



University of Nairobi

**PREVALENCE AND ASSOCIATED RISK FACTORS OF
DEVELOPING THYROID HORMONE DYSFUNCTION IN
CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME
FOLLOWED UP AT KENYATTA NATIONAL HOSPITAL**

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**A Research Dissertation submitted to the University of Nairobi in part of
the fulfillment of the requirements for the degree of Masters of Medicine in
Paediatrics & Child Health, Faculty of Health Sciences, University of
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2023

DECLARATION

I, Dr. Maureen Kwamboka Machungo, declare that this dissertation for Master of Medicine in Paediatrics & Child Health is my original work and has not, to the best of my knowledge, been presented by any other individual for review and approval at any other learning institution.

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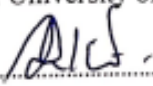
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1. The University of Nairobi.
2. Kenyatta National Hospital.

FUNDING.

The research endeavor is self-funded in its entirety.

LIST OF ABBREVIATIONS AND ACRONYMS

E	Degree of Accuracy
ERC	Ethics Review Committee
FSGS	Focal Segmental GlomeruloSclerosis
GDP	Gross Domestic Product
GFR	Glomerular Filtration Rate
H.I.V	Human Immunodeficiency Virus
H.S.P	Henoch SchonleinPurpura
I.N	Idiopathic Nephrotic Syndrome
H	Kenyatta National Hospital
MCNS	Minimal Change Nephrotic Syndrome
mls	Milliliters
N	Sample Size
N.S	Nephrotic Syndrome
P	Proportion
RT3	Reverse Triiodothyronine
S.L.E	Systemic Lupus Erythematosus
SD	Standard Deviation
SRNS	Steroid Resistant Nephrotic Syndrome
T.H	Thyroid Hormones
T3	Triiodothyronine
T4	Thyroxine
TBG	Thyroxine Binding Globulin
TSH	Thyroid Stimulating Hormone
UON	University of Nairobi

OPERATIONAL DEFINITION OF TERMS

Child: A young individual between ages zero and eighteen.

Children on follow up: Children attending renal clinic as a referral or 4 weeks after discharge from the ward after management of an acute phase of idiopathic nephrotic syndrome.

Frequent Relapse: After preliminary diagnosis, more than 2 relapses in 6 months or more than 4 events of relapse in a year.

Idiopathic Nephrotic Syndrome: Nephrotic syndrome unrelated to any systemic causes.

Nephrotic syndrome: kidney disease that increases the ability to penetrate the entire glomerular filter barrier. It is characterized by high proteinuria (over 40mg / m² per hour) causing hypoalbuminemia (less than 30g / L), and the result of hyperlipidemia, edema, and other complications.

Relapse: Increase in the first morning urine protein to creatinine ratio >0.2 or 2+ proteinuria for > 3 consecutive days.

Remission: Attainment of + 1 proteinuria on urine dipstick for more than 3 consecutive days.

Response: Remission within the first four weeks of corticosteroid treatment.

Steroid dependent: Relapse with steroid tapering or within 2 weeks of steroid discontinuance.

Steroid resistant: Inability to induce remission within 4 weeks of daily steroid therapy.

Steroid responsive: Ability to induce remission in the first 4 weeks of steroid therapy.

Thyroid Hormone Derangements: Abnormally elevated or reduced level of any or all thyroid hormone parameters

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ABSTRACT

Background: Evidence from publications done globally show that a significant percentage of children diagnosed with idiopathic nephrotic syndrome complicate with deranged thyroid hormone levels despite being in remission, and this affects the outcome of treatment and disease progression. Thyroid hormone derangements in children with idiopathic nephrotic syndrome have not been studied in Kenya.

Objectives: The broad objective of this study was to determine the prevalence of thyroid hormone imbalances in children undergoing nephrotic syndrome follow-up at the Kenyatta National Hospital paediatric renal clinic.

Methodology: This study used a prospective cross-sectional study in the outpatient paediatric renal clinic of Kenyatta National Hospital on approximately 65 children between ages 1-17years who have been diagnosed with idiopathic nephrotic syndrome. The study ran a course of five months and included participants who matched the inclusion criteria.

Data collected was filled in a data collection tool designed. The information was using SPSS version 21. Categorical data was analyzed and presented as frequencies and proportions, continuous data was summarized and presented as means and standard deviations.

Results: The study participants were aged 4-17 years old with a median age of 11.038 out of 65 had less than 2 relapses per year. Most of the participants were in remission. 71% of the children had albumin levels in the normal range. 94% of the study participants were using immunosuppressive agents. In this study, 51% were euthyroid whereas 49% had hypothyroidism. Of the study participants with hypothyroidism, 47% had subclinical hypothyroidism, 31% had low T3 syndrome and 22% had overt hypothyroidism.

Both albumin level and proteinuria were significantly associated with derangement of thyroid hormones at 5% significance level, p values 0.01 and 0.02, respectively.

Conclusion: The prevalence of thyroid hormone derangements among children on follow up for idiopathic nephrotic syndrome in this study is 49%. Proteinuria and albuminemia showed increase in the odds of developing deranged thyroid hormone levels among children on follow up for idiopathic nephrotic syndrome in this study despite being tagged as in remission.

CHAPTER 1: INTRODUCTION

1.1. Background

Preservation of homeostasis of metabolic functions in all body organs is fundamental. Key regulatory organs or actions of hormones are involved in achieving this balance. Thyroid hormones are important in the early structural development of the kidney, as well as the regulation of main glomerular and tubular functions, along with water and electrolyte balance(1). Contrastingly, the kidney functions by regulating the concentration of hydrogen, sodium, potassium, phosphate and other extracellular ions enabling maintenance of fluid and acid-base balance, excretion of metabolic waste products, secretion and metabolism of certain hormones involved in hemodynamic control, mineral metabolism, and red cell production(2). As a result, a dysfunction in one of the organs is likely to have negative ramifications in both systems.

Amongst the most diagnosed renal diseases in children is nephrotic syndrome. It is a clinical state induced by renal disorders that causes the glomerular filtration barrier to become more permeable. The cumulative prevalence rate is approximately 16 cases per 100,000 individuals (3). A systemic review by Rachel Wine et al on the trends of epidemiology of childhood nephrotic syndrome in Africa deciphered that only a third of African countries have data on nephrotic syndrome in children (4). Most countries with data are listed in the top 20 of nominal gross domestic product in Africa, which reflects differential access to care and nephrology training across the continent(4). In Kenya, scanty data is available pertaining to nephrotic syndrome and in particular complications associated with nephrotic syndrome.

Many patients with nephrotic syndrome have a good prognosis with no sequelae. However, some of these children may develop complications related to the disease process or secondary to the therapy used in the treatment. Various endocrine abnormalities, in particular thyroid hormone derangements have been associated with Nephrotic Syndrome (5). Through a negative feedback loop involving the hypothalamus and pituitary gland, the thyroid gland generates, stores, and secretes thyroid hormones. When any phase of this process is impaired, thyroid dysfunction can develop, resulting in high or low concentrations of thyroid stimulating hormone (TSH).

Nephrotic Syndrome is a clinical syndrome defined by massive proteinuria(more than 40mg/m² per hour) leading to hypoalbuminemia (less than 30g/L), which contributes to hyperlipidemia, edema and other complications(6). Although albumin constitutes the major fraction of protein excreted Due to the selective

character of proteinuria, many other essential globulins, hormones, and hormone binding proteins are also excreted in substantial numbers, resulting in clinical implications other than renal insufficiency. (7).

The loss of thyroid hormones and thyroid binding globulins (TBG) in the urine is a major source of concern. In the early stages, no metabolic consequences are projected since levels of free thyroxine (fT4) and free triiodothyronine (fT3) are normal, but prolonged excretions of thyroid binding globulin can lower levels of free thyroid hormones, leading to an increase in thyroid stimulating hormone (TSH) levels as the thyroid gland begins to over function to preserve the steady hormone levels. (8).

Table 1: Table showing the different classification of thyroid dysfunction(9)

Serum TSH	Serum free T4	Serum T3	Assessment
Normal hypothalamic-pituitary function			
Normal	Normal	Normal	Euthyroid
Normal	Normal or high	Normal or high	Euthyroid hyperthyroxinemia
Normal	Normal or low	Normal or low	Euthyroid hypothyroxinemia
Normal	Low	Normal or high	Euthyroid: T3 therapy
Normal	Low-normal or low	Normal or high	Euthyroid: thyroid extract therapy
High	Low	Normal or low	Primary hypothyroidism
High	Normal	Normal	Subclinical hypothyroidism
Low	High or normal	High	Hyperthyroidism
Low	Normal	Normal	Subclinical hyperthyroidism
Abnormal hypothalamic-pituitary function			
Normal or high	High	High	TSH-mediated hyperthyroidism
Normal or low*	Low or low-normal	Low or normal	Central hypothyroidism

T3: triiodothyronine; T4: thyroxine; TSH: thyroid-stimulating hormone.

* In central hypothyroidism, serum TSH may be low, normal, or slightly high.

Hypothyroidism and hyperthyroidism both cause significant changes in electrolyte and water homeostasis(10). Changes in thyroid hormone secretion, synthesis, metabolism, and excretion occur in tandem with the reduction in kidney function. Other factors that predispose patients with nephrotic syndrome to thyroid hormone derangements include hypoalbuminemia, duration of illness, number of relapses, use of glucocorticoids, kidney failure and the renal histology type of Nephrotic Syndrome(11).

Datta et al(12) conducted a research on 30 children between 1-8 years old with Nephrotic Syndrome looking at the levels of thyroid hormones. Results were that these children had low T3 and T4 levels with high TSH levels. This indicates that there is a high prevalence of hypothyroidism in children with nephrotic syndrome.

Ebadi et al year 2016(13) noted low levels of T3 and T4 with high TSH levels in children in remission with nephrotic syndrome.

Prevalence of thyroid hormone derangements has been recorded in children with nephrotic syndrome.

CHAPTER 2: LITERATURE REVIEW

2.1 Nephrotic Syndrome

Nephrotic Syndrome results from an increase in permeability across the kidneys glomerular filtration barrier. The first two clinical features are utilized to diagnose it because the remaining two may not appear in all cases.(14) :

- Nephrotic range proteinuria- proteinuria $> 3.5\text{g}/24\text{hr}$.
- Hypoalbuminemia- serum albumin concentration of $< 3\text{g}/\text{dL}(30\text{g}/\text{L})$.
- Edema
- Hyperlipidemia.

The overall prevalence rate in the United States is around 16 cases per 100,000 people. (3).

Most children with N.S have a primary/ idiopathic form of nephrotic syndrome. Glomerular lesions associated with Idiopathic Nephrotic Syndrome include minimal change disease accounting for approximately 80% of the disease, focal segmental glomerulosclerosis, membranous nephropathy. Nephrotic syndrome may also be secondary to systemic diseases such as Systemic Lupus Erythematosus (S.L. E), Human Immunodeficiency Virus (H.I. V), Malaria, Henoch Schonlein Purpura (H.S.P).

Corticosteroids are the mainstay therapy for primary nephrotic syndrome. With corticosteroids many children respond and attain remission while some relapse or are either steroid responsive or steroid dependent. Most patients with Minimal Change Nephrotic Syndrome have good outcomes without complications. However, some of these children have lesions associated with foot process effacement and scarring of the glomerular capillaries. This is termed Focal Segmental Glomerulosclerosis (F.S.G.S). This permanent damage to the glomerular capillaries results in prolonged proteinuria that is refractory to corticosteroids therefore posing higher risk of developing complications associated with focal segmental glomerulosclerosis.

Table 2: Table below illustrates different complications associated with nephrotic syndrome disease process and its treatment.(5)

COMPLICATIONS	EXAMPLES
Disease-associated complications	Infections: Spontaneous Bacterial peritonitis, sepsis, cellulitis Thromboembolism: VTE, Pulmonary embolism Hypovolemic crisis Anemia Acute Renal Failure Hormonal and mineral alterations: Hypothyroidism, Hypocalcemia, Bone disease
Drug associated complications	Corticosteroids-cushingoid features, growth retardation, hormonal disturbance Cyclosporin: nephrotoxicity, neurotoxicity Alkylating Agents: bone marrow examples Mycophenolate mofetil: bone marrow suppression

2.2 Thyroid hormone synthesis, transport, metabolism, and function.

The thyroid gland, from thyroglobulin (an iodinated glycoprotein) produces two hormones: thyroxine (T4) and triiodothyronine (T3). These hormones have an important function in fetal cell development and in maintaining metabolic homeostasis and thermogenic characteristics in human life. The anterior pituitary secretes Thyroid Stimulating Hormone (TSH), which is important for thyroid axis regulation(15). T4 is produced at a twenty-fold higher percentage than T3 by the thyroid gland. Protein-bound thyroxine binding globulin, albumin, and transthyretin bind both hormones. Plasma binding proteins enhance the amount of hormone in circulation, delay clearance, and may modify hormone distribution to specific tissue sites. (2) . Protein binds 99.98 percent of T4 and 99.7 percent of T3.

2.3 Thyroid hormone and renal physiology.

During childhood, thyroid hormones are required for kidney growth and development as well as the maintenance of water and electrolyte homeostasis(16). Thyroid hormones are metabolized and excreted via the kidney, which is a major target organ for thyroid hormones(16). Thyroid hormone imbalances cause significant changes in the water and electrolyte metabolism. (17). Changes in thyroid hormone secretion, metabolism, and excretion precede a reduction in kidney function. The liver is the major site of thyroid hormone metabolism. Thyroid hormones metabolism is deiodination-based, with only 25% conjugated(17), deaminated, or decarboxylated thyroid hormone. The kidneys play a limited role in T4 to T3 conversion by deamination and decarboxylation.

2.3 Effect of Nephrotic Syndrome on Thyroid Dysfunction

Between March 2016 and March 2018, Saffari et al (18) conducted a case-control study in a paediatric hospital in Qazvin, Iran, to investigate thyroid dysfunction in children with idiopathic nephrotic syndrome. The case group consisted of 73 nephrotic children (49 with active disease and 24 in remission), while the control group consisted of 74 healthy children. Total t4 levels were normal in all the controls. Thyroid stimulating hormone levels were found to be higher in nephrotic children than in controls (34.2 percent versus 10.8 percent). When compared to patients in remission, a significantly lower number of active illness patients were euthyroid (51 percent versus 95.8 percent).

Thyroid screen tests may be required in nephrotic children due to the prevalence of subclinical and even overt hypothyroidism, according to the findings of this study. This can be described by urinary losses of binding proteins such as thyroid binding globulins (TBG), transthyretin or prealbumin, albumin, and thyroid hormone bound. This causes a drop in serum total thyroxine levels and, in rare cases, T3 levels. The severity of proteinuria and the resulting drop in serum albumin levels cause hormonal alterations (18). The thyroid, on the other hand, is effective to compensate for urine losses of thyroid hormones, and the patients preserve euthyroid status(19). Overt hypothyroidism can develop in patients with a depleted thyroid reserve.

Datta et al investigated thyroid hormones in 60 children aged 1 to 8 years, 30 of whom were hospitalized for conditions other than nephrotic syndrome (excluding known cases of thyroid disease) and 30 of whom were diagnosed with nephrotic syndrome (12). T4 and T3 levels were low in nephrotic syndrome patients. In the nephrotic syndrome group, thyroid stimulating hormone levels were higher. Children under the age of six years were shown to have a higher prevalence of hypothyroidism (12).

In 2016, Ebadi A et al, conducted a study on 20 children diagnosed with Nephrotic syndrome who were randomly participated in the study to assess their thyroid markers levels, two groups of children: a normal group and a group of nephrotic syndrome patients. The participants were divided into two groups: a normal group and a group of nephrotic syndrome patients. Blood samples were tested weekly for serum T3, T4, and thyroid stimulating hormone levels by ELISA (Enzyme linked immunosorbent assay) to determine the actual state of their thyroid function, as well as urine protein to determine whether patients had Nephrotic syndrome. T4 and T3 levels were low in nephrotic syndrome patients and thyroid stimulating hormone levels were high, indicating hypothyroidism. However, T4 levels were much lower in nephrotic syndrome patients when compared to the normal group.(13)

Primary hypothyroidism, both overt and subclinical, is more prevalent in patients with nephrotic syndrome, but not hyperthyroidism. (20).

Patients who respond well to steroids have an excellent long-term prognosis and a low risk of developing chronic kidney disease, despite they often experience frequent relapses and have a protracted illness course(21) . Approximately 20% of patients with Idiopathic Nephrotic Syndrome will not respond to glucocorticoid therapy. The prognosis is poorer for patients with idiopathic steroid-resistant nephrotic syndrome., as kidney survival rate in white children is approximately 50% at 10 years and even worse in Blacks or Hispanic children(22).

In 2017, Marimuthu V et al published a document in which they recruited 30 children (ages 1 to 18) with idiopathic Steroid resistant nephrotic syndrome and 30 healthy controls for a cross-sectional research.(23). This study sought to determine how often nonautoimmune subclinical and overt hypothyroidism is in children with idiopathic Steroid Resistant Nephrotic Syndrome. In 10 of the 30 children with idiopathic SRNS, overt hypothyroidism was identified. When compared to controls, children with Steroid Resistant Nephrotic Syndrome had a higher mean (SD) TSH value of 4.55 (4.64) mIU/L. According to the study, the prevalence of subclinical and overt hypothyroidism in idiopathic Steroid Resistant Nephrotic Syndrome appears to be high, with over one-third of children having overt or subclinical non-autoimmune hypothyroidism.

Hypothyroidism has been described in children with steroid-resistant nephrotic syndrome. Dagan et al (24) published a case report on five children aged 3 to 11 years with Steroid Resistant Nephrotic Syndrome who were observed for 5-42 months. Without any signs of autoimmune thyroiditis, the children developed hypothyroidism (low free thyroxine and high thyrotropin levels). These patients' renal functions deteriorated

over time, ultimately unresponsive to all treatments. Only after achieving end-stage renal illness and starting hemodialysis did the thyroid hormone level return to normal (26).

Steroid resistant idiopathic nephrotic syndrome as well as steroid dependent have been noted to be high contributors to progressive decline in renal functions associated with further loss of protein resulting in loss of Thyroid Hormones, Thyroid Binding Globulin and becomes a vicious cycle without treatment.

Thyroid hormone derangements can persist in the remission period, according to the research mentioned above, necessitating thyroid hormone screening and monitoring.

2.5 Risk factors associated with thyroid hormone dysfunction.

2.5.1 Corticosteroids.

The mainstay treatment of idiopathic nephrotic syndrome is prolonged durations of high dose glucocorticoids with an aim of achieving remission. (25). The exact mechanism of action of corticosteroids is unknown but has been postulated to suppress T- cell dysfunction that causes podocytes foot processes effacement due to a rise in circulating factors(26). Thyroid function is altered by these glucocorticoids, which decrease Thyroid Stimulating Hormone secretion while increasing FT4 and FT3 levels.(27) , and decrease in conversion of T4 to T3 (28). In untreated nephrotic syndrome, continued urinary losses of T4,T3 and Thyroid binding globulin gradually results in developing mild hypothyroidism.(29).

Kano et al., 1994 carried out a study on five children with idiopathic nephrotic syndrome without renal insufficiency investigating the effect of prednisone on thyroid function these children. Prednisone was administered to each patient once a day for four weeks, followed by a two-week taper. Over the next 18 weeks, the daily dose was lowered every two weeks. Thyroid function tests was undertaken during the active period of the disease, while it was untreated, 4 days after prednisone treatment, 3 weeks later, and during remission. (25)

Untreated nephrotic children had large decreases in serum T4, T3, and Thyroid binding globulin concentrations and significant increases in thyroid stimulating hormone concentrations, according to the findings. The hormones continually decreased with intake of prednisone and increased after 9 weeks of cessation of prednisone.

In nephrotic children, blood T4, T3, and Thyroid binding globulins levels were much lower than in normal children, according to Etling and Fouque (1982)(29). There was no change in free T4 but a slight increase in levels of thyroid stimulating hormone. Thyroid hormone serum levels were lower than normal during total

or partial remission, but higher than during nephrotic syndrome. The excretion was similar to normal excretion during entire remission.(29)

2.5.2 Renal Insufficiency.

Thyroid function abnormalities are frequently more severe when impaired kidney function complicates the nephrotic syndrome than when either renal failure or the nephrotic syndrome are present alone. (24).

A cross-sectional study was conducted in a specialized pediatric medical care center in Madrid investigating thyroid dysfunction in children with chronic renal failure. Findings to the study was 14 out of the 50(28%) patients in the study had thyroid dysfunction. Nine children had hypothyroidism in the subclinical stage, three had euthyroid sick syndrome, and two had primary hypothyroidism. It was concluded that a systematic screening of thyroid hormone levels was paramount in children with chronic kidney disease(30)

Hypothyroidism is linked to a reduction glomerular filtration rate(GFR) and the total renal blood flow, which leads to higher serum creatinine levels, decreased sodium reabsorption, hyponatremia, and a decreased ability to dilute urine(31). Increased renal blood flow, glomerular filtration rate and tubular reabsorption are all associated with hyperthyroidism, resulting in lower serum creatinine levels(32). These changes normalize after treatment of thyroid dysfunction (33)

2.5.3 Relapses and duration of illness.

There is scanty literature around relapses and duration of Nephrotic syndrome being factors associated with thyroid hormone derangements. Low thyroid hormones may be linked to long-term disease and recurrent relapses due to the gradual loss of proteins in urine over time and long-term usage of corticosteroids. Also, nephrotic syndrome may complicate and result in chronic kidney disease further worsening the level of proteinuria leading to decreased levels of thyroid hormones, thyroid binding globulin and elevated thyroid stimulating hormone.

2.4 SUMMARY OF LITERATURE REVIEW

Table 3: Summary of Literature Review Articles

STUDY TITLE, AUTHOR, YEAR& COUNTRY	STUDY TYPE STUDY POPULATION STUDY SETTING	RESULT
Thyroid dysfunction in children with idiopathic nephrotic syndrome attending a paediatric hospital in Qazvin, Iran Saffari et al, March 2016- March 2018 Qazvin, Iran	Case control study 73 with nephrotic syndrome (49 active disease, 24 in remission) 74 healthy participants Paediatric hospital in Qazvin, Iran	34.2% of those with nephrotic syndrome had elevated TSH levels. 51% of those in active disease and 95.8% of those in remission had euthyroid
The relationship between thyroid dysfunction and nephrotic syndrome: a clinicopathological study. Ling Z et al 2019 China	Clinicopathological Study 317 patients with nephrotic syndrome	82% had an abnormality on TFTs. 32% Hypothyroidism, 24% SCH, 37% Euthyroid sick syndrome Associated with high urine protein levels, dyslipidemia, hypoalbuminemia and high creatinine
Subclinical Hypothyroidism in children with idiopathic Nephrotic syndrome in a tertiary institution in Southwest Nigeria. A.U Solarin et al, October 2022 Southwest, Nigeria	Comparative Cross Sectional Study 200 children between ages 1-15 years: 100 children with N.S and 100 Children of the same age and gender matched without Nephrotic Syndrome. Lagos State University Teaching Hospital, Nigeria	The prevalence of SCH, was significantly higher in N.S subjects (24.1% vs 2% p=0.006) Of these 24.1% were aged 11-15 years old and majority were female (19.4%) 26.3% of the SCH subjects had SRNS.3 folds odd of developing SCH.

		Average values of serum albumin and protein were also low in this patient with SCH.
Non-autoimmune subclinical and overt hypothyroidism in idiopathic steroid resistant nephrotic syndrome in children. Marimuthu et al, 2017	Cross sectional study 30 children aged 1 to 18 years with idiopathic Steroid resistant nephrotic syndrome and 30 healthy controls.	Nonimmune subclinical and overt hypothyroidism was detected in 10 out of 20 children with idiopathic SRNS
Hypothyroidism in children with steroid resistant nephrotic syndrome Dagan et al, 2012 Tel Aviv University, Israel	Case report of 5 children between age 3-11 years. These children had a diagnosis of idiopathic steroid resistant nephrotic syndrome	All patients presented with hypothyroidism. In 2 children hypothyroidism resolved in those that nephrotic syndrome remitted. In 1 patient the thyroid levels were still low despite remission, One child died
Thyroid function in patients with idiopathic Nephrotic syndrome. Shivendra Singh et al, 2021	Prospective observational study 100 patients: 42 children and 58 adults.	3% overt hypothyroidism 18% had subclinical hypothyroidism, Most hypothyroid cases belonged to SRNS subgroup. Serum TSH showed a negative correlation with 24h proteinuria and a negative correlation with serum albumin

STUDY JUSTIFICATION AND OBJECTIVES

2.6 Justification

Childhood idiopathic nephrotic syndrome in Africa is one of the commonest renal diagnoses and an attributable cause to chronic kidney disease (CKD). Impaired kidney functions can affect thyroid hormone metabolism. Hypothyroidism has been noted to have negative impact on the outcome of nephrotic syndrome such as prolonged duration to remission, progression to renal failure.

Moreover, more complications associated with nephrotic syndrome may be exacerbated by thyroid hormone derangements for example, decreased growth velocity, mental retardation, and progression to renal failure.

Therefore, thyroid hormone evaluation is crucial in patients with childhood nephrotic syndrome as it will have impact on the response to treatment, minimize complications and improve the health of the patient.

This study seek data to describe the nature and magnitude of thyroid hormone derangements in nephrotic syndrome children given the absence of data in Kenya.

The data will enable guidelines to be established in screening, timely recognition, and treatment of thyroid hormone derangements as one of the complications of nephrotic syndrome that may lead to further morbidity or mortality.

2.7 Objectives

2.7.1 Research Question

What is the prevalence of thyroid hormone imbalances in children aged 1-17 years with Idiopathic Nephrotic Syndrome who attend the Kenyatta National Hospital's paediatric renal clinic?

2.7.2 Broad objective

To determine the prevalence of thyroid hormone derangement among children with paediatric Idiopathic Nephrotic Syndrome

2.7.3 Specific objective

Describe the various thyroid dysfunction classifications in children with nephrotic syndrome.

2.7.4 Secondary Objective

To identify the various risk factors linked to thyroid dysfunction in children with Nephrotic Syndrome. This includes duration of illness, duration of corticosteroid or immunosuppressant use and number of relapses per year.

CHAPTER 4: METHODOLOGY

4.1 Study Design

A prospective cross-sectional study evaluating the prevalence of thyroid hormone derangements in children diagnosed with idiopathic nephrotic syndrome.

4.2 Study site

The research took place at Kenyatta National Hospital's paediatric renal clinic. Kenyatta National Hospital is the country's largest and most important referral hospital. Which is also the teaching facility for the College of Health Sciences, University of Nairobi. Patients from Nairobi and its environs, as well as referrals from all other hospitals in Kenya and its bordering countries, are treated at the hospital.

The paediatric renal clinic takes place every Friday morning and is run by a team of certified paediatric nephrologists, paediatric nephrology fellows and paediatric registrars under university of Nairobi attached to renal rotation. Approximately 15 to 20 patients are reviewed at the day of clinic. This is when there is first contact with new patients or follow-up based on date dependent on the urgency of their condition of patients who were admitted in the K.N.H paediatric wards. Routine evaluation of urine analysis, kidney function tests and albumin levels. Thyroid evaluation tests are not routinely done in the paediatric renal clinic at Kenyatta National Hospital, and this study will be completely financed, with no fees borne to the study participants.

4.3 Study duration

The study was conducted over a period of 5 months in the paediatric renal clinic located in Kenyatta National Hospital.

4.4. Study Population

Children aged 1-17 years with a diagnosis of nephrotic syndrome based on clinical and laboratory findings undergoing care at Kenyatta National Hospital.

Inclusion Criteria

1. Patients with nephrotic syndrome- based on clinical and laboratory findings.
2. Patients more than 3 weeks post discharge from the wards.
3. Patients aged 1-17 years attending Paediatric renal clinic.
4. Informed consent given.

Exclusion Criteria

1. Preexisting thyroid disease before/ on diagnosis of Nephrotic syndrome or hypothalamic pituitary axis dysfunction (trauma to pituitary gland, pituitary tumors)
2. Children with a confirmed secondary cause of Nephrotic syndrome. This includes Systemic Lupus Erythematosus, chronic hepatitis B Infection, Vasculitides, HIV, Malignancies, Drugs.
3. Patients in relapse of disease. Defined as proteinuria >+2 for 3 consecutive days.
4. Children with malabsorption or moderate to severe protein energy deficiency or protein losing enteropathy.
5. Children with chronic liver diseases.
6. Children with less than 1 month in duration of Nephrotic Syndrome diagnosis.

4.5. Sample Size

- For a descriptive and analytical investigation, the sample size was estimated. All subjects who fulfilled the inclusion requirements were included. Data of patients discharged from the paediatric ward and on follow up in the paediatric renal clinic with a diagnosis of nephrotic syndrome between the years 2018-2021 was retrieved from the Health & Information centre based in Kenyatta National Hospital. Data is stored in the servers with codes according to International Code of Diseases. The average estimated study population that fits the inclusion criteria is 80 children. A representative sample as drawn from this finite population and sample size will be determined as follows: Where,

n: = sample size with finite population correction

N= size of the target population= 80

Z= Z statistic for 95% level of confidence=1.96

e = margin of error= 5%

P= is the effect proportion from past studies (34.2%)

The study by Saffari et al. 2020 on Thyroid dysfunctions among children with idiopathic nephrotic syndrome in Iran showed that 34.2% had deranged thyroid function. Sample size formula is as below(34)

$$n = N \times \frac{Z^2 \times P \times (1-P)}{e^2} \div \left(N-1 + \frac{Z^2 \times P \times 1-P}{e^2} \right)$$

e²

$$n = 80 \times \frac{1.96^2 \times 0.34(1-0.34)}{0.05^2}$$
$$\frac{80-1 + [1.96^2 \times 0.34(1-0.34)]}{0.05^2}$$

$$n = 80 \times \frac{[345]}{[(79+345)]}$$

n = 65

Sampling Method

To achieve the targeted sample size, all patients who met the inclusion criteria were sampled consecutively in order of attendance to the clinic in the time interval of the research.

Study Tool

Participant's data was collected from the participants and from parents/caregivers of the participants and from the patient's hospital files using an interviewer guided data collection tool.

4.6 Study Procedures

RECRUITMENT

The lead investigator retrieved a list of patients who are scheduled for paediatric renal clinic that week. The files were scrutinized, and those who meet the inclusion criteria and have a diagnosis of idiopathic nephrotic syndrome were selected. The patients who were present during the clinic day were taken through the second step of the recruiting procedure, which involves obtaining informed consent and assent.

SAMPLING TECHNIQUE

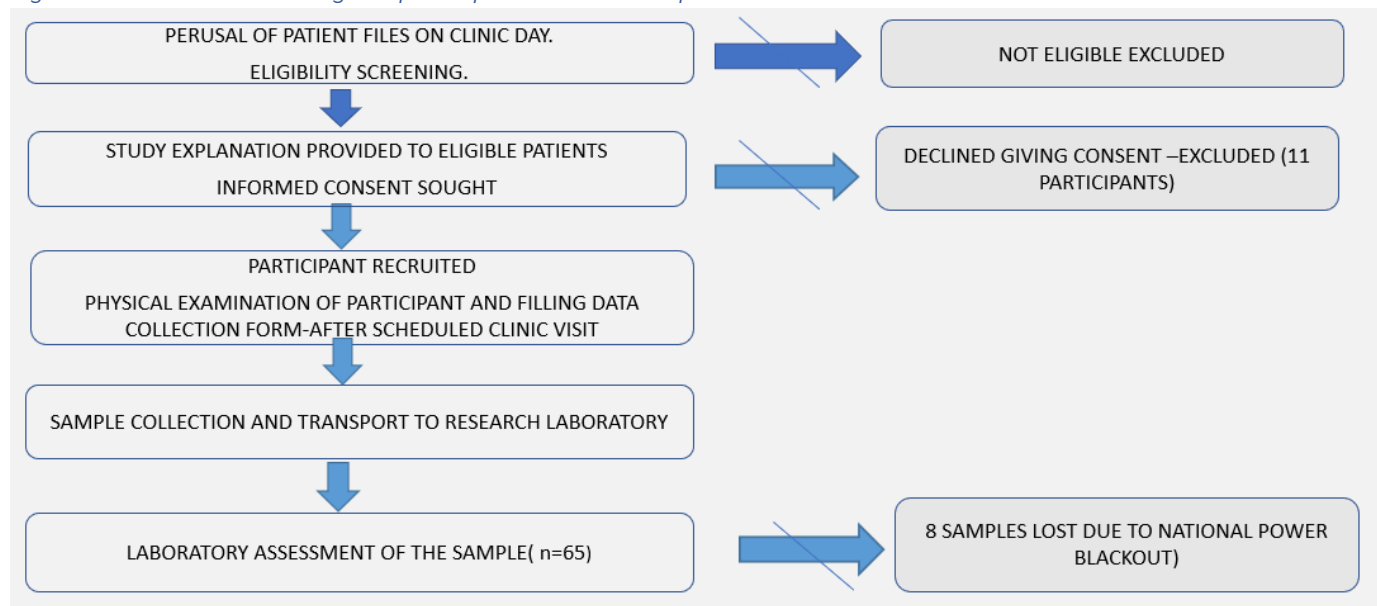
All consecutive patients who meet the inclusion criteria were assessed for eligibility and recruited until the sample size is achieved.

ADMINISTRATION OF CONSENT FORM

Patients who met the inclusion criteria were approached as they signed up for the clinic visit. A brief introduction was made to the details of research and selected participants were requested to spare some time after completing their scheduled clinic visit for detailed information of the research. On acceptance, after the scheduled visit the study participant were moved to a secluded room and a written consent in English or Kiswahili will be obtained. The parent or care giver of children were requested for informed consent, which includes information about the study's goal, benefits, and risks. Participants aged 7 to 17 signed an assent form to participate in the study. The consent process was free of coercion and entirely voluntarily. Any questions or concerns regarding the study were addressed at this point. Participants were notified that they can withdraw from the research at any time before their data is processed, with no implications. The researcher obtaining the consent countersigned the consent form. The participant remained with a copy of the consent form which included contacts of the investigators. A serial number was provided representing each patient partaking the study for privacy of patient information.

The study subjects did not incur any financial costs, as the research is sponsored by the principal investigator.

Figure 1: Flow chart showing the participant recruitment process



4.7 Study Variables

4.7.1 Independent Variables

Table 4: Table Summarizing Study Variables

INDEPENDENT VARIABLE	DEFINITION
Hypoalbuminemia	Serum albumin concentrations of less than 3 g/dL (30 g/L) are considered low.
Persistent Proteinuria	Defined as presence of protein in urine >+1 on 3 consecutive days despite being on treatment
Prolonged Glucocorticoid use	Defined as the use of glucocorticoids for longer than 3 months regardless of the dosing and frequency.
Cyclosporine Use	Defined as patients who are on management using cyclosporine

Frequent N.S relapses	Relapses are defined as four or more each year or two or more in the first six months after diagnosis.
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Sociodemographic factors	This includes: -age of the patient -gender of the patient -residence: whether rural or urban
Age at diagnosis of Nephrotic Syndrome	Ages between 1 to 17 years at diagnosis of idiopathic Nephrotic Syndrome

4.7.2 Dependent Variables

The study dependent variable was thyroid hormone levels in children aged 1-17 years who have a diagnosis of Nephrotic syndrome.

The thyroid hormone levels can either be high, low, or normal levels in reference to the ranges provided by the laboratory evaluating the samples.

4.8 Data Collection Procedures and Quality Assurance Procedures

Patients who met the inclusion criteria were requested to have a small individual interview after being attended to at their scheduled clinic visit. Selected participants were taken through the study details and its requirements together with the consent form. Those who volunteer to the study signed a consent form and assent form those between ages 7-17. After consenting to the study, a study data collection tool which includes physical examination – weight, thyroid exam was administered according to the inclusion criteria above. Recent results from the routine laboratory tests done – urinalysis, liver function test and Kidney function tests was input in the data collection tool. Target oriented history of symptoms and physical

examination findings was filled in the data collection form. Later specimen collection was carried out by the principal investigator.

Approximately 2 mls of venous blood collected in the appropriate serial number tagged vacutainer, stored in a laboratory cooler box. Pre-analytical quality measures include exclusion of hemolyzed samples or minimal sample amounts. The samples will be transported to a laboratory that has been certified by the Kenya National Accreditation System (KENAS) and is also ISO certified.

Post analytical measures including data interpretation was carried out using the reference ranges given by the reagents manufacturer and results counter checked and signed by two laboratory personnel to ensure there was no transcription error.

The files were marked with a sticker which contained the serial number assigned to the patient so as to avoid duplication in the recruitment process.

4.9 Ethical Consideration

Ethical approval and permission were obtained from the respective ethics boards and administrative offices in the University of Nairobi (UoN) and Kenyatta National Hospital (KNH) Ethics and Research Committee (KNH/UoN, ERC). Approval number P226/03/2022

Informed consent was taken and patients who decline were excluded from the study without bias. Pre consent counselling involved:

1. Adequately explaining and informing participants on research nature and primary goal.
2. Detailed explanation of the procedures with any risk or discomfort explained.
3. Assurance that participation in the study is entirely optional, with no consequences if one chooses to leave at any time.
4. Confidentiality of patient information, specimen and results will be maintained.
5. Assurance of free access to the results and medical interpretations.

During the data collection period measures to prevent COVID-19 transmission were included: wearing surgical masks, hand hygiene before and after handling any patient and ensuring physical distance at least 1.5 meters when interviewing the caregivers/patients. Instruments used to collect data and collect blood samples of the children were sterile before and after use to prevent contact spread of the virus. This study

also excluded all sick patients who require admission including those who may have COVID-19 and only involves patients who are attending their routine outpatient follow up clinics. Throughout the study period the investigators complied with all laws and regulations put in place to prevent the spread of COVID-19.

Results obtained was analyzed with the primary investigator and the supervisors of the research. Thereafter the primary investigator explained the study to the primary physician in KNH paediatric renal clinic and discussed the abnormal test results. Any abnormal result was communicated via the mobile number provided during consent taking first to the caregiver of the study participant.

Participants in the study with the caregiver will be required to come for a scheduled review and further discussion of the test result and if treatment is needed.

4.10 Data Management and Analysis.

The data recorded in data collection tool was coded and entered to Excel using excel data entry forms. Afterwards, the data was imported into R 4.1.2 for cleaning and analysis. Recoding responses, deleting duplicate variables, and identifying the levels of a variable are all part of the data cleaning process.

Exploratory analysis was conducted in form of charts and tables. Descriptive analysis was carried out by use of means and standard deviations for continuous variables e.g., weight, age, and duration of steroid use. Categorical variables e.g., persistence of proteinuria or cyclosporine use will be presented using frequencies and proportions.

The prevalence of thyroid dysfunction was presented as a percentage and as a proportion with 95% confidence interval.

The association between the outcome i.e., thyroid dysfunction versus normal thyroid function and albumin levels whether normal or not, persistent proteinuria or not and whether on cyclosporine use was evaluated using Pearson's chi square test or Fisher's exact test. The relationship between the outcome and each categorical predictor variable, such as thyroid dysfunction and duration of illness and assessed using crude odds ratios.

A proportional ordinal logistic regression model was fitted to assess for the impact of each independent variable on the three categories of thyroid hormones. The significance of the results was evaluated using p-values and odds ratios. P-values equal to or less than 0.05 was considered significant. Odds ratios was presented with their 95% confidence intervals. A confidence interval containing the value 1 was considered statistically insignificant. A multivariable regression model was fitted for factors that were significant

under bivariate analysis to assess the net effect of the independent variables after adjusting for the effect of confounding.

STUDY RESULTS DISSEMINATION PLAN

The study's findings were presented to the Department of Paediatric and Child Health at the University of Nairobi (UON) as part of the Master of Medicine program's requirements. Hard copies were submitted to the University of Nairobi's repository for record keeping. The findings were shared with the KNH Office of the Head of Department to improve patient care. Finally, the findings will be submitted to scientific publications for publication.

CHAPTER 5: RESULTS

This chapter will commence by presenting the sample population demographic data to understand the composition and representativeness of the sample. Later descriptive statistics of the study population will be analyzed to assess prevalence and risk factors of thyroid hormone dysfunction in children with nephrotic syndrome.

5.1 Demographic Characteristics of Study Group

This study attained a total of 65 participants on follow up for nephrotic syndrome who fulfilled the inclusion criteria and after obtaining consent and assent. The study participants were aged 1- 17 years old with the youngest participant being 4 years old and the oldest being 17 years old. The median age of the participants was 11.0 years with an interquartile range of 8.0 to 14.0 years. In terms of age groups, 24% (16 out of 65) of the participants were aged below 8 years, and 34% (22 out of 65) were aged between 8-12 years. Those aged between 13-17 years were the majority at 42% (27 out of 65).

The majority, 68% (44 out of 65) of the children were males and the rest were females. Urban dwellers represented the majority, 58% (35 out of 65) of the children and 42 % (30 out of 65) were rural dwellers (table 5)

Table 5:Demographic Characteristics

<i>Variable</i>	<i>Detail</i>	<i>Frequency/Median</i>	<i>Percent (%) /IQR</i>
<i>N = 65</i>			
<i>Age</i>	<8 years	16	24
	8-12 years	22	34
	13-17 years	27	42
<i>Age</i>	Age in years	Median = 11.0	IQR = 8.0, 14.0
<i>Gender</i>	Male	44	68
	Female	21	32
<i>Residence</i>	Urban	35	58
	Rural	30	42

Clinical characteristics

Under clinical characteristics of the children, number of relapses, current medications, presence of protein in the urine, albumin levels and physical thyroid examination were analysed. Majority of the children, 58% (38 out of 65) had less than 2 relapses per year. The median number of relapses was 1 with an interquartile range of 1 to 2 relapses. Most of the participants were in remission although having proteinuria of less than

+2, this accounted for 57% (37 out of 65) of the children. Majority of the children had albumin levels in the normal range, 71% (46 out of 65). Majority, 98.5 (64 out of 65) had normal thyroid glands and only one child had an enlarged thyroid.

Table 6: Clinical Characteristics

<i>Variable</i>	<i>Detail</i>	<i>Frequency</i> <i>N = 65</i>	<i>Percent</i> <i>(%)</i>
<i>Number of relapses</i>	Below 2	38	58
	2 and above	27	42
<i>Medication</i>	Cyclophosphamide + Prednisolone	4	6
	Cyclosporine + Prednisolone	14	22
	Prednisolone	37	57
	Prednisolone + Tacrolimus + Mycophenolate mofetil	1	1
	Tacrolimus + Prednisolone	5	8
	None	4	6
	<i>Proteinuria</i>	Yes	37
	No	28	43
<i>Albumin levels</i>	Normal	46	71
	Low	19	29
<i>Thyroid exam</i>	Normal	64	98.5
	Enlarged	1	0.5

On medication, the majority, 57% (37 out 65) of the children were on prednisolone only followed by those on cyclosporine and prednisolone combination at 22% (14 out of 65). Those on cyclophosphamide and prednisolone combination were 6% (4 out of 65) with an equal proportion that was not on medication. Eight percent (5 out of 65) were on tacrolimus and prednisolone combination and 1% on tacrolimus, prednisolone, and mycophenolate mofetil combination. Figure 1 below summarizes this information.

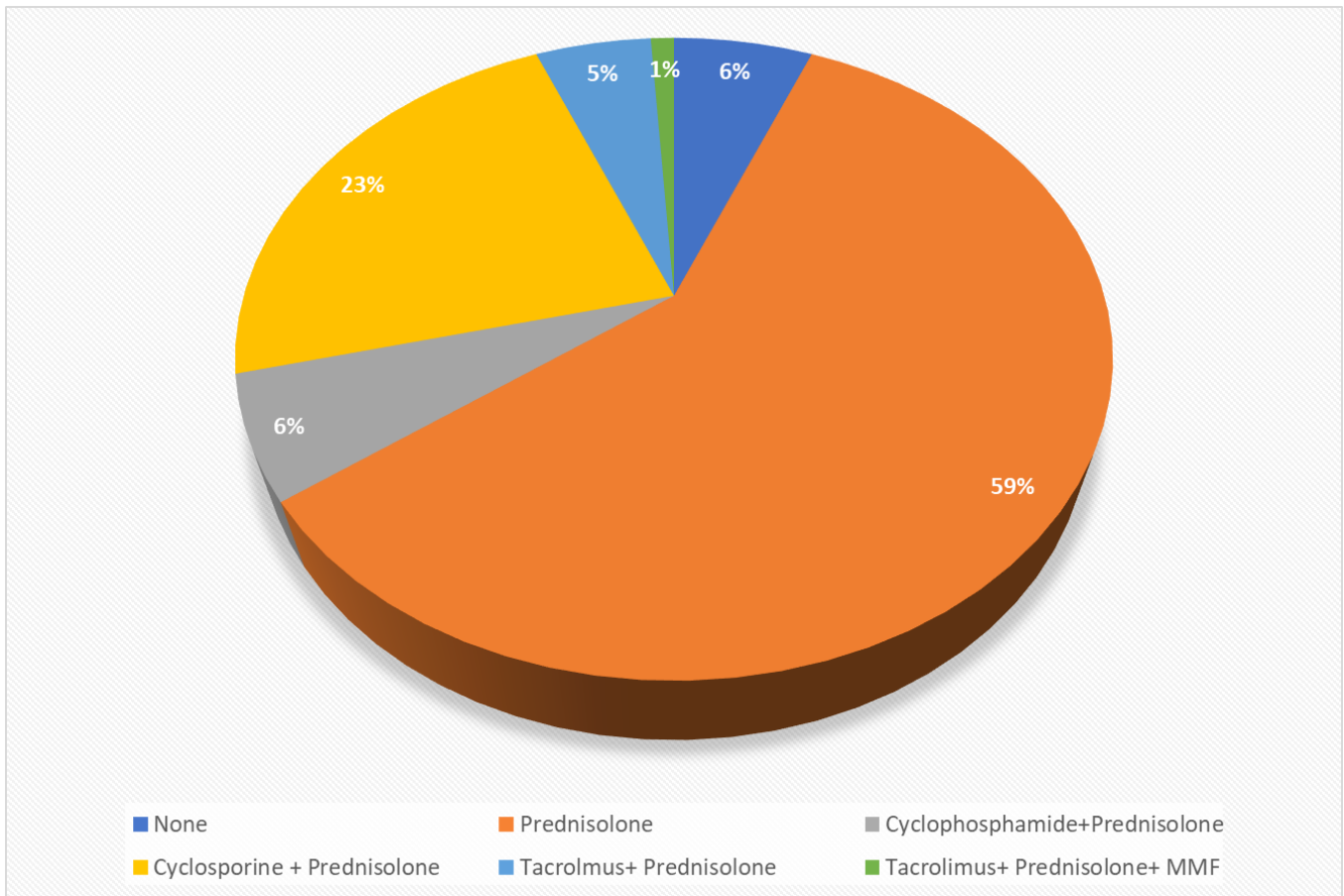


Figure 2: Pie Chart -Summarizing medication use in Study Participants

5.2 Prevalence of Thyroid Hormone Dysfunction in Children with Nephrotic Syndrome

The broad objective of this study was to determine prevalence of thyroid hormone derangements in children aged 1-17 years old with nephrotic syndrome. Most of the study participants had normal thyroid hormone levels, the percentage normal ranging from 70.8% for free T4, to 70.8% for TSH and 87.7% free T3. Of the sample population 29.2 % had elevated TSH levels whereas 0% was recorded for low TSH levels. Free T3 and Free T4 had minimal elevation and reduced levels.

Table 7: Thyroid Hormone Levels as Compared to the reference ranges.

		N= 65 (%)	Mean	S. D	95% C. I
ft3 Reference range (2.2-4.2pg/ml)	Normal	57 (87.7)	3.33(pg/ml)	0.72	3.16-3.50
	Low	5 (7.7)			
	High	3 (4.6)			
ft4 Reference range (0.8-1.7ng/dl)	Normal	46 (70.8)	1.65(ng/dl)	2.29	1.09-2.20
	Low	13 (20)			
	High	6 (9.2)			
TSH Reference range (0.3-3.6iu/ml)	Normal	46 (70.8)	2.88 (uIU/ml)	2.11	2.37-3.39
	Low	0			
	High	19 (29.2)			

The majority, 70.8% of the participants had normal thyroid stimulating hormone levels of 0.3 to 3.6 uIU/ML. The remaining 29% had high levels of TSH above 3.6 uIU/ML. Free triiodothyronine (ft3) level was evaluated in terms of low (<2.2 pg/ML), normal (2.2-4.2 pg/ML) and high levels (>4.2 pg/ML).

Free thyroxine (Ft4) levels, the reference values were low (<0.8 ng/dL), normal (0.8-1.7 ng/dL) and high (>1.7 ng/dL). The prevalence of low FT3 levels was 8% (95% CI 3.8%, 15.6%). The prevalence of low thyroxine levels was 20% (95% CI 12.9%, 29.4%) while that of high thyroxine levels was 9% (95% CI 4.5%, 16.8%) valence of high FT3 levels was 4% (95% CI 1.3%, 10.5%)

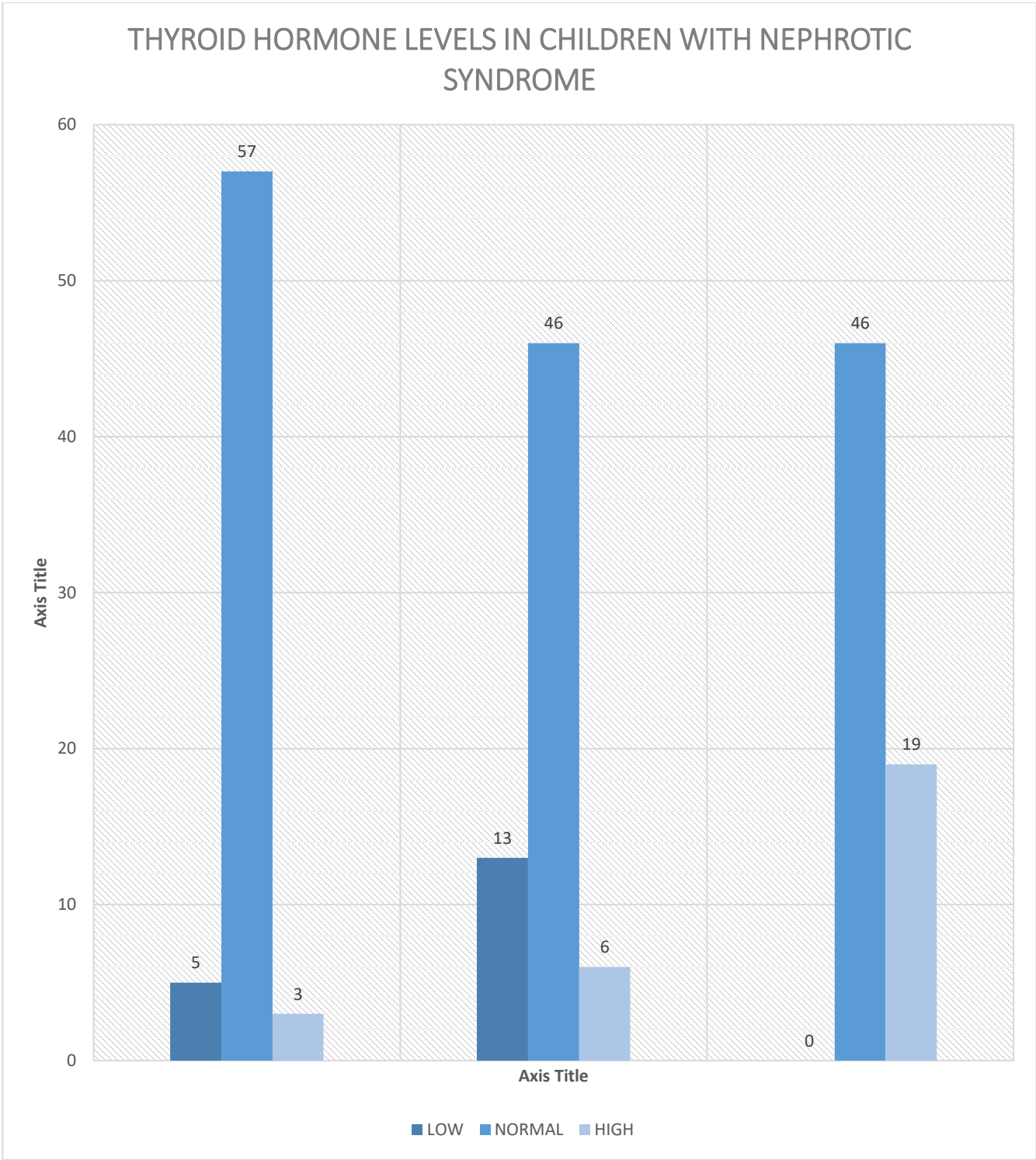


Figure 3: Thyroid Hormone Levels in Children with Nephrotic Syndrome

5.3 Thyroid dysfunction classifications in children with nephrotic syndrome

Thyroid dysfunction is defined as the disruption of thyroid hormone production+/- function characterized by the presence of high or low levels of thyroid stimulating hormone and free thyroid hormone. Various combinations of thyroid hormone levels are used to be able to classify thyroid hormone derangements.

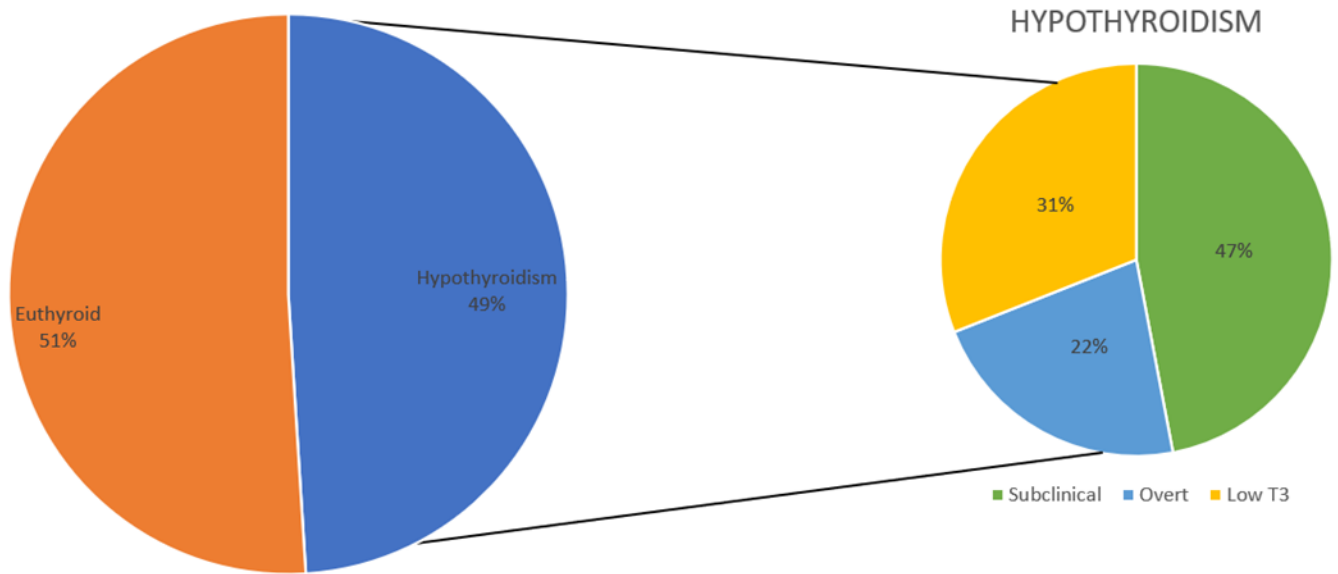
Table 8: Table Below Summarizes The classification of Thyroid Hormone Dysfunction

Clinical state	TSH	fT4	fT3
Euthyroid	Normal	Normal	Normal
Overt Hypothyroidism	High	Low	Normal/low
Subclinical Hypothyroidism	High	Normal	Normal
Hyperthyroidism	Low	High	Normal/High

In this study, 51% (n= 33) were euthyroid- normal levels of thyroid hormone parameters whereas 49% had hypothyroidism (n= 32).

Hypothyroidism was further categorized as subclinical, overt, and low T3 based on the table above. Of the study participants with hypothyroidism, 47% (n= 15) had subclinical hypothyroidism, 31% (n=10) had low T3 syndrome and 22% (n=7) had overt hypothyroidism. The figure below illustrates the above data.

Figure 4: Prevalence of Hormone Dysfunction and the Classifications



12 of the 15 (80%) study participants with subclinical hypothyroidism are of the male gender. 10 out of the 15 (67%) were aged more than 9 years. Most of the children with subclinical hypothyroidism had less than 2 relapses per year (67%). 60% of those with subclinical hypothyroidism had steroid resistant nephrotic syndrome whereas 40% had steroid sensitive nephrotic syndrome. The table below summarizes details related to subclinical hypothyroidism in the study participants.

Table 9: Summary of characteristics associated with subclinical hypothyroidism.

SUBCLINICAL HYPOTHYROIDISM(n=15)		
Gender	M=12	F=3
Age	< 9years= 5	> 9years=10
Relapses	< 2/year=10	> 2/year=5
SSNS	6	
SRNS	9	

5 of the 7 (71%) study participants with overt hypothyroidism are of the male gender. 5 out of the 7 (71%) were aged more than 9 years. Many of the children with overt hypothyroidism had less than 2 relapses per year (57%). All the study participants with overt hypothyroidism had steroid resistant nephrotic syndrome. The table below summarizes the information below:

Table 10: Summary of characteristics associated with overt hypothyroidism.

OVERT HYPOTHYROIDISM (n=7)		
Gender	M=5	F=2
Age	< 9years=2	> 9years=5
Relapses	< 2 years=4	> 2years=3
SSNS	0	
SRNS	7	

5.4 Risk Factors Linked to Thyroid Dysfunction in Children with Nephrotic Syndrome

For the factors associated with the derangement of thyroid hormones, we fitted a binary logistic regression model (the outcome has two levels; hypothyroidism vs. euthyroid) to assess whether the factors under study were significantly associated with thyroid hormone derangement. The p-values were generated either using Fisher's exact test (more than 20% of the cells have counts less than 5) or chi square test.

Table 11: Factors associated with hypothyroidism in nephrotic syndrome.

Variable	Detail	Thyroid hormone		Crude OR (95% CI)	P value
		Hypothyroidism	Euthyroid (Ref)		
		32	33		
Gender	Female	7	14	0.38 (0.13, 1.13)	0.08
	Male	25	19	Reference	
Relapses	2 and above	17	10	2.61 (0.94, 7.20)	0.06
	Below 2	15	23	Reference	
Age	<8 years	8	7	Reference	
	8-12 years	7	15	0.60 (0.16, 2.28)	0.45
	>12 years	18	9	2.57 (0.72, 4.82)	0.14
Duration of illness	4 years and above	8	7	1.23 (0.39, 3.93)	0.72
	Less than 4 years	24	26	Reference	
Proteinuria	Present	24	13	4.62 (1.60, 13.35)	0.04*
	Absent	8	20	Reference	
Albumin	Low	15	4	6.40 (1.82, 22.4)	0.002*
	Normal	17	29	Reference	
Medication	Combination	16	8	Reference	
	None	0	4	NA	0.14
	Prednisolone	16	21	0.38 (0.13, 1.11)	0.11

As shown in table 11 above, proteinuria and albumin levels were significantly associated with thyroid hormone levels at 5% significance level; p values are above 0.04 and 0.002 respectively.

Interpretation of the odds ratios

The odds of having hypothyroidism for a female child were 0.38 those of a male child OR 0.38 (95% CI 0.13, 1.13)

The odds of having hypothyroidism for children who had 2 or more relapses were 2.61 times the odds of the children who had had less than 2 relapses OR 2.61 (95% CI 0.94, 7.20).

The children who had proteinuria were 4.62 times more likely to have hypothyroidism compared to those who did not have proteinuria OR 4.62 (95 % CI 1.60, 13.35). children who had low albumin levels were 6.40 times more likely to have hypothyroidism compared to those who had normal albumin levels.

Multivariable analysis

We fitted a multivariable model for the factors that were significant under bivariate analysis for the purpose of adjustment.

Table 12: Factors associated with deranged thyroid hormone levels.

Variable	Detail	Deranged thyroid hormones		Crude OR (95% CI)	P value
		Hypothyroidism (n=32)	Euthyroid (Ref) (n=33)		
Proteinuria	Present	24	13	3.94 (1.31, 12.75)	0.02
	Absent	8	20	Reference	
Albumin	Low	15	4	5.46 (1.57, 22.74)	0.01
	Normal	17	29	Reference	

Both albumin level and proteinuria remained significantly associated with derangement of thyroid hormones at 5% significance level, p values 0.01 and 0.02, respectively.

After adjusting for proteinuria, children who had low albumin levels were 5.46 times more likely to have hypothyroidism compared with those who had normal albumin OR 5.46 (95% CI 1.57, 22.74). On the other hand, after adjusting for albumin levels, children who had proteinuria were 3.94 times more likely to have hypothyroidism compared to those who did not have proteinuria OR 3.94 (95% CI 1.31, 12.75).

CHAPTER 6: DISCUSSION

In both the acute phase and remission of nephrotic syndrome, abnormalities in thyroid hormone levels have been observed. This study was conducted to determine the prevalence of thyroid hormone imbalances and to evaluate the classifications and associated risk factors of thyroid dysfunction in children with idiopathic nephrotic syndrome undergoing follow-up care at the paediatric nephrology clinic of Kenyatta National Hospital.

The prevalence of thyroid hormone derangements was 49% among children with idiopathic nephrotic syndrome undergoing follow-up, compared to 51% among those who were euthyroid. 32 of the 65 study participants (49%) with thyroid hormone derangements were classified as having hypothyroidism. This is lower than that reported in previous studies carried out evaluating the prevalence of thyroid hormone derangements in children with nephrotic syndrome. Atish Kumar et al reported (2020-2021) 62% had altered thyroid hormone levels. Contrastingly, Shikha Sharma et al showed a lower prevalence of 20% of the children with nephrotic syndrome (36).

The thyroid hormone derangements were applied to categorize the various thyroid hormone clinical states: - Hypothyroidism (Subclinical, Overt, and Low t3) and Hyperthyroidism. Zero cases of Hyperthyroidism (low TSH, high fT4 and normal/high fT3) were identified among the study subjects. This is similar to a study by Gilles et al that reported no hyperthyroidism states in a study group of 200 participants with nephrotic syndrome(35). This results can be explained by the progressive loss of proteins that are used in the synthesis of thyroid hormones and thyroid binding globulins in urine in patients with nephrotic syndrome .

In this study, of those with hypothyroidism, 23% (n=15) of the study participants had subclinical hypothyroidism, 11% (n= 7) had overt hypothyroidism and 15% (n=10) had low t3 syndrome. These findings are like those reported by A.U. Solarin et al in Nigeria that reported 24.1% of the study participants had subclinical hypothyroidism and 9.3% had overt hypothyroidism(37) . Similarly, in a study by of the 31 patients, 16 (51.6%) showed abnormal thyroid hormone profiles: 6 had overt hypothyroidism, 8 had subclinical hypothyroidism, and 2 had low T3 syndrome(38). Contrastingly, Shivendra et al (2014), reported 18% and 30% of the participants had Subclinical Clinical Hypothyroidism and Overt hypothyroidism, respectively(39). Subclinical hypothyroidism is noted due to the progressive loss of small amounts of protein in urine due to nephrotic syndrome that ,regardless of being in remission, and this leads to loss of thyroid binding globulin protein that aids in transportation and secretion of thyroid hormones. Overt hypothyroidism is not realized due to loss of minimal protein in children in remission.

Choudhury et al. (40) reported that children with NS had an increased risk of SCH, particularly in the younger age groups. However, we found a higher proportion of children with SCH in the older age group of more than 9 years of age. This may be due to the possibility that older children have a more advanced disease than younger children, resulting in a prolonged duration of NS diagnosis in the older age group. In advanced diseases, functional defects in hormone reabsorption from the proximal tubule are more severe, according to studies (3). In the current study, SCH

was more prevalent in males, although this difference was not statistically significant. Lazar et al. (41) concluded that girls are at a higher risk for persistently aberrant TSH levels and identified female gender as a predictor of elevated TSH levels.

It has been reported in previous studies that there is a difference in protein selectivity and renal handling of free and protein bound thyroid hormone and Thyroid Stimulating Hormone in steroid sensitive and steroid-resistant Nephrotic Syndrome. This study noted that 72.2 % of the participants with Hypothyroidism had a diagnosis of Steroid Resistant Nephrotic Syndrome. This is comparable to a study by A.U Solarin et al that reported Steroid Resistant Nephrotic Syndrome had 3 folds odds of developing hypothyroidism as compared to Steroid Sensitive Nephrotic Syndrome (37). However, 33% of study participants with steroid resistant nephrotic syndrome in Marimuthu et al study had hypothyroidism, 27 % with subclinical hypothyroidism and 6% with overt hypothyroidism(23). This low numbers may be due to less numbers of study participants in the Marimuthu et al study (n=30)(7)

Most of the children, 59% (n=37) in this study were on prednisolone treatment only. Hypothyroidism among children on prednisolone only treatment was 25% (n=16). Children on prednisolone had minimal odds of developing hypothyroidism OR 0.38(0.13-1.11). Corticosteroids act on the hypothalamus to reduce thyrotropin releasing hormone messenger ribonucleic acid levels and on the anterior pituitary gland to decrease TSH secretion which explains why SCH is more common than overt hypothyroidism in NS.

Proteinuria and low serum albumin levels were statistically significant risk factors of deranged thyroid hormone levels in children with idiopathic nephrotic syndrome in this study. Children who had low albumin levels were 5.46 times more likely to have hypothyroidism compared with those who had normal albumin OR 5.46 (95% CI 1.57, 22.74). On the other hand, after adjusting for albumin levels, children who had proteinuria were 3.94 times more likely to have hypothyroidism compared to those who did not have proteinuria OR 3.94 (95% CI 1.31, 12.75). Similarly, A.U. Solarin et al (2022) reported SCH was associated with lower albumin & protein levels AOR 0.754 (95 CI 0.283-2.742) and AOR 0.592 (95% CI 0.183-2.005) respectively (37). Based on our results, the most important predictor of hypothyroidism is hypoalbuminemia which results in five- fold odds of developing hypothyroidism in comparison to normal albumin levels.

Our findings on proteinuria being a significant risk factor to developing thyroid hormone derangements is similar to that of Gilles et al , which illustrated that TSH levels were higher in patients with proteinuria in children with nephrotic syndrome as compared to healthy controls(35). Urinary losses of thyroid hormones in patients with proteinuria result in a stimulation of TSH production. SCH was associated with significantly reduced levels of serum albumin and protein and increased levels of urine protein. Mohamed et al (40) reported that patients with NS in relapse had significantly lower levels of total serum albumin and protein in comparison with cases in remission and control group.

Study Strengths

This study was conducted in a well-established nephrology clinic that follows many children referred from all over Kenya and are reviewed by nephrologists.

Minimal nonparticipation Bias- Most of the caregivers and children approached for the study agreed to participate.

Study Limitations

This study used a cross sectional descriptive design and is a limitation to establish a causal relationship.

Unavailability of Test Reference index in most laboratories in Kenya. Correct evaluation of thyroid health status is centered on the use of suitable reference intervals (RI) e.g., age, gender, body mass index and genetic variants, of the thyroid function tests (TFT) to evaluate the readings of different components of TFT.

Conclusion

Most of the participants in this study were euthyroid (51%) and the prevalence of thyroid hormone derangements among children on follow up for idiopathic nephrotic syndrome in this study was 49%

Subclinical hypothyroidism was the most diagnosed thyroid dysfunction-23%, followed by low T3 levels at 15 % and overt hypothyroidism at 11%.

Steroid Resistant Nephrotic Syndrome, proteinuria & low albumin levels showed an increase in the odds of developing hypothyroidism among children with idiopathic nephrotic syndrome.

Cases of Hyperthyroidism were not derived from the study on children with Nephrotic Syndrome.

Recommendations

There is a need to monitor thyroid hormone profiles in patients with Nephrotic Syndrome especially in those with Steroid resistant Nephrotic syndrome.

Further research on the effects of hypothyroidism on children with idiopathic nephrotic syndrome is needed.

Further research is needed to establish a causal relationship between deranged thyroid hormone levels and Idiopathic nephrotic syndrome.

STUDY BUDGET

Category	Remarks	Units	Unit Cost (KSh)	Total (KSh)
Proposal Development	Printing drafts	200 pages	3	600
	Proposal Copies	10 copies	350	3,500
Data Collection	Stationery Packs (Pens, Paper and Study Definitions)	20	100	2000
	Thyroid Function Test (65 participants)	65	1400	91000
Data Analysis	Statistician	1		20,000
Thesis Write Up				
	Printing drafts	1000 pages	5	5,000
	Printing Thesis	10 copies	500	5,000
Contingency funds (15%)				20,000
Total				147,100

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APPENDIXES

APPENDIX 1: PARENTAL CONSENT FORM IN ENGLISH

Date(date/month/year):

Title of Study: PREVALENCE OF THYROID DYSFUNCTION IN CHILDREN WITH NEPHROTIC SYNDROME ATTENDING CLINIC AT KENYATTA NATIONAL HOSPITAL.

Principal Investigator and institutional affiliation:

Dr. Maureen Machungo (MChB)

Department of Paediatrics and Child health, University of Nairobi.

Telephone Number: 0724-801772

Co-Investigators and institutional affiliation:

Dr. Bashir Admani & Dr. Paul Laigong

Department of Paediatrics and Child Health, University of Nairobi

Introduction:

I would like to inform you about a study being conducted by the above-listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether your child should participate in the study. Feel free to ask any questions about the purpose of the research, what happens if your child participates in the study, the possible risks and benefits, the rights of your child as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide if you want your child to be in the study or not. This process is called 'informed consent'. Once you understand and agree for your child to be in the study, I will request you to sign your name on this form.

You should understand the general principles which apply to all participants in medical research:

- (i) Your child's decision to participate is entirely voluntary.
- ii) You child may withdraw from the study at any time without necessarily giving a reason for his/her withdrawal.

iii) Refusal to participate in the research will not affect the services your child is entitled to in this health facility or other facilities.

May I continue? YES / NO

For children under 18 years of age we give information about the study to parents or guardians. We will go over this information with you and you need to give permission for your child to participate in this study. We will give you a copy of this form for your records.

If the child is between the ages of 7-17 years, he/she can appreciate what is being done and he/she will also be required to agree to participate in the study after being fully informed.

WHAT IS THE PURPOSE OF THE STUDY?

The researchers listed above are interviewing individuals who are on follow up for idiopathic nephrotic syndrome at the paediatric renal clinic at Kenyatta National Hospital. The purpose of the interview is to find out if children with nephrotic syndrome have associated thyroid hormone dysfunction. Participants in this research study will be asked questions about their treatment regimen and a general physical examination will be done. Participants will also have the choice to undergo a blood test that will help check the thyroid levels in the participants.

There will be approximately 65 participants in this study randomly chosen. We are asking for your consent to consider your child to participate in this study.

WHAT WILL HAPPEN IF YOU DECIDE YOU WANT YOUR CHILD TO BE IN THIS RESEARCH STUDY?

If you agree for your child to participate in this study, the following things will happen:

You will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions. The interview will last approximately 15 minutes. The interview will cover explaining the role

of thyroid hormones in humans and the effects associated with deranged thyroid hormones in relation to nephrotic syndrome.

Afterwards in the private examination room, goal-oriented history will be taken and filled in a form attached. Thereafter a general physical examination will be done checking the vital signs, any sign of edema, weight, height and examination of the thyroid gland. This will also be filled in in a form attached.

After the interview has finished, 2 milliliters of your child's blood will also be drawn using aseptic technique. With authorization from the KNH-UoN ERC, the specimen will be sent in a cooler box to a licensed and accredited laboratory to analyze the thyroid hormone levels.

You will be informed about the results.

We will ask for a telephone number where we can contact you if necessary. If you agree to provide your contact information, it will be used only by people working for this study and will never be shared with others. The reasons why we may need to contact you is to convey the results to you and if needed ask for an appointment if treatment may be required if the thyroid hormones are deranged.

ARE THERE ANY RISKS, HARMS, DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify your child in a password-protected computer database and will keep all our paper records in a locked file cabinet. However, no system of protecting confidentiality can be secure so it is still possible that someone could find out your child was in this study and could find out information about your child.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview, or any questions asked during the interview.

We will do everything we can to ensure that the whole interview and examination is done in private.

Furthermore, all study staff and interviewers are professionals with special training in these examinations/interviews.

Your child may feel some discomfort when drawing a blood sample and may have a small bruise or swelling in the puncture area. The utmost care and expertise will be guaranteed during the whole procedure. In case of an injury, illness or complications related to this study, contact the study staff right away at the number provided at the end of this document. The study staff will treat your child for minor conditions or refer the child for treatment for conditions that require more extensive care.

ARE THERE ANY BENEFITS IN THIS STUDY?

Your child may benefit by receiving free thyroid hormone testing, you may be counseled on management of nephrotic syndrome so as your child can have a quality life. We will refer your child to a hospital for care and support if necessary. Also, the information you provide will help us better understand if thyroid hormone derangements is a common complication in children with nephrotic syndrome. This information is a major contribution to science and patient care and may assist in formulating guidelines to better care for children with nephrotic syndrome.

The results from the blood sample will be discussed further with the two research coordinators who are paediatric kidney and endocrine (thyroid) specialists. If the results are normal, you will be called with the principal investigator and results explained to you and will be filed in your hospital file, free for you and your primary doctor to access when needed.

If the results are abnormal, you will be required to come in for a review, where treatment will be started after consultation with the two research coordinators. Results will be filed in your hospital file.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

Since this is a study that does not involve routine blood investigations, the principal investigator will cover all the costs needed.

You will not be required to give any financial aid towards this study.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about your child participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your child's rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to have your child participate in this research is voluntary. You are free to decline or withdraw participation of your child in the study at any time without injustice or loss of benefits.

Just inform the study staff and the participation of your child in the study will be stopped. You do not have to give reasons for withdrawing your child if you do not wish to do so. Withdrawal of your child from the study will not affect the services your child is otherwise entitled to in this health facility or other health facilities.

CONSENT FORM (STATEMENT OF CONSENT)

The person being considered for this study is unable to consent for him/herself because he or she is a minor (a person less than 18 years of age). You are being asked to give your permission to include your child in this study.

Parent/guardian statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered by him or her in a language that I understand. The risks and benefits have been explained to me. I understand that I will be given a copy of this consent form after signing it. I understand that my participation and that of my child in this study is voluntary and that I may choose to withdraw it any time.

I understand that all efforts will be made to keep information regarding me and my child's personal identity confidential.

By signing this consent form, I have not given up my child's legal rights as a participant in this research study.

I voluntarily agree to my child's participation in this research study: Yes No

I agree to have my child undergo testing: Yes No

I agree to provide contact information for follow-up: Yes No

Parent/Guardian signature /Thumb stamp: Date _____

Parent/Guardian printed name: _____

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 knowingly given his/her consent.

Printed Name: _____

Date: _____

Signature: _____

If you have any questions, please contact:

1. Name: Dr. Maureen Machungo
Mobile Number: 0724801772
Email: maureenkwamby91@gmail.com
2. Dr. Bashir Admani
Phone Number: 0721967818
Email: falseir@uonbi.ac.ke
3. Dr. Paul Laigong
Phone Number: 0735769615
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4. 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

APPENDIX 2: FOMU YA RIDHAA YA MZAZI KWA KISWAHILI

Tarehe (siku/mwezi/mwaka):

Kichwa cha Utafiti: KUENEA KWA UKOSEFU WA THYROID KWA WATOTO WENYE NEPHROTIC SYNDROME WANA OHUDHURIA KLINIKI KATIKA HOSPITALI YA TAIFA YA KENYATTA.

Mpelelezi Mkuu na uhusiano wa kitaasisi:

Maureen Machungo (MBChB) Dk.

Idara ya Madaktari wa Watoto na Afya ya Mtoto, Chuo Kikuu cha Nairobi.

Nambari ya Simu: 0724-801772

Wachunguzi-wenza na uhusiano wa kitaasisi:

Dkt. Bashir Admani na Dk. Paul Laigong

Idara ya Madaktari wa Watoto na Afya ya Mtoto, Chuo Kikuu cha Nairobi

UTANGULIZI

Ningependa kukuarifu kuhusu utafiti unaofanywa na watafiti walioorodheshwa hapo juu. Madhumuni ya fomu hii ya idhini ni kukupa taarifa utakayohitaji ili kukusaidia kuamua kama mtoto wako atashiriki au la. Jisikie huru kuuliza maswali yoyote kuhusu madhumuni ya utafiti, nini kitatokea ikiwa mtoto wako atashiriki katika utafiti, hatari na manufaa yanayoweza kutokea, haki za mtoto wako kama mtu wa kujitolea, na jambo lingine lolote kuhusu utafiti au fomu hii ambayo sivyo. wazi. Wakati tumejibu maswali yako yote kwa kuridhika kwako, unaweza kuamua kama ungependa mtoto wako awe kwenye utafiti au la. Utaratibu huu unaitwa 'ridhaa iliyoarifiwa'. Ukishaelewa na kukubali mtoto wako awe kwenye utafiti, nitakuomba utie sahihi jina lako kwenye fomu hii.

Unapaswa kuelewa kanuni za jumla zinazotumika kwa washiriki wote katika utafiti wa

matibabu:

- (i) Uamuzi wa mtoto wako kushiriki ni wa hiari kabisa
- ii) Mtoto wako anaweza kujiondoa kwenye utafiti wakati wowote bila ya lazima kutoa sababu ya kujiondoa kwake.
- iii) Kukataa kushiriki katika utafiti hakutaathiri huduma anazostahiki mtoto wako katika kituo hiki cha afya au vituo vingine.

Naweza kuendelea? NDIO LA

Kwa watoto walio chini ya umri wa miaka 18 tunatoa taarifa kuhusu utafiti kwa wazazi au walezi. Tutapitia maelezo haya nawe na unahitaji kutoa ruhusa ili mtoto wako ashiriki katika utafiti huu. Tutakupa nakala ya fomu hii kwa rekodi zako.

Ikiwa mtoto ana umri wa kati ya miaka 7-17, anaweza kufahamu kinachofanywa na atahitajika pia kukubali kushiriki katika utafiti baada ya kufahamishwa kikamilifu.

NINI KUSUDI LA MASOMO HAYO?

Watafiti walioorodheshwa hapo juu wanawahoji watu ambao wanafuatilia ugonjwa wa nephrotic wa idiopathic katika kliniki ya magonjwa ya figo ya watoto katika Hospitali ya Kitaifa ya Kenyatta. Madhumuni ya mahojiano ni kujua ikiwa watoto walio na ugonjwa wa nephrotic wamehusishwa na shida ya homoni ya tezi. Washiriki katika utafiti huu wataulizwa maswali kuhusu regimen ya matibabu yao na uchunguzi wa jumla wa kimwili utafanywa. Washiriki pia watakuwa na chaguo la kupitiwa damu

Kutakuwa na takriban washiriki wa 65 katika utafiti huu waliochaguliwa kwa nasibu. Tunaomba idhini yako ya kuzingatia mtoto wako kushiriki katika utafiti huu.

JE, NINI KITAENDELEA UKIAMUA KUTAKA MTOTO WAKO AWE KATIKA UTAFITI HUU?

Ukikubali mtoto wako kushiriki katika utafiti huu, mambo yafuatayo yatafanyika: Utahojiwa na mhojiwa aliyefunzwa katika eneo la faragha ambapo unahisi vizuri kujibu maswali. Mahojiano yatachukua takriban dakika 15.

Mahojiano yatashughulikia kuelezea jukumu la homoni za tezi kwa wanadamu na athari zinazohusiana na homoni zilizoharibika za tezi kuhusiana na ugonjwa wa nephrotic.

Baadaye katika chumba cha uchunguzi wa kibinafsi, historia yenye lengo la dalili za utendaji wa tezi iliyoharibika itachukuliwa na kujazwa katika fomu iliyoambatanishwa. Baada ya hapo uchunguzi wa jumla wa kimwili utafanyika kuangalia ishara muhimu, ishara yoyote ya uvimbe, uzito, urefu na uchunguzi wa tezi ya tezi. Hii pia itajazwa katika fomu iliyoambatanishwa

Baada ya mahojiano kukamilika, mililita 2 ya damu ya mtoto wako pia itatolewa kwa kutumia mbinu ya aseptic. Kwa idhini kutoka kwa KNH-UoN ERC, kielelezo kitatumwa katika kisanduku baridi kwa maabara iliyoidhinishwa na iliyoidhinishwa ili kuchanganua viwango

vya homoni za tezi. Utajulishwa kuhusu matokeo. Tutaomba nambari ya simu ambapo tunaweza kuwasiliana nawe ikibidi. Ukikubali kutoa maelezo yako ya mawasiliano, yatatumiwa na watu wanaofanya kazi katika utafiti huu pekee na kamwe hayatahirikiwa na wengine. Sababu ambazo tunaweza kuhitaji kuwasiliana nawe ni kukujulisha matokeo na ikihitajika omba miadi ikiwa matibabu yanaweza kuhitajika ikiwa homoni za tezi zimeharibika.

JE, KUNA HATARI, MADHARA, FURAHA ZINAZOHUSIANA NA UTAFITI HUU?

Utafiti wa kimatibabu una uwezo wa kuanzisha hatari za kisaikolojia, kijamii, kihisia na kimwili. Jitihada zinapaswa kuwekwa kila wakati ili kupunguza hatari. Hatari moja inayoweza kutokea ya kuwa katika utafiti ni kupoteza faragha. Tutaweka kila kitu unachotuambia kama siri iwezekanavyo.

Tutatumia nambari ya msimbo kumtambua mtoto wako katika hifadhidata ya kompyuta iliyolindwa na nenosiri na tutaweka rekodi zetu zote za karatasi kwenye kabati ya faili iliyofungwa. Hata hivyo, hakuna mfumo wa kulinda usiri unaoweza kuwa salama kabisa kwa hivyo bado kuna uwezekano kwamba mtu anaweza kujua mtoto wako alikuwa katika utafiti huu na kupata taarifa kuhusu mtoto wako.

Pia, kujibu maswali katika mahojiano kunaweza kuwa na wasiwasi kwako. Ikiwa kuna maswali yoyote ambayo hutaki kujibu, unaweza kuyaruka. Una haki ya kukataa mahojiano au maswali yoyote yaliyoulizwa wakati wa mahojiano. Tutafanya kila tuwezalo kuhakikisha kuwa mahojiano na mitihani yote inafanyika kwa faragha.

Zaidi ya hayo, wafanyakazi wote wa utafiti na wahojaji ni wataalamu walio na mafunzo maalum katika mitihani/mahojiano haya. Mtoto wako anaweza kuhisi usumbufu wakati wa kuchora sampuli ya damu na anaweza kuwa na michubuko ndogo au uvimbe katika eneo la kuchomwa. Utunzaji wa hali ya juu na utaalumu utahakikishiwa wakati wa utaratibu mzima. Iwapo kuna jeraha, ugonjwa au matatizo yanayohusiana na utafiti huu, wasiliana na wafanyakazi wa utafiti mara moja kwa nambari iliyotolewa mwishoni mwa waraka huu. Wafanyakazi wa utafiti watamtibu mtoto wako kwa hali ndogo au kuelekeza mtoto kwa matibabu kwa hali zinazohitaji utunzaji wa kina zaidi.

JE, KUNA FAIDA YOYOTE KUWA KATIKA UTAFITI HUU?

Mtoto wako anaweza kufaidika kwa kupokea upimaji wa homoni za tezi bila malipo, unaweza kushauriwa kuhusu udhibiti wa ugonjwa wa nephrotic ili mtoto wako aweze kuwa na maisha

bora. Tutampeleka mtoto wako hospitali kwa matunzo na usaidizi ikibidi. Pia, maelezo utakayotoa yatusaidia kuelewa vyema ikiwa mabadiliko ya homoni ya tezi ni tatizo la kawaida kwa watoto walio na ugonjwa wa nephrotic. Maelezo haya ni mchango mkubwa kwa sayansi na utunzaji wa wagonjwa na yanaweza kusaidia katika kuunda miongozo ya utunzaji bora kwa watoto walio na ugonjwa wa nephrotic.

Matokeo kutoka kwa sampuli ya damu yatajadiliwa zaidi na waratibu wawili wa utafiti ambao ni wataalamu wa figo za watoto na endocrine (tezi). Ikiwa matokeo ni ya kawaida, utaitwa pamoja na mpelelezi mkuu na matokeo yatafafanuliwa kwako na yatawasilishwa katika faili yako ya hospitali, bila malipo kwa wewe na daktari wako mkuu kufikia inapohitajika.

Ikiwa matokeo si ya kawaida, utahitajika kuja kwa ukaguzi, ambapo matibabu yataanza baada ya kushauriana na waratibu wawili wa utafiti. Matokeo yatawasilishwa katika faili yako ya hospitali.

JE, KUWA KWENYE SOMO HILI LITAKUGHARIMU LOLOTE?

Kwa kuwa huu ni utafiti ambao hauhusishi uchunguzi wa kawaida wa damu, mpelelezi mkuu atagharamia mahitaji yote. Hutahitajika kutoa usaidizi wowote wa kifedha kwa utafiti huu.

VIPI IKIWA UNA MASWALI BAADAYE?

Ikiwa una maswali zaidi au wasiwasi kuhusu mtoto wako kushiriki katika utafiti huu, tafadhali piga simu au tuma ujumbe mfupi wa maandishi kwa wafanyikazi wa utafiti kupitia nambari iliyotolewa chini ya ukurasa huu. Kwa maelezo zaidi kuhusu haki za mtoto wako kama mshiriki wa utafiti unaweza kuwasiliana na Katibu/Mwenyekiti, Hospitali ya Kitaifa ya Kenyatta-Kamati ya Maadili na Utafiti ya Chuo Kikuu cha Nairobi Nambari 2726300 Ext. 44102 barua pepe uonknh_erc@uonbi.ac.ke.

Wafanyikazi wa utafiti watakurudishia malipo yako kwa nambari hizi ikiwa simu ni ya mawasiliano yanayohusiana na masomo.

UCHAGUZI WAKO MENGINE NI GANI?

Uamuzi wako wa kumfanya mtoto wako ashiriki katika utafiti huu ni wa hiari. Uko huru kukataa au kuondoa ushiriki wa mtoto wako katika utafiti wakati wowote bila dhuluma au hasara ya faida. Wajulishe tu wafanyakazi wa utafiti na ushiriki wa mtoto wako katika utafiti

utasitishwa. Sio lazima utoe sababu za kumwondoa mtoto wako ikiwa hutaki kufanya hivyo. Kuondolewa kwa mtoto wako kutoka kwa utafiti hakutaathiri huduma ambazo mtoto wako anastahili kupata katika kituo hiki cha afya au vituo vingine vya afya.

Nambari ya serial:

FOMU YA RIDHAA (TAARIFA YA RIDHAA)

Mtu anayezingatiwa kwa utafiti huu hana uwezo wa kujikubali kwa sababu yeye ni mtoto mdogo (mtu aliye chini ya miaka 18). Unaombwa kutoa idhini yako ya kujumuisha mtoto wako katika utafiti huu. Taarifa ya mzazi/mlezi Nimesoma fomu hii ya idhini au nimesomewa maelezo.

Nimepata nafasi ya kujadili utafiti huu na mshauri wa utafiti. Nimejibu maswali yangu kwa lugha ninayoelewa. Hatari na faida zimeelezwa kwangu. Ninaelewa kuwa nitapewa nakala ya fomu hii ya idhini baada ya kuitia saini. Ninaelewa kuwa ushiriki wangu na wa mtoto wangu katika utafiti huu ni wa hiari na kwamba ninaweza kuchagua kuuondoa wakati wowote.

Ninaelewa kuwa juhudi zote zitafanywa ili kuweka maelezo kunihusu na ya mtoto wangu kuwa siri. Kwa kutia saini fomu hii ya idhini, sijaachana na haki za kisheria za mtoto wangu kama mshiriki katika uamuzi huu.

Ninakubali kwa hiari ushiriki wa mtoto wangu katika utafiti huu wa utafiti: Ndiyo Hapana

Ninakubali mtoto wangu afanyiwe uchunguzi: Ndiyo Hapana

Ninakubali kutoa maelezo ya mawasiliano kwa ufuatiliaji: Ndiyo Hapana

Sahihi ya Mzazi/Mlezi /Muhuri wa kidole gumba:

Tarehe Jina lililochapishwa la Mzazi/Mlezi:

Kauli ya mtafiti

Mimi, aliyetia sahihi hapa chini, nimeeleza kikamilifu maelezo muhimu ya utafiti huu kwa mshiriki aliyetajwa hapo juu na ninaamini kuwa mshiriki ameelewa na ametoa ridhaa yake akijua.

Jina Lililochapishwa:

Sahihi:

Tarehe:

Jukumu katika utafiti:

Ikiwa una maswali yoyote, tafadhali wasiliana na:

1. Jina: Dkt. Maureen Machungo

Nambari ya simu: 0724801772

Barua pepe: maureenkwamby91@gmail.com

2. Dr. Bashir Admani

Nambari ya simu: 0721967818

Barua Pepe: falseir@uonbi.ac.ke

3. Dr. Paul Laigong

Nambari ya simu: 0735769615

Barua Pepe: drlaigongp@gmail.com

4. Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee
College of Health Sciences

Simu: (254-020) 2726300-9 Ext 44355: Barua pepe: uonknh.erc@uonbi.ac.ke

APPENDIX 3: ASSENT FORM FOR CHILDREN AGED 7-17 YEARS

STUDY TITLE: PREVALENCE OF THYROID HORMONE DERANGEMENTS IN CHILDREN WITH NEPHROTIC SYNDROME IN KENYATTA NATIONAL HOSPITAL.

Principal Investigator and institutional affiliation:

Dr. Maureen Machungo (MBChB)

Department of Paediatrics and Child health, University of Nairobi.

We are doing a research study about a study looking into the number of cases of thyroid hormone changes in children with nephrotic syndrome who attend clinic at K.N.H. Thyroid hormones are substances that are produced by a gland that is in the neck. These substances help your body in various functions such as: growth, heat changes, mood and bone growth.

Permission has been granted to undertake this study by the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UoN ERC Protocol No.

This research study is a way to learn more about people. At least 65 children will be participating in this research study with you.

If you decide that you want to be part of this study a brief interview taking approximately 15 minutes will be carried out. You will be asked if you have some symptoms, and a physical examination will be carried out.

There are some things about this study you should know. The study requires taking a

blood sample from you, and this will be done with the most care and technique to minimize excess bleeding and pain.

When we are finished with this study, we will write a report about what was learned. This report will not include your name or that you were in the study.

You do not have to be in this study if you do not want to be. If you decide to stop after we begin, that's okay too. Your parents know about the study too.

Not everyone who takes part in this study will benefit. A benefit means that something good happens to you. We think the study will benefit you to be able to be checked for thyroid disease and treatment started so that you may be of good health and grow as appropriate.

If you decide you want to be in this study, please sign your name.

I, _____ want to be in this research study.

(Signature/Thumb stamp)

(Date)

APPENDIX 5: DATA COLLECTION TOOL

Serial Number.....

Date.....

Patient’s demographics

Age (months/years)

Gender: Male () Female ()

Residence: Rural () Urban ()

Patient physical exam:

Weight: Height.

Blood Pressure: Pulse rate:

Presence of edema: Present () Absent ()

Thyroid exam: Normal () Enlarged ()

Patients’ comorbidities:

Thyroid disease: Yes () No ()

If yes, specify duration: ...

Past medical history

Duration of nephrotic syndrome diagnosis.....(months/years)

Number or relapses/retreatment due to Nephrotic syndrome in a year or past 6 months since diagnosis.....

Current treatment (exact drug)

Duration on the current treatment regimen.....(months/years)

Laboratory results

Serum albumin (g/L)

Urine dipstick.....

Thyroid Functions Tests: Thyroxine

Triiodothyronine.....

Thyroid Stimulating Hormone.....



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KNH-UON ERC

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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

Pay 1,500/= Access patients records (4020)
Client's code

Ref: KNH-ERC/A/376

28th September, 2022

Dr. Maureen Kwamboka Machungo
Reg. No. H58/37832/2020
Dept. of Paediatrics and Child Health
Faculty of Health Sciences
University of Nairobi



Dear Dr. Machungo,

RESEARCH PROPOSAL: PREVALENCE OF THYROID HORMONE DYSFUNCTION IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME FOLLOWED UP AT KENYATTA NATIONAL HOSPITAL (P226/03/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P226/03/2022**. The approval period is 28th September 2022 – 27th September 2023.

This approval is subject to compliance with the following requirements;

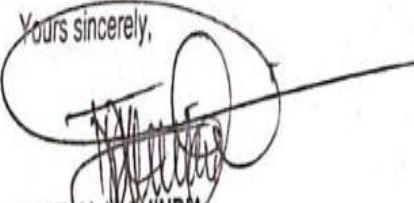
- i. Only approved documents including (informed consents, study instruments, MTA) will be used.
- ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
- iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
- iv. Any changes, anticipated or otherwise that may increase the risks or affected 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.
- v. Clearance for export of biological specimens must be obtained from relevant institutions.
- vi. 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.
- vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Protect to client

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.

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

Yours sincerely,



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

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chair, KNH- UoN ERC
The Dean, School of Medicine, UoN
The Chair, Dept of Diagnostic Imaging & Radiation Medicine, UoN
Supervisors: Dr. Timothy Musila Mutala, Dept. of Diagnostic Imaging & Rad. Medicine, UoN
Dr Jasper Muruka, Dept. of Diagnostic Radiology, KNH