wenye umri wa miaka hadi 18.
- Ninafanya hivyo kwa ufahamu kamili kwa madhumuni ya utafiti na taratibu zilizohusika. Taratibu hizi ni pamoja na kujaza dodoso la utafiti na ku na kuwa mililita 7 za damu kuondolewa kwa ajili ya vipimo vya maabara, yaani; Seram vitamini D, madini ya kalisiamu, fosfati na homoni ya paradundumio. Vipimo hivi vitatusaidia kujua viwango vyao katika mwili.

  Saini ya mzazi/ mlezi_____

  Saini ya shahidi_____

  Tarehe_____

Taarifa ya Mtafiti.

- Mimi, aliyechaguliwa , nimeezelewa
- kikamilifu maelezo muhimu ya utafiti huu wa utafiti kwa mshiriki aliyechaguliwa hapo juu na kuamini kuwa mshiriki ameelewa na ametoa idhini yake kwa hiari na kwa hiari.
- Jina la mtafiti_____
- Saini_____ Date_____

Nini ikiwa una maswali / wasiwasi baadaye?

Ikiwa una maswali Zaidi au unahitaji maelezo Zaidi au ufafanuzi kuhusu ushiriki katika utafiti, tafadhali piga simu au tuma ujumbe wa maandishi kwa :Dk. Zanuba Chepkoech Mohammed(mtafiti mkuu), nambari la simu na barua pepe, 0722854703, chepzanuba@gmail.com. Waelekezaji wakuu: Dk. Lucy Mungai, nambari la simu barua pepe ,0724654135, dr.lmungai@gmail.com :Dk.Bashir Admani, nambari la sim u,na barua pepe,0721967818,pedbashir@yahoo.com

Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee, college of health science, Sanduku la posta 19676 00202,nambari la simu na Barua Pepe: (254-020) 2726300-9 Ext 44355, uonknh-erc@uonbi.ac.ke.

Je, ni uchaguzi Gani mwingine?

- Uamuzi wako wa kushiriki katika utafiti ni wa hiari. Wewe ni huru kupungua kushirika katika utafiti na unaweza kujiondoa kwenye utafiti wakati wowote bila udhalimu na kupoteza faida yoyote.

Funa ya Kufuna (Kwa Watoto Zaidi Ya Miaka 6 Na Chini Ya Miaka 18)

- Jina langu ni DK. Zanuba Chep'koech Mohammed, mtaalamu wa Watoto katika hospitali ya Taifa ya Kenyatta anafanya shahada ya Mwalimu katika Watoto wa afya na afya ya Watoto, katika shule ya Dawa, Idara ya Maabara ya Afya na Afya ya Watoto, Chuo Kikuu cha Nairobi.
- Utafiti huu unafanyika kwa idhini ya hospitali ya Taifa ya Kenyatta- Chuo Kikuu cha Nairobi na Kamati ya Ma'adili na Utafiti (Protocol ya KNH-UON ERC hakuna……..)
- Ninafanya utafiti juu ya upungufu wa vitamini d, madini ya kalisiamu, fosfati na homoni ya paradundumio kwa Watoto wenye ugonjwa wa figo wa muda mrefu wenye umri wa miaka 18 na chini, waliona hospitali ya kitaifa ya Kenyatta. Unatakiwa kushiriki kikamilifu katika utafiti kwa sababu unakabiliana na masharti ya kuingizwa katika utafiti.

Mafunzo

- Una ugonjwa sugu. Pia unakuja hospitali mara kwa mara kwa daktarin ili uone kama unafanya vizuri. Ili kuwawezesha daktarin kujua jinsi unavyofanya vizuri ni muhimu kujua vipimo vya vitamini d, madini ya kalisiamu na fosfati katika mwili wako.

Kusudio

- Tunataka kujua kama ngazi vya vipimo hivyo katika mwili wako ni nzuri ya kuruhusu mwili wako kufanya kazi vizuri. Wakati mwingine kutokana na ugonjwa wako sugu viwango hivyo vinaweza kupunguka.

Taratibu

- Ikiwa unakubali, nitakuuliza baadhi ya maswali ili nisaidie kujua Zaidi kuhusu wewe na ugonjwa wako.
- Nitawachunguza kabla ya kuchukua damu kutoka mkono wako.
- Tutachukua kuhusu vijiko vitatu vya damu.
- Tutatuma damu kwenye maabara kwa ajili ya vipimo.

- Tutatoa matokeo haya kwa daktari wako kila wakati na kisha atakuwezesha kwqa njia bora Zaidi.

Hatari au Wasiwasi Wowote

- Njisi tunavyotumia kutoa damu inaweza kuumiza.
- Unaweza kupata maradhi juu ya mkono wako.
- Wakati mwingine, unaweza keundeleza uvimbe kwenye tovuti pia.
- Ikiwa hii itatokea, tafadhali piga simu ili tupate kukusaidia.

Unawafuna Nini Unafuna Kusafu Au Uwe Na Maswali Yoyote?

Ikiwa una maswali Zaidi au unahitaji maelezo Zaidi au ufafanuzi kuhusu ushiriki katika utafiti, tafadhali piga simu au tuma ujumbe wa maandishi kwa: Jina: DK. Zanuba CHEPKOECH Mohammed,(mtafiti mkuu) Nambari ya simu: 07228547034 Barua pepe: chepzanuba@gmail.com.Jina: DK. Lucy Mungai, Nambari ya simu: 0724654135Barua pepe: dr.lmungai@gmail.com. Jina: DK. Bashir Admani, Nambari ya simu: 0721967818Barua pepe: pedbashir@yahoo.com. Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee,College of health sciences, 19676 00202,Nambari ya simu: (254-020) 2726300-9 Ext 44355 Barua pepe: uonknh-erc@uonbi.ac.ke

Taarifa Nyingine

Hatuwezi kumwambia yeyote aliyeshiriki katika utafiti huu. Jina lako halitakuwa kwenye sampuli ya damu tunayochukua. Huna budi kushiriki katika utafiti huu ikiwa hutaki. Hakuna mtu atakayekuwa na furaha na wewe. Tutakupa nakala ya karatasi hii kuweka

_____ _____ _____

Saini Jina Tarehe ya uchunguzi

Taarifa Ya Somo

- Utafiti huu wa utafiti umeelezewa kwangu. Nakubali kushiriki katika utafiti huu. Nimekuwa na nafasi ya kuuliza maswali. Ikiwa nina maswali Zaidi, ninaweza kumuliza dakatri.
- _____ _____

  Saini na Jina la somo Tarehe

  _____

  _____

  Saini na jina la mzazi/ mlezi wa sharia Tarehe

Appendix VI: Data Collection Form Tool

Study Questionnaire

Vitamin D Deficiency And Insufficiency In Children With Ckd At Knh.

Primary Researcher: Dr Zanuba Mohammed

Serial No_____ Date of Interview_____

Part 1: Patients details

1. Age (months) _____
2. Gender: ☐Male ☐
3. Skin: Dark_____ Light _____
4. Etiology of CKD (as recorded in the hospital records) _____
5. Date /Duration of the diagnosis_____
6. Is the patient on dialysis: Yes_____ No_____
7. Has the patient ever been on dialysis_____

a) If yes, indicate whether on hemodialysis or peritoneal dialysis_____

b) Date of commencement and termination of dialysis (termination date if only temporary dialysis) _____

8. Anthropometry measurements and vital sign

Anthropometric measurements	Vital signs
Height (cm)	B/P (mmHg)
Weight (kg)	Heart rate
MUAC (cm)	Respiratory rate
BMI	Temp (°C)

9. Nutritional status categorization

WHZ_____ WAZ_____ HAZ_____ BMI for age Z score_____

Part 2: Parents/caregivers details

Mothers' details	Fathers' details	Caregivers' details
Age (years)	Age	Age
Occupation	Occupation	Occupation
Education level	Education level	Education level
Marital status	Marital status	Marital status

Part 3: Use of medication

Drug	Dose	Duration	Commencement

Part 4: Stage of CKD

Estimated GRF (as recorded in the file)	Stage of CKD

Part 6: Study laboratory results

Lab	Results
Vitamin D (calcidiol)(ng/ml)	Adequate
	Insufficient
	Deficient
Calcium (mmol/l)	
Phosphate (mmol/l)	
Parathyroid hormone (mmol/l)	

Part 8: General examination (Tick where appropriate)

Sign	Yes	No
Uremic frost on the skin		
Edema		
Widening of the wrist		
Bowlegs		
Teeth		

Interviewers

Name_____ Signature_____

Appendix VII: KNH/UoN-ERC Letter of Approval

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

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 08 SEP 2020 KNH/UoN-ERC P. O. BOX 20723 - 00202 NAIROBI

Ref: KNH-ERC/A/293

8th September 2020

Dr.Zanuba Chepkoech Mohammed
Reg. No.H58/11279/2018
Dept.of Paediatrics and Child Health
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Mohammed

RESEARCH PROPOSAL – SUBOPTIMAL VITAMIN D LEVELS IN CHILDREN WITH CHRONIC KIDNEY DISEASE AT KENYATTA NATIONAL HOSPITAL (P134/ 02/2020)

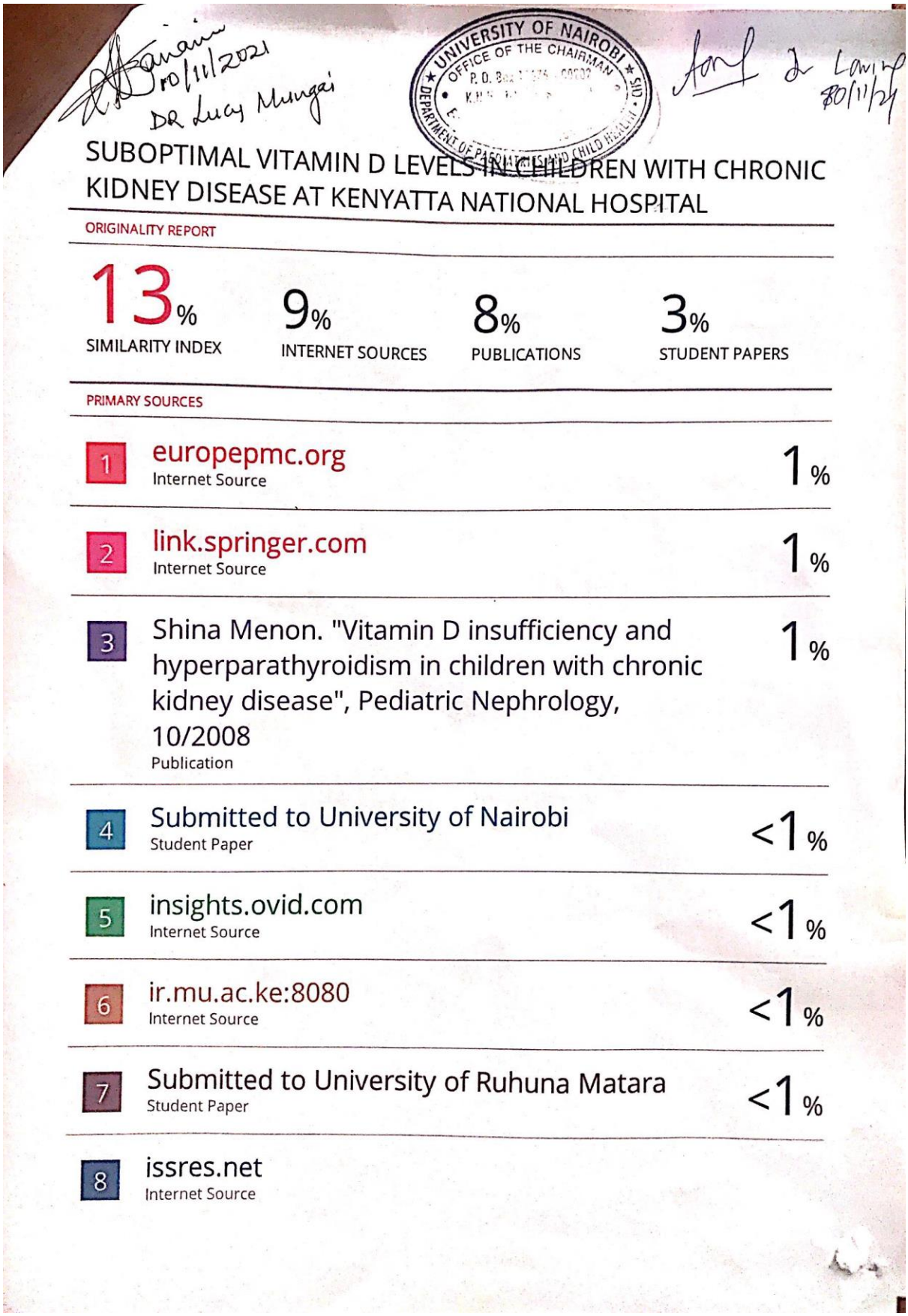
This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 8th September 2020 – 7th September 2021.

This approval is subject to compliance with the following requirements:

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

Protect to discover

Appendix: VIII: Certificate of Plagiarism



10/11/2021
DR Lucy Mungai

UNIVERSITY OF NAIROBI
OFFICE OF THE CHAIRMAN
DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH

Prof J Lavin
30/11/21

SUBOPTIMAL VITAMIN D LEVELS IN CHILDREN WITH CHRONIC KIDNEY DISEASE AT KENYATTA NATIONAL HOSPITAL

ORIGINALITY REPORT

13%	9%	8%	3%
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PRIMARY SOURCES

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3	Shina Menon. "Vitamin D insufficiency and hyperparathyroidism in children with chronic kidney disease", Pediatric Nephrology, 10/2008 Publication	1%
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