UNIVERSITY OF NAIROBI

HYPERLIPIDEMIA AMONG CHILDREN ON FOLLOW UP FOR IDIOPATHIC NEPHROTIC SYNDROME AT KENYATTA NATIONAL HOSPITAL.

PRINCIPAL INVESTIGATOR: DR. UMMULKHEIR ADHAN HASSAN

REGISTRATION NUMBER: H58/80871/15

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF A MASTER OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH AT THE UNIVERSITY OF NAIROBI.

2018

DECLARATION

I declare that this dissertation is my own work and has not been published or presented for a degree in any other institution.

……. ……

Signature Date

Dr. Ummulkheir Hassan.

Senior House Officer, Department of Paediatrics and Child Health.

University of Nairobi.

This dissertation had been submitted to the University of Nairobi with my approval as University supervisor

……. ……

Signature Date

Dr. Bashir Admani

Paediatrician Nephrologist, Senior Lecturer, Department of Pediatrics and Child Health, University of Nairobi

……. ……

Signature Date

Dr. Daniel Njai

Pediatrician, Senior Lecturer, Department of Pediatrics and Child Health, University of Nairobi.

ACKNOWLEDGEMENTS

I would like to acknowledge and express my sincere gratitude to:

1. The Almighty God for giving me strength and seeing me through to this point.
2. My supervisors :Dr Bashir Admani and Dr Daniel Njai for continuous support and guidance
3. Kenyatta National Hospital for allowing me to conduct the study at the nephrology clinic.
4. Lancet laboratory for speedy and efficient sample analysis
5. All the children and their guardians who participated in this study

TABLE OF CONTENTS

DECLARATION ..... **ii**
ACKNOWLEDGEMENTS ..... **iii**
LIST OF TABLE ..... **vi**
LIST OF FIGURES ..... **vii**
DEFINITION OF TERMS ..... **viii**
ABBREVIATIONS AND ACRONYMS ..... **ix**
ABSTRACT ..... **x**
CHAPTER ONE: INTRODUCTION **1**
CHAPTER TWO: LITERATURE REVIEW **3**
2.1. Prevalence of hyperlipidemia in nephrotic syndrome 3
2.2 Risk factors associated with hyperlipidemia 4
CHAPTER THREE:JUSTIFICATION AND OBJECTIVES **9**
3.1. Study justification and utility 9
3.2. Research Question 9
3.2.1 Primary Objective 9
3.2.2 Secondary Objectives 10
CHAPTER FOUR: METHODOLOGY **11**
4.0 Study design 11
4.1 Study Area 11
4.2. Study outcomes 11
4.3 Study Population 11
4.3.1 Inclusion Criteria 12
4.3.2 Exclusion criteria 12
4.4 Sample size determination 12
4.5 Sampling technique 12
4.6 Study tool 13
4.7 Study procedure 13
4.8 Data processing and analysis 15
4.9 Ethical considerations 16

CHAPTER 5:RESULTS 17
5.0.Demographic characterisation of study group 17
5.1. Prevalence of hyperlipidemia..... 19
5.2 correlation between hyperlipidemia and known risk factors 20
CHAPTER 5: DISCUSSION 22
Strengths 24
Limitations 24
Conclusion 25
Rrecommendations 25
REFERENCES..... 26
APPENDICES 30
APPENDIX 1: STUDY SCHEDULE..... 30
APPENDIX 2: CONSENT FORM 31
APPENDIX 3: IDHINI 35
APPENDIX 4: ASSENT FORM 39
APPENDIX 5: QUESTIONNAIRE..... 46
APPENDIX 6:: BUGDET 48

LIST OF TABLE

Table 1: Plasma lipid levels for children and adolescents in mg/dl 1

Table 2: Descriptive Characteristics of the Study Population 18

Table 3: Proportion of children with abnormal components of the lipid profile 19

Table 4: Univariate and multivariate analysis of known risk factors 20

Table 5: Interaction between prednisolone and cyclosporine 21

LIST OF FIGURES

Figure 6: Prevalence of hyperlipidaemia 19

DEFINITION OF TERMS

Dyslipidemia:	Abnormal amount of lipids, example: Triglyceride, Total cholesterol or fat phospholipid in blood. Most dyslipidemias are hyperlipidemia.
Hyperlipidemia:	Abnormally elevated level of any or all lipids or lipoproteins in blood
Nephrotic syndrome:	Kidney disease that increases permeability through the glomerular membrane. It presents with: nephrotic range proteinuria of urine protein creatinine ratio more than 2gram per gram creatinine, hypoalbuminemia defined as serum albumin concentration less than 30 grams per liter, edema and hyperlipidemia.
Idiopathic Nephrotic syndrome:	Nephrotic syndrome unrelated to any systemic causes.
Frequent relapse:	More than 4 episodes of relapse in a year or more than 2 relapses in six months after initial diagnosis.
Infrequent relapse:	Less than 4 relapse in a year or less than 2 relapses in six months after initial diagnosis.
Children on follow up:	Children attending clinics six weeks after discharge from the ward after the acute phase of idiopathic nephrotic syndrome has been managed.
Child:	Individual between two and fourteen years of age
Remission:	Urine protein creatinine ratio less than 2 grams protein per gram of creatinine
Relapse:	Recurrence of proteinuria more 2 grams per gram creatinine after initial relapse.

ABBREVIATIONS AND ACRONYMS

BMI	Body Mass Index
C.K.D	Chronic Kidney Disease
ESRD	End Stage renal disease
G/L	Grams per Liter
H.D.L	High Density Lipoprotein
I.N.S	Idiopathic Nephrotic Syndrome
K.N.H	Kenyatta National hospital
KDIGO	Kidney Disease Improving Global Outcomes
LDL	Low Density Lipoprotein
MCNS	Minimal Change nephrotic syndrome
Mg/dl	Milligrams per deciliter
N.S	Nephrotic syndrome
T.C	Total Cholesterol
T.G	Triglyceride
VLDL	Very Low-Density Lipoprotein

ABSTRACT

Background

Hyperlipidemia is present during the acute phase of the disease but disappears with the resolution of proteinuria. Children with nephrotic syndrome have been noted to have hyperlipidemia despite being in remission. There have been many publications globally concluding that hyperlipidemia among children with nephrotic syndrome persists even after clinical remission. There is no published work on lipid profile of children with nephrotic syndrome in Kenya. A study on prevalence of hyperlipidemia among children on follow up for idiopathic nephrotic syndrome and the evaluation of the correlation between the known risk factors and hyperlipidemia would improve management and follow up.

Objectives

To determine the prevalence of hyperlipidemia among children on follow up for idiopathic nephrotic syndrome.

To evaluate the correlation between hyperlipidemia and the known risk factors among children on follow up for idiopathic nephrotic syndrome at the K.N.H nephrology clinic.

Methods

This study used a cross sectional study design. Consecutive sampling was used to study sixty-six children on follow up for idiopathic nephrotic syndrome at the K.N.H paediatric nephrology clinic who met the inclusion criteria. Data was collected from files and guardians of the participants using an interviewer guided questionnaire. Then samples were taken for measuring: fasting lipid profile and serum albumin. Urine samples taken for protein creatinine ratio analysis. The study was carried out between November 2017 and February 2018.

Results

The study participants were aged 2-14 years with a mean of 8.84 (3.15 SD) .Majority of the participants 32 (48.5%) were aged less than 9 years. There were more male 37 (56.1%).Sixty two children (93.9%) had normal BP levels and over half 35 (53%) had normal BMI.

Majority of the children 41 (62%) had INS for less than 21 months. Almost half the participants had infrequent relapses 42 (63.3%).Most of the participants were in remission 47 (71.7%).

More than half the children 40 (60.6%) were on prednisolone, 19 (28.8%) were on no treatment, 3(4.5%) on cyclosporine and 4 (6.1%) were on both prednisolone and cyclosporine.

Prevalence of hyperlipidemia among children on follow up for idiopathic nephrotic syndrome was 81.8% [95% CI (70.39-90.24)] .There is an increase in odds of hyperlipidemia among frequent relapsers compared to infrequent relapsers, OR 2.91 (0.43-19.78).Children with a duration of illness more than 21 months has an increased odds of hyperlipidemia compared to those with INS for less than 21 months, OR 1.35 (0.25-7.41). The odds of hyperlipidemia among children on cyclosporine is 1.39 (0.06-36.77), those on prednisolone OR 5.39 (0.89-32.48), without statistical significance value p= 0.066 and those on both prednisolone and cyclosporine is 2.18 (0.04-129.8) compared to those on no treatment.

Conclusion

The prevalence of hyperlipidaemia among children on follow up for idiopathic nephrotic syndrome in this study is 81.8% [95% CI (70.39-90.34].

64.8% of children in remission had hyperlipidaemia, therefore hyperlipidaemia can be present despite disappearance of proteinuria.

Frequent relapses, prolonged duration of illness, use of prednisolone and cyclosporine treatment shows an increase in the odds of hyperlipidemia among children on follow up for INS in this study.

CHAPTER ONE: INTRODUCTION

The nephrotic syndrome is a kidney diseases that increase the permeability of the glomerular membrane. It presents with : nephrotic range proteinuria of urine protein creatinine ratio ≥2g/g, hypoalbuminemia defined as serum albumin levels less than 30 g/L, edema and hyperlipidemia (1).

Hyperlipidemia in children as defined by the United States National Heart Lung and Blood institute in 2011 is values ≥95th percentile :Total cholesterol >200mg/dl or low density lipoprotein >130mg/dl or non-high density lipoprotein cholesterol >145mg/dl and triglyceride >130mg/dl (2).There is no literature on lipid reference ranges for African children.

Category	**Desirable level**	**Borderline levels**	**Abnormal levels**
Total Cholesterol	<170mg/dl	170-199mg/dl	>200mg/dl
Low Density Lipoproteins	<110mg/dl	110-129mg/dl	>130mg/dl
Non High Density Lipoprotein - C	<120mg/dl	120-144mg/dl	>145mg/dl
Triglyceride (0-9years)	<75mg/dl	75-99mg/dl	>100mg/dl
Triglyceride(10 -19years)	<90mg/dl	90-129mg/dl	>130mg/dl
High Density Lipoprotein	>45mg/dl	40-45mg/dl	<40mg/dl

Table 1: Plasma lipid levels for children and adolescents in mg/dl

Hyperlipidemia has been known to present during the acute phase of nephrotic syndrome and disappear when proteinuria resolves. There is a rise in serum triglycerides, low density

lipoprotein and low high density lipoprotein (3).However, studies have noted hyperlipidemia despite being in remission (4)

A study by Merouni *et al* indicated that 48% of the children with nephrotic syndrome in remission had serum Triglyceride and LDL levels above the ninety fifth percentile for sex and age (5). Moreover, children with frequent relapses were more likely to have hyperlipidemia even during remission.

Hyperlipidemia plays a role in initiation and acceleration of renal injury(6),(7), (8),(9) .In 1982 Moorhead *et al* formulated the lipid nephrotoxicity hypothesis .It explained that lipid abnormalities can lead to chronic progressive kidney disease (10). There is evidence showing that inflammatory stress, oxidative stress and endothelial dysfunction associated with dyslipoproteinemia can contribute to renal pathophysiological changes (11).
Muntner *et al* studied risk of developing renal dysfunction among adults in the atherosclerosis risk communities study. They studied the relationship between plasma lipids and the rise in serum creatinine among patients 12,728 in the atherosclerosis risk communities (ARIC). They followed the participants up for a mean of 2.9 years. They concluded predictors of renal dysfunction as increased triglyceride and low HDL (12)

Hyperlipidemia is also a known risk factor for atherosclerosis(13). Atherosclerosis has been noted to begin in childhood(14), as early as nine years of age (2). The occurrence of hyperlipidemia is of concern due to the associated morbidities.

CHAPTER TWO: LITERATURE REVIEW

2.1. Prevalence of hyperlipidemia in nephrotic syndrome

Hyperlipidemia among children with nephrotic syndrome has been reported in several studies. Merouni *et al* studied plasma lipid profiles of 25 children in remission with idiopathic nephrotic syndrome with or without prednisolone treatment. The results indicated that plasma low density lipoprotein and total cholesterol levels were above the 95th percentile for sex and age in 12 of the 25 patients (48%) , 6 had borderline (75^{th} -95^{th} percentile) cholesterol and low density lipoprotein levels.7 of them had triglyceride and apolipoprotein B concentrations above 95th percentile (5).

A study was done in Miami on lipid abnormalities among 59 children with idiopathic nephrotic syndrome. Out of the 59 children, 24 were in remission for at least two months. The study found a number of children with Minimal change nephrotic syndrome during prolonged remission had elevated lipid parameters; 46%, 29% and 40 % had elevated TC, LDL and VLDL respectively. Among 32 children not in remission 42%,81%,60% had elevated TC,LDL and VLDL respectively (4).

Mahmud *et al* studied hyperlipidemia in children with idiopathic nephrotic syndrome, during relapse and remission among 26 children at two nephrology centers in Bangladesh.10 out the 26 (38%) children had abnormal lipid profiles even during remission (15).

A comparative study on lipid abnormalities in the first episode and relapse cases among 50 children with nephrotic syndrome and compared them to a healthy matched control. Lipid parameters remain raised even during remission compared to the controls as follow: TC 282.7+/-47.5 vs. control 175.37+/-18.32, TGD 178.15+/- 15 vs. 94.10+/- 19.39 and LDL 191.4+/- 52 vs. 107.33+/-16.6. (16).

A study in Sudan among children with idiopathic nephrotic syndrome found the prevalence of dyslipidemia as 78%. 66% had total cholesterol >200mg/dl, 63.3%LDL > 130mg/dl ,63% had triglycerides>150mg/dl, , 26.7%HDL <35mg/dl (17).

There are no published studies on prevalence of hyperlipidemia among children with nephrotic syndrome in Kenya.

2.2 Risk factors associated with hyperlipidemia

2.2.1 Hypoalbuminemia

Friedman and Bayer's postulated that hyperlipidemia was caused by hypoalbuminemia (18).The pathogenesis of hyperlipidemia is multi factorial, one of the factors being proteinuria resulting into low plasma oncotic pressures that stimulates hepatic lipoprotein synthesis (19).

A study among Sudanese children with nephrotic syndrome observed an inverse correlation between albumin levels hyperlipidemia. Children were classified into two groups based on serum albumin, those with $\leq$ 15g/L and those $\geq$16 but $\leq$ 30 g/L. Out of the children with serum albumin levels between 16g/L and 30g/L ;52% ,50% and 54.7% of them had elevated TC,TGD and LDL respectively vs. 100%,69% and 83% among those with serum albumin less than 15g/L .Upon further analysis, abnormal TC and LDL was significantly more prevalent among children with serum albumin less than 15g/L compared to those with serum albumin between 16-30 g/L ,p=0.002 and p=0.04 (17).

A study in Bangladesh by Hossain et al concluded that there is an inverse correlation between serum cholesterol and albumin levels in children with nephrotic syndrome .The lower the serum albumin level the higher the cholesterol level. (20).Sreevinisa et al study in India observed an inverse correlation between albumin and cholesterol (16). Both Indumati et al and Dnyanesh et al also found an inverse correlation between serum albumin and serum cholesterol levels (3),(21).

Zilleruelo et al found a poor correlation between serum cholesterol and albumin values. The study noted many patients had raised serum cholesterol despite normal albumin levels during

remission and relapse. Moreover, no correlations were established between the severity of proteinuria and the extent of hyperlipidemia (4).

2.2.2 Relapses and duration of illness

Merouni et al found a significant correlation between hyperlipidemia and the number of relapse episodes. This was observed in children with and without prednisone treatment. The number of relapses was noted to influence the TC ($p=0.003$)and LDL ($p=<0.003$) levels (5). The duration of illness was not an influencing factor.

Zilleruelo et also observed a good correlation between the severity of lipid abnormalities and the frequency of relapses and the duration of illness (4).

On comparison of lipid profiles between frequent and infrequent relapsing nephrotic syndrome Eltigani et al concluded the following :TC ≥200mg/dl was in 71% of the frequent relapsing vs. 28% in the infrequent relapsing (p value 0.00);LDL ≥130mg was in 76.9% in frequent relapsing vs. 23.1% in infrequent relapsing (p value 0.000). Children with frequent relapses were more likely to have hyperlipidemia even during remission (17)

A prospective observational study done in Bangladesh recruited 26 children with idiopathic nephrotic syndrome and followed them up for six months. Their lipid profile at remission was used to group them, 50% the patients who had abnormal lipid profiles during remission relapsed during the six months period they were being followed up yet none of the patients with normal lipid profiles relapsed. It could be concluded from this study that hyperlipidemia at remission may predict relapse in idiopathic nephrotic syndrome (15).

Screenvasa et al observed that that lipid profile in first episode of nephrotic syndrome reached normal value during remission. Whereas in relapse cases, there was persistent elevation in the lipid profiles even during the remission (16). Dnyanesh et al noted that in relapse nephrotic syndrome there was insignificant reduction in serum lipid levels even at the end 8 weeks of steroid treatment (3).

2.2.3 Cyclosporine

Cyclosporine treatment is associated with impairment of lipid metabolism, characterized by elevation of LDL,TC, TGD and apolipoprotein (22).However studies on impact of cyclosporine monotherapy on hyperlipidemia are limited, there is evidence that cyclosporine alone can independently elevate serum triglycerides and cholesterol in humans .Cyclosporine is thought to decrease synthesis of bile from cholesterol by inhibiting enzyme 26 hydroxylase. It is also reported to increase serum LDL by binding to LDL receptors ,it decreases clearance of serum VLDL and LDL by decreasing lipoprotein lipase activity and hepatic lipase activity (23).

Eighty five adults who had undergone heart transplant were randomized into two groups to receive either cyclosporine (n=46) or tacrolimus (39).Serum lipid profile was done at 3, 6 and 12 months. The total cholesterol and LDL was higher in the group of patients on cyclosporine at 239 vs. 205 mg/dl at 3 months, 246 vs. 191 mg/dl at 6 months, 212 vs. 186 mg/dl at 12 months. After twelve months of treatment 71% of the patients on cyclosporin and 41 % on tacrolimus received therapy for hypercholesterolemia (24).

A study looked at the effect of cyclosporine monotherapy on 58 adult patients at one year after a renal transplant. These patients were compared against a healthy control that was matched by age, sex, exercise level and social background. The patients on cyclosporine had a higher mean of :TC (263 +/-58 vs. 220+/- 34 mg/dl),TGD (167.2 vs. 99 mg/dl) and lower HDL (47+/-13 vs. 55.7+/-13mg/dl) compared to the controls (25).

In Netherlands, the effect of cyclosprin withdrawal was studied among 6 children after liver transplantation. All the children were on daily cyclosporine, azathioprine and alternate day prednisolone .After rejection of the graft was excluded, there lipid profile was analyzed .Cyclosporin was gradually discontinued over seven days, another sample for lipid profile was analyzed after four weeks. TC,LDL TGD reduced by 18%,27% and 23% respectively (26)

2.2.4. Corticosteroids

Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines recommend prednisolone as initial treatment of childhood idiopathic nephrotic syndrome (27).The exact mechanism of action of corticosteroids unknown in the treatment of idiopathic nephrotic syndrome. Nephrotic syndrome is thought to be due T-cell dysfunction that causes release of a circulating factor that results in effacement of the podocytes foot processes and proteinuria (28). Corticosteroids are presumed to suppress T-cell-mediated factor and act on the oocytes by stabilizing the actin cytoskeleton and altering gene expression (29)

Corticosteroids are postulated to be a secondary cause of dyslipidemia with varying degrees of lipid abnormalities and multifactorial mechanisms. Studies report conflicting findings.

Increase in TGD is thought to be due to redistribution of body fat to the trunk and face. This reduces the number of glucocorticoid receptors leading to the increased insulin levels and resistance.(30). Insulin resistance caused by glucocorticoids has a role in lipid abnormalities in that hyperglycemia: increases VLDL production, inhibits fatty acid β-oxidation and enhances hepatic lipogenesis.

Abnormal changes in lipid profile has been noted in 73 out of 100 patients with systemic lupus erythematous. The raised TC,LDL,TGD was associated with high dose of prednisolone more than 30 milligrams per day and renal involvement .HDL levels were significantly low in patients receiving high dose prednisolone ($p < 0.05$) (31).

A study among post-transplant children looked at the benefits of steroid withdrawal in the era of cyclosporine. Ten children with stable graft were gradually tapered off prednisolone and maintained on 6mg/kg/day of cyclosporine, their lipid profile was compared to 13 children on prednisolone after six months. Both TC (176 +/- 9.2 vs. 265 +/- 8.3 mg/d) and LDL (109 +/- 10 vs. 167 +/- 9.2 mg/dl)) was high in the group of children on prednisolone (32).

Zilleruelo et al explained that there could be profound metabolic abnormalities resulting from prolonged corticosteroid use that could cause persistent hyperlipidemia (4).

In the study by Merouni et al, out of the 12 patients with hyperlipidemia 8 of them were on prednisolone treatment. However, upon further analysis the difference was not statistically significant (p= 0.2262) (5)

The third national health and nutritional survey among 15004 Americans older than twenty years, demonstrated no association between glucocorticoid use and raised lipid profiles among the United States of America's population (33).

CHAPTER THREE:JUSTIFICATION AND OBJECTIVES

3.1. Study justification and utility

Many publications have shown that hyperlipidemia among children with idiopathic nephrotic syndrome persists even after clinical remission. Hyperlipidemia has been noted to accelerate progression to chronic kidney disease and increases the risk of premature atherosclerosis. With survival of children with a nephrotic syndrome improving, the occurrence of hyperlipidemia with its associated morbidity is of concern.

Regular monitoring of lipid profiles even during remission is thus recommended especially among those with frequent relapses yet routine lipid profile for children on follow up at KNH paediatric nephrology clinic is not done.

There has been no published work in Kenya on hyperlipidemia among children with nephrotic syndrome. This study will determine the prevalence of hyperlipidemia among children on follow up for idiopathic nephrotic syndrome. It will determine the risk factors associated with hyperlipidemia so as to improve follow up and management of children with nephrotic syndrome at the nephrology clinic.

3.2. Research Question

What is the proportion of children on follow up for idiopathic nephrotic syndrome have hyperlipidemia?

3.2.1 Primary Objective

To determine the prevalence of hyperlipidemia in children on follow up for idiopathic nephrotic syndrome at KNH.

3.2.2 Secondary Objectives

To evaluate the correlation between hyperlipidemia and the known risk factors

- Hypoalbuminemia
- Number of relapses
- Duration of illness
- Use of cyclosporine
- Use of prednisolone

CHAPTER FOUR: METHODOLOGY

4.0 Study design

This study adopted a cross sectional study design.

4.1 Study Area

This study was conducted at Kenyatta National Hospital paediatric nephrology clinic. KNH is a national referral hospital located in Nairobi, the Kenyan capital city. It has 50 wards, 22 out-patient clinics, 24 theaters, 1800 bed capacity and an accident and emergency department. The pediatric nephrology clinic follows up all children below 14years of age with renal conditions. The clinic is conducted on Friday mornings by pediatric nephrologists and residents. Approximately 120 children were attended to at the paediatric nephrology clinic from January 2016-November 2016, there no records on number of patients on follow up for nephrotic syndrome.

4.2. Study outcomes

The study achieved the following:

- Determination the prevalence of hyperlipidaemia among children on follow up for idiopathic nephrotic syndrome
- Evaluation of correlation between hyperlipidemia and the known risk among children on follow up for idiopathic nephrotic syndrome

4.3 Study Population

The study was conducted among children on follow up for idiopathic nephrotic syndrome at KNH paediatric nephrology clinic for the period of November 2017 to February 2018.Idiopatic nephrotic syndrome in this study defined as patient with confirmed nephrotic syndrome with no identifiable systemic disease attending the clinic. All patients had :normal complement levels, negative hepatitis B and C,None reactive HIV test , negative antinuclear antibody and anti-double stranded DNA previously tested and available in patients records.

4.3.1 Inclusion Criteria

a. Children on follow up for idiopathic nephrotic syndrome aged 2 years to 14years.

b. Children with obtained written informed consent/assent from guardian/parent.

4.3.2 Exclusion criteria

a. Children with newly diagnosed nephrotic syndrome.

b. Children with known liver disease.

c. Children with known diabetes mellitus.

d. Children recruited into the study previously

4.4 Sample size determination

Substituting in the fisher's formula:

$$N = \frac{Z^2 * P * Q}{D^2}$$

N=Sample size,

=66 children on follow up for nephrotic syndrome

Z = is the value from standard normal distribution corresponding to desired confidence level

(Z=1.96 for 95% CI)

P = is the expected true proportion of outcome

(Prevalence of hyperlipidemia estimated at 78% in children on follow up for nephrotic syndrome in Sudan (17).)

Q = Probability of failure = (1 – P)

D=Desired margin of error (0.1)

4.5 Sampling technique

Consecutive sampling was done among all the patients who met the inclusion criteria.

4.6 Study tool

Data was collected from the parents/guardians of the participants and their files using an interviewer guided questionnaire.

4.7 Study procedure

The principal investigator at the start of every week visited the records office, got details of the patients scheduled for nephrology clinic that week. Files of the patients were retrieved and those with a diagnosis of idiopathic nephrotic syndrome and fulfilled the inclusion criteria were selected. All the patients had a confirmed diagnosis of nephrotic syndrome with results of laboratory tests ruling out systemic causes of nephrotic syndrome in patient files being negative. Consecutive sampling was used until the sample size was attained without including children re-visiting the clinic. Their caregivers were called so as to seek a tentative consent. Those that accepted were requested to make their children fast for a minimum of eight hours and pack breakfast for them when coming for the appointment.

On arrival at the nephrology clinic for the appointment, the study was explained. Written consent from the caregivers and assent for children above seven years was sought in Kiswahili/English according to participant's preference. An interviewer guided questionnaire was filled by the principal investigator with information from the guardian and the participant's file. Vital signs and anthropometric measurement were taken. Blood pressure was measured using and electronic blood pressure machine with an appropriate cuff size, BP by gender age and height percentile charts were used to classify reading into hypertension or normal. Height was measured in centimeters using a stadiometer and weight using a stand on weighing scale in kilograms. Thereafter, body mass index was calculated in kilograms per meters squared. CDC charts for BMI for age percentile used to classify children into overweight or normal. Soon after the measurements were finished, two milliliters fasting venous blood sample was collected for measuring: lipid profile and albumin levels and 5mls of urine was collected for protein creatinine ratio.

4.7.1. Laboratory procedure

Sample collection

On wearing clean gloves, the venipuncture site was cleaned with a spirit swab.2mls of venous blood was drawn using a disposable syringe. Blood collected was put into a plain vacutainer tube that was coded with a serial number. Thereafter participant was requested to put approximately 5mls of urine in a plain urine tube that was coded with a serial number.

Sample transportation

The specimens were properly sealed, placed on a rack in a cool box and taken to the Lancet laboratory. The samples were be taken to the laboratory within 1-2 hours of sample collection.

Sample processing and analysis

The blood and urine specimen were received by a laboratory technologist at Lancet laboratory. The specimens were logged in a book and assigned a specimen lab number, then processed immediately.

Venous blood sample was centrifuged to get serum. Using Cobas Integra auto analyzer machine TC, TGD and HDL were determined .LDL was calculated using Friedewald formula. Thereafter serum albumin was measured using dye-binding technique.

The urinary protein and creatinine was measured using Cobas Integra auto analyzer Systems which uses absorbance measuring mode.

Result interpretation

The lipid profile were interpreted using ranges recommended by the United States National Heart Lung and Blood institute in 2011:

- TC: <170-200mg/dl
- LDL :<110-130mg/dl
- HDL: >45-<35mg/dl
- TGD:<125->125mg/dl

Albumin: 30-50g/L

Urine protein creatinine ratio: ≤2g protein / grams creatinine

Sample storage

In case of delays in samples processing at the laboratory, the specimen were refrigerated at 2-8^{0}c.

Quality control of the laboratory

The laboratory is accredited by the Kenya National Accreditation System (KENAS) and is also international standard certification (ISO 15189:2012). Internal quality control is carried out daily at the laboratory prior to sample analysis. External quality control of the laboratory is under the THISTLE system

4.8 Data processing and analysis

Quantitative data from questionnaires was checked daily for completeness and coded for appropriate computer entry. Quantitative data was entered into the Microsoft Excel for data cleaning and preparation for analysis. Descriptive analysis was done using counts and respective percentages. The prevalence of hyperlipidemia was computed as a proportion with 95% confidence interval. Bivariate associations of risk factors (independent variables) with hyperlipidemia (dependent variable) was explored using chi squared tests and presenting the p values. Univariable (unadjusted) and multivariable (adjusted) logistic regression using Penalized

maximum likelihood was used due to small sample resulting in small or zero value categories. Odds Ratios, 95% confidence intervals and respective p values were reported. P values were evaluated at the 5% level (0.05). All the statistical data analysis was done using Stata Version 15.1 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).Tables and pie and bar charts were used to display the results.

4.9 Ethical considerations

4.9.1 Research Ethics Committee Approval

Ethical approval was obtained from the Kenyatta National Hospital/University of Nairobi ethics review committee approval number P402/07/2017

4.9.2 Consent for the questionnaire

Before administration of the questionnaire, informed written consent was obtained from each caregiver and written assent from children aged 7 years and above. This was done after an explanation had been given to the participants about the purpose of the study.

Participants were assured of confidentially and that the data collected would only be accessible to the research team. Anonymity was maintained with participants using serial numbers instead of their names. Participants were informed of their right to refuse to participate in the study.

CHAPTER FIVE:RESULTS

5.0.Demographic characterisation of study group

A total of 66 children on follow up for idiopathic nephrotic syndrome who fulfilled the inclusion criteria were enrolled after obtaining consent and assent. The study participants were aged 2-14 years with a mean of 8.84 (3.15 SD) .Using the mean age for further analysis majority of the participants 32 (48.5%) were aged less than 9 years. There were more male 37 (56.1%).Using BP by gender age and height percentile charts 62 (93.9%) had normal BP levels. Using BMI for age percentile CDC charts over half 35 (53%) had normal BMI.

The mean duration of illness was 20.74 (SD 17.08), and majority of the children 41 (62%) had INS for less than 21 months. Almost half the participants had infrequent relapses 42 (63.3%).Most of the participants were in remission 47 (71.7%) with normal albumin levels 48 (72.7%).More than half the children 40 (60.6%) were on prednisolone, 19 (28.8%) were on no treatment, 3(4.5%) on cyclosporine and 4 (6.1%) were on both prednisolone and cyclosporine. The patient characterisation is summarized in Table 4.

Characteristics	**Total=66** **N (%)**
Age	
>9	34 (51.5)
<9	32 (48.5)
Gender	
Male	37 (56.1)
Female	29 (43.9)
BP	
Normal	62 (93.9)
Hypertension	4 (6.1)
BMI	
Normal	35 (53)
Overweight	32 (47)
Duration of illness	
<21months	41 (62)
>21 months	25 (37.9)
Relapses	
Infrequent	42 (63.3)
Frequent	24 (36.4)
Disease status	
Remission	47 (71.2)
Not remission	19 (29.8)
Treatment	
None	19 (28.8)
Prednisolone	40 (60.6)
Cyclosporine	3 (4.5)
Prednisolone & cyclosporine	4 (6.1)
Serum Albumin	
Normal	48 (72.7)
hypoalbuminemia	18 (27.3)

Table 2: Descriptive Characteristics of the Study Population

5.1. Prevalence of hyperlipidemia

Prevalence of hyperlipidemia among the 66 children on follow up for INS in this study was 81.8% [95% CI (70.39-90.24)]

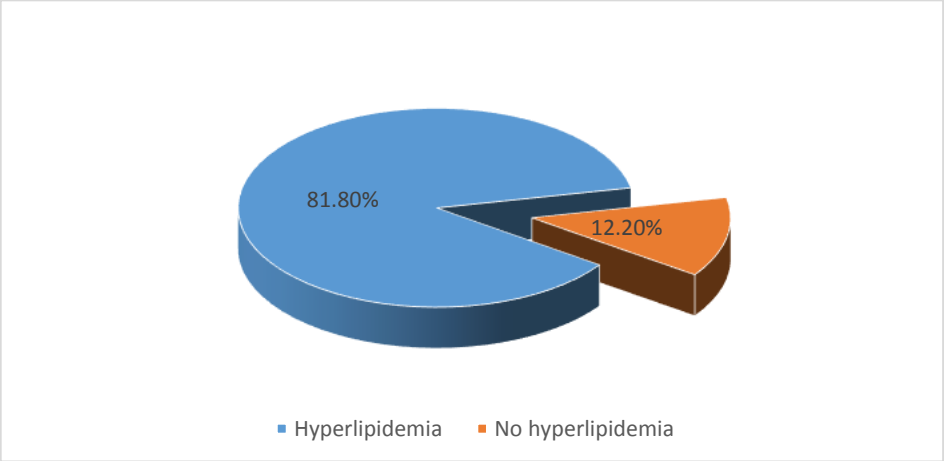

Figure 6: Prevalence of hyperlipidaemia

Over half the participants 35 (53%) had elevated serum total cholesterol, 46 (69.7%) had high triglyceride, 23 (34.8%) with elevated LDL and 10 (15.5%) with low HDL. Table 3 summarizes proportion of children with abnormal components of lipid profile.

Category	**Total** **N (%)**
Total cholesterol	35 (53)
Triglyceride	46 (69.7)
Low density lipoprotein	23 (34.8)
High density lipoprotein	10 (15.5)
Total	**66 (100)**

Table 3: Proportion of children with abnormal components of the lipid profile

5.2 correlation between hyperlipidemia and known risk factors

VARIABLE	UNIVARIABLE ANALYSIS		MULTIVARIABLE ANALYSIS	
	95% CI	P value	95% CI	P value
Age <9 years >9 years	0.32 (0.08-1.21)	0.093	0.20 (0.03-1.22)	0.08
Gender Male Female	0.9 (0.27-3.1)	0.884	0.93 (0.23-3.77)	0.922
Relapses Infrequent Frequent	2.91 (0.66-12.78)	0.158	2.91 (0.43-19.78)	0.274
Duration of illness <21 months >21 months	0.55 (0.16-1.86)	0.336	1.35 (0.25-7.41)	0.729
Albumin Normal Hypoalbuminemia	3.58 (0.6-21.51)	0.164	0.28 (0.02-3.83)	0.339
Prednisolone No Yes	5.28 (1.45-19.18)	0.012	Analyzed for interaction	
Cyclosporine No Yes	1.03 (0.16-6.79)	0.978	Analyzed for interaction	

Table 4: Univariate and multivariate analysis of known risk factors

As summarized on table 4 above, there is a decrease in the odds of hyperlipidemia among children aged more than 9 years compared to those less than 9 years, OR 0.20 (0.03-1.22) .The odds of hyperlipidemia in males compared to females is 0.93 (0.23-3.77).There is an increase in odds of hyperlipidemia among frequent relapsers compared to infrequent relapsers ,OR 2.91 (0.43-19.78).Children with a duration of illness more than 21 months has an increased odds of hyperlipidemia compared to those with INS for less than 21 months, OR 1.35 (0.25-7.41).Children with hypoalbuminemia had a decrease in odd of hyperlipidemia compared to those with normal albumin level, OR 0.28 (0.02-3.83).

The odds of hyperlipidemia among children on cyclosporine compared to those on no treatment is 1.39 (0.06-36.77).There is an increase in odds of hyperlipidemia among children on prednisolone compared to children on no treatment, OR 5.39 (0.89-32.48), without statistical significance value 0.066.The odds of hyperlipidemia among children on both prednisolone and cyclosporine is 2.18 (0.04-129.8) compared to those on no treatment. The interaction between prednisolone and cyclosporine is shown below on table 5.

Variable	Univariate		multivariate	
	95 % CI	P values	95% CI	P value
No prednisolone & no cyclosporine	Ref			
Cyclosporine & no prednisolone	1.16 (0.09-14.77)	0.908	1.39 (0.06-36.77)	0.922
Prednisolone & no cyclosporine	5.09 (1.28-20.15)	0.020	5.39 (0.89-32.48)	0.066
Prednisolone & cyclosporine	5.33 (0.25-113.94)	0.280	2.18 (0.04-129.8)	0.708

Table 5: Interaction between prednisolone and cyclosporine

CHAPTER FIVE: DISCUSSION

Hyperlipidemia has been noted in nephrotic syndrome in both the acute phase and during remission. This study was undertaken to determine the prevalence of hyperlipidemia and to evaluate the correlation between hyperlipidemia and the known risk factors among children on follow up at the paediatric nephrology clinic for idiopathic nephrotic syndrome.

The prevalence of hyperlipidemia among children on follow up for idiopathic nephrotic syndrome was 81.8% [95% CI (70.39-90.34)]. Elevated serum lipid profile components above 95th percentile for age for the study group was as follows:53% had elevated TC, 69% had hypertriglyceridemia,34.4% had high LDL and 15.2% had low HDL .These findings are similar to those among Sudanese children that reported 78% dyslipidaemia, with 66.7% high TC,63.3% elevated TGD,63.3% raised LDL above 95th percentile for age (17).This findings are also similar to those reported by Zilleruelo et al that showed 46% had elevated TC, 42% and 29% with elevated TGD and LDL respectively(4).)Our study shows a higher prevalence of hyperlipidaemia compared to that reported by Merouni el al as 48%, the difference could be explained by the fact that merouni study included only patients in remission unlike this study that included all children on follow up for idiopathic nephrotic syndrome regardless of the remission status.

Majority of the children in this study, 71.2% (n=47) were in remission .Among those in remission, 64.8% (n=35) had hyperlipidemia. Those not in remission were 28.8% (19), out of whom only 35.2 % (n=19 had hyperlipidemia. This differs with the findings of zillerullo that found higher prevalence of hyperlipidemia among children not in remission. They observed TC,LDL, and VLDL among those in remission was elevated in 46% ,29% and 40 % vs. 42%,81% and 60% respectively among children not in remission (4).Over half of the children in remission ,55.3% (n=26) in were on prednisolone treatment,36.2% (n=17) off treatment,4.3% (n=2) on cyclosporine and 4.3% (n=2) were on both cyclosporine and prednisolone.

In this study the correlation between hypoalbuminemia and hyperlipidaemia was not statistically significant, OR 0.28 (0.02-3.83) and p value =0.338.In this study only 27.3% (18) of the children had hypoalbuminemia and 31.5 % of the children with hypoalbuminemia has hyperlipidemia. Zilleruelo had noted that many patients has elevated serum lipid concentration despite normal

serum albumin levels (4).In this study 68.5% (n=37) had hyperlipidemia despite having normal serum albumin levels. However ,this study contradicts many studies that have established a negative correlation between hyperlipidemia and hypoalbuminemia (16), (17),(20).

The mean duration of illness among children in this study was 20.74 months (SD 17.08).Using the mean as cut off for analysis, most of the children 61.1% (n=41) had the illness for less than 21months.Hyperlipidemia was observed in 64.8% among those with illness for less than 21 months and in 35.2% of children with the illness for more than 21 months. On further analysis the correlation between the duration of illness and hyperlipidemia was not statistically significant ,OR 1.35 (0.25-7.41),p=0.729.This in keeping with a study by merouni et that concluded that duration of illness did not influence hyperlipidemia (5) but contradicts Zillerullo et al that showed a good correlation (4)

In this study 63.8% had infrequent relapses and 36.3% had frequent relapses since being diagnosed with idiopathic nephrotic syndrome. Moreover, 40.7% (22) of the children with frequent relapses had hyperlipidemia. Those with frequent relapses had over two fold odds of hyperlipidemia, OR 2.91 (0.43-19.78), however not statistically significant p=0.274.This conquers with the study by Merouni that showed number of relapses significantly influenced hyperlipidemia and correlated with elevated TC (p=0.003) and LDL (p=0.003) (5).It also agree with other studies (4),(17).

In this study, 10.6% (n=7) were on cyclosporine treatment .Out of the 7 children, 3 were on cyclosporine alone and 4 were on cyclosporine and prednisolone combination. Hyperlipidemia was noted in 3.7% of those on cyclosporine alone and 7.4% among those on combination of cyclosporine and prednisolone. There is an increase in the odds of hyperlipidemia among those on cyclosporine only compared to those not on any treatment, OR 1.39 (0.06-36), with no statistical significance=0.503. This study agrees with studies by Hulzebo and Brown (25),(26).The odds of hyperlipidemia among children on prednisolone and cyclosporine compared to those on no treatment is increased, OR 2.18 (0.04-129.9) without statistical significance p=0.922.

Majority of the children, 60.6% (40) in this study were on prednisolone treatment only. Hyperlipidemia among children on a prednisolone only was 66.7% (n=36).Children on prednisolone had over fivefold increase in odds of hyperlipidaemia, OR 5.39 (0.89-32.48) ,without statistical significance p=0.066.This agrees with a study by Leong ,that's showed 73% of the patients on prednisolone for systemic lupus erythematous has hyperlipidemia (31).It contradicts merouni study that noted that ,despite most of the patients with hyperlipidemia in the study being on prednisolone treatment the correlation between prednisolone use and hyperlipidemia was not statistically significant p=0.22 (5).

Strengths

This study was conducted in a well-established nephrology clinic that follows many children referred from all over the country and is supervised by paediatric nephrologists.

The study was conducted at the largest referral hospital that captures patients from all over the country.

All the caregivers and children approached for the study accepted to participate meaning there was minimal non participation bias.

Limitations

This study using crossectional descriptive design is a limitation in that it wasn't possible to establish causal relationship.

Poor record keeping and incomplete documents and missing investigation in patient's file made participants to be excluded from the study.

Conclusion

The prevalence of hyperlipidaemia among children on follow up for idiopathic nephrotic syndrome in this study is 81.8% [95% CI (70.39-90.34].

64.8% of children in remission had hyperlipidaemia, therefore hyperlipidaemia can be present despite disappearance of proteinuria.

Frequent relapses, prolonged duration of illness, use of prednisolone and cyclosporine treatment shows an increase in the odds of hyperlipidemia among children on follow up for INS in this study.

Rrecommendations

Regular monitoring of lipid profile of children on follow up for idiopathic nephrotic syndrome

Further research on the effects of hyperlipidemia on children with idiopathic nephrotic syndrome.

REFERENCES

1. DeBaun MR, Vichinsky E. Nelson Textbook of Pediatrics - 18e. 2008.
2. Goldwire M. Screening and treatment of pediatric dyslipidemias. US Pharm. 2014;39(5):52–8.
3. Dr. Dnyanesh DK1. A Study of Serum Lipids in Nephrotic Syndrome in Children\n. IOSR J Dent Med Sci. 2014;13(3):01–6.
4. Zilleruelo G, Hsia SL, Freundlich M, Gorman HM, Strauss J. Persistence of serum lipid abnormalities in children with idiopathic nephrotic syndrome. J Paediatr. 1984;104:61–4.
5. merouani A, Levy E, Mongeau JG, Robitaille P, Lambert M DE. Hyperlipidemic profiles during remission in childhood idiopathic nephrotic syndrom. Clin Biochem. 2003;36(7).
6. Saland JM, Pierce CB, Mitsnefes MM, Flynn JT, Goebel J, Kupferman JC, et al. dyslipidemia in Children with Chronic Kidney Disease : A Report of the Chronic Kidney Disease in Children (CKiD) Study. kidney Int. 2010;78(11):1154–63.
7. Hassan Thabet MAE, Salcedo JR, Chan JCM. Hyperlipidemia in childhood nephrotic syndrome. Pediatr Nephrol. 1993;7(5):559–66.
8. Keane, William F.; Mulcahy, Wayne S.; Kasiske, Bertram L.; Youngki Kim; O'Donnell MP. Hyperlipidemia and progressive renal disease. Kidney Int. 1991;39(Suppl 3(31):S-41-S-48.
9. Wheeler DC, Bernard DB. Lipid Abnormalities in the Nephrotic Syndrome : Causes , Consequences , and Treatment. Am J Kidney Dis. 23(3):331–46.
10. Moorhead JF, Chan MK, El-Nahas M VZ. Lipid nephrotoxicity in chronic progressive glomerular and tubulo-interstitial disease. 1982.
11. Ruan XZ, Varghese Z, Moorhead JF. Inflammation modifies lipid-mediated renal injury. Nephrol Dial Transplant. 2003;18(1):27–32.
12. Muntner P, Coresh J, Smith JC, Eckfeldt J, Klag MJ. Plasma lipids and risk of developing renal dysfunction: The atherosclerosis risk in communities study. Kidney Int. 2000;58(1):293–301.
13. Querfeld U. Disturbances of lipid metabolism in children with chronic renal failure. Pediat Nephro 1993;7(6):749–57.
14. McGill H.C. J, McMahan CA, Herderick EE, Malcom GT, Tracy RE, Jack P. Origin of

atherosclerosis in childhood and adolescence. Am J Clin Nutr. 2000;72(5 SUPPL.):102-5.

15. Mahmud S, Jahan S, Hossain MM. Hyperlipidemia in childhood idiopathic nephrotic syndrome during initial remission and relapse. Mymensingh Med J. 2011;20(3):402–6.
16. Sreenivasa B, Manjunatha B, Joseph N. Comparative study of lipid profile abnormalities in first episode and relapse cases of childhood nephrotic syndrome. 2016;3(4):1297–300.
17. Ali EMA, Bushara HMM, Abdelraheem MB. Original Articles Dyslipidemia among children with nephrotic syndrome in Sudan. 2013;06(03):915–22.
18. Rosenman RH, Friedman M, Byers SO, Smith MK. The causal role of plasma defficiency in experimental hyperlipemia and hypercholesteremia. J Clin Invest. 1956;(group 8):522–32.
19. Attman PO, Alaupovic P. Pathogenesis of hyperlipidemia in the nephrotic syndrome. Am J Nephrol. 1990;10:69–75.
20. Hossain MA. Correlation between Serum Cholesterol and Serum Albumin Level in Childhood Nephrotic Syndrome. Urol Nephrol. 2016;3(4):13–6.
21. Krishnaswamy D***, Indumati.V**, Satishkumar D*, Vijay V*, Maharudra.Shekanawar* AM& RV, ***Professor. SERUM PROTEINS , INITIAL AND FOLLOW-UP LIPID PROFILE IN CHILDREN WITH NEPHROTIC SYNDROME Krishnaswamy D ***, Indumati . V **, Satishkumar D *, Vijay V *, Maharudra . Shekanawar *, Amareshwara . Maligi * & Rajeshwari . V *. Int J Appl Biol Pharm Technol. 2011;2(3):59–64.
22. Badiou S, Cristol J-P, Mourad G. Dyslipidemia following kidney transplantation: Diagnosis and treatment. Curr Diab Rep [Internet]. 2009;9(4):305–11.
23. Kobashigawa, Jon A, Kasiske BL. HYPERLIPIDEMIA IN SOLID ORGAN TRANSPLANTATION. Transplantation. 1997;63(3):331–8.
24. DO1 T, , Barr ML, Radovancevic B, Renlund DG, Mentzer RM Jr, Smart FW, Tolman DE, Frazier OH Y, JB VPA. A randomized , multicenter comparison of tacrolimus and cyclosporine immunosuppressive regimens in cardiac transplantation : decreased hyperlipidemia and hypertension with. J Hear Lung Transpl. 1999;18(4):336–445.
25. J. H. Brown, N. Anwar, C. D. Short, D. Bhatnager, M. I. Mackness LPH and PND. Serum lipoprotein (a) in renal transplant recipients receiving cyclosporin monotherapy. Nephrol Dial Transplant. 1993;8(January):863–7.

26. Hulzebos C V, Bijleveld CMA, Stellaard F, Kuipers F, Fidler V, Slooff MJH, et al. Cyclosporine A – Induced Reduction of Bile Salt Synthesis Associated With Increased Plasma Lipids in Children After Liver Transplantation. Liver Transplant. 2004;10(7):872–80.
27. Rm L, Ds G, Em H. Treatment of steroid-sensitive nephrotic syndrome : new guidelines from KDIGO . Pediatr Nephrol. 2013;28(3):415–26.
28. Davin J. The glomerular permeability factors in idiopathic nephrotic syndrome. Pediatr Nephrol. 2016;31:207–15.
29. Rf R, Ng L, Ma H, Sj A, We S. Glucocorticoids protect and enhance recovery of cultured murine podocytes via actin filament stabilization . Kidney Int. 2005;68(6):2473–83.
30. Arnaldi G, Scandali VM, Trementino L, Cardinaletti M, Appolloni G, Boscaro M. Pathophysiology of dyslipidemia in Cushing's syndrome. Neuroendocrinology. 2010;92(SUPPL. 1):86–90.
31. Leong KH, Koh ET, Feng PH, Boey ML. Lipid profiles in patients with systemic lupus erythematosus. J Rheumatol. 1994;21(7):1264–7.
32. Ingulli E, Tejani A, Markell M. The beneficial effects of steroid withdrawal on blood pressure and lipid profile in children posttransplantation in the cyclosporine era. Transplantation. 1993;55(5):1029–33.
33. Choi HK, Seeger JD. Glucocorticoid use and serum lipid levels in US adults: The third national health and nutrition examination survey. Arthritis Rheum. 2005;53(4):528–35.
34. Dietz WH. Health consequences of obesity in youth: Childhood predictors of adult disease. Pediatrics. 1998;(101):518–25.
35. Lai SW, Ng KC, Lin HF, Chen HL. Association between obesity and hyperlipidemia among children. Yale J Biol Med. 2001;74(4):205–10.
36. Chang CJ, Jian DY, Lin MW, Zhao JZ, Ho LT, Juan CC. Evidence in Obese Children: Contribution of Hyperlipidemia, Obesity-Inflammation, and Insulin Sensitivity. PLoS One. 2015;10(5):1–12.
37. Boyd GS, Koenigsberg J, Falkner B, Gidding S HS. Effect of Obesity and High Blood Pressure on Plasma Lipid Levels in Children and Adolescents. Pediatrics. 2005;116(2):442–6.

38. Korsten-Reck U, Kromeyer-Hauschild K, Korsten K, Baumstark MW, Dickhuth HH, Berg A. Frequency of secondary dyslipidemia in obese children. Vasc Health Risk Manag. 2008;4(5):1089–94.

APPENDICES

APPENDIX 1: STUDY SCHEDULE

ACTIVITY	ESTIMATED TIME
Proposal development and presentation	Jan2017-May 2017
Submission of proposal for ethical approval	June 2017
Data collection	November 2017-January 2018
Data analysis	February 2018
Dissertation writing	2018
Dissertation submission	2018

APPENDIX 2: CONSENT FORM

HYPERLIPIDEMIA AMONG CHILDREN ON FOLLOW UP FOR NEPHROTIC SYNDROM AT KENYATTA NATIONAL HOSPITAL

Informed Consent form for _____ _____

The principal investigator is Dr Ummulkheir Hassan under supervision from Dr Daniel Njai and Dr Bashir Admani on a study looking into hyperlipidemia among children on follow up for nephrotic syndrome. The study is being done under the department of Paediatrics and Child Health in the University of Nairobi.

This Informed Consent Form has two parts:

- Information Sheet (to share information about the research with you)
- Certificate of Consent (for signatures if you agree to take part)

You will be given a copy of the full Informed Consent Form

Introduction

I am a Student currently doing my Masters in Paediatrics and Child health at the University of Nairobi. I am doing a study looking at hyperlipidemia among children on follow up for nephrotic syndrome. Information will be given to you and you may feel free to ask questions before participating in the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them to me.

Purpose of the research

Hyperlipidemia is a hallmark of nephrotic syndrome. Hyperlipidemia is usually present during the acute phase of the disease and disappears with the resolution of proteinuria. However, children with nephrotic syndrome have been noted to have hyperlipidemia despite being in remission. Doing this study will enable us to determine lipid profile of children with nephrotic syndrome and so as to improve management and follow up.

Risks

The study poses no risk to the participant and all information given will be treated with utmost confidentiality.

Benefits

The study will improve patient management and follow up.

Participant selection

We invite all children who are on follow up for nephrotic syndrome at Kenyatta National Hospital to participate in the research.

Voluntary Participation

Your participation in this research is entirely voluntary as such no remuneration or compensation will be offered to the participants of the study. It is your choice to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose not to participate in this research project, you will still be offered the treatment that is routinely offered in this clinic for nephrotic syndrome.

Procedures and Protocol

Description of the Process

Once consented, a set of questions will be presented to you mainly asking on the condition of the child. Details on duration of illness and number of admission due to nephrotic syndrome. There after we will request to take 2mls of blood sample for lipid profile, total protein and albumin and also 5mls of urine to determine protein creatinine ratio.

Duration

We will just require 15 minutes of your time to gather information from you after which we proceed to sample collection.

Confidentiality

This research will improve follow up of children with nephrotic syndrome. We will not be sharing the identity of those participating in the research.

The information that we collect from this research project will be kept confidential. Information about you and your child that will be collected during the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up. It will not be shared with or given to anyone except the department of Paediatrics and Child Heath in the University of Nairobi.

Right to Refuse

You do not have to take part in this research if you do not wish to do so and refusing to participate will not affect your treatment at this clinic in any way. You will still have all the benefits that you would otherwise have at this clinic.

This proposal has been reviewed and approved by the department of Paediatrics and Child health and the Ethics committee in Kenyatta National Hospital, which is a committee whose task it is to make sure that research participants are protected from any harm.

You can ask me any more questions about any part of the research study, if you wish to. Do you have any questions?

PART II: Certificate of Consent Serial Number: _____

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it .Questions that I have asked have been answered to my satisfaction. I as a guardian/parent to: _____consent voluntarily to participate as a participant in this research.

Name of Participant_____ Researchers: Dr Ummulkheir Hassan

Signature of Participant _____ _____

Date _____ Date _____

Who to Contact

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following:

Name: Ummulkheir Hassan (Primary Researcher)

Mobile Number: 0724087388

Email: umulkheirhassan.uh@gmail.com

Name: Dr Daniel Njai

Mobile Number: 0722682929

Email: drdanielnjai@yahoo.com

Name: 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

APPENDIX 3: IDHINI

HAIPALIPIDEMIA KATIKA WATOTO WANAOFUATILIWA KWA MARADHI YA FIGO NEPHROTIC SYNDROME KWA HOSPITALI YA KENYATTA

Fomu ya Idhini ya _____ _____

Mpelelezi mkuu ni Daktari Ummulkheir Hassan chini ya usimamizi wa Dkt Daniel Njai na Dkt Bashir Admani katika utafiti wa kuangalia haipalipidemia katika watoto wenye kufuatiliwa kwa maradi ya nephrotic syndrome . Utafiti itafanyika chini ya Idara ya Afya ya Watoto katika Chuo Kikuu cha Nairobi.

Hi fomu ya idhini ina sehemu mbili:

- Sehemu ya Maelezo (kukuelezea zaidi kuhusu utafiti)
- Shahada ya Idhini (sahihi ikiwa umekubali kujihusisha na utafiti huu)

SEHEMU YA I: Maelezo

Mimi ni mwanafunzi katika chuo kikuu cha Nairobi, ninasomea shahada kuu kwenye Idara ya Afya ya watoto. Ningependa pamoja na wasimaizi wangu kutafiti haipalipidemia katika watoto wenye kufuatilia kwa maradhi ya nephrotic syndrome. Kando na haya utapewa maalezo zaidi kuhusu mada na pia una uhuru wa kuuliza maswali yoyote ili kuelewa uafiti huu zaidi.

Nia

Haipalipidemia ni mmoja wapo wa shida unaosababishwa maradhi ya figo nephrotic syndrome.Utafiti huu utasaidia kuboresha matibabu ya watoto wenye maradhi ya nephrotic syndrome.

Hatari

Hakuna hatari yoyote itakayotarajiwa utakaposhiriki utafiti huu.

Faida ya utafiti

Utafiti huu utasaidia kuboresha maisha ya watoto wetu na matibabu yao.

Waanaoalikwa kujihusisha na utafiti

Mtafiti anawakaribisha watoto wote wanaofuatiliwa katika clinic ya figo katika Hospitali ya Taifa Ya Kenyatta .

Kushiriki

Kushiriki utafiti huu utakuwa kwa njia ya kujitolea na kwa hivyo hakuna malipo yoyote atakayolipwa mshiriki wa utafiti huu. Iwapo hungependa kushiriki ,uamuzi huu hautakuathiri kwa njia yoyote iwe matibabu yako au utakavyiohudumiwa.

Maelezo kuhusu mchakato

Iwapo utakubali kushiriki utaulizwa maswali chache kuhusu hali ya mtoto amabayo itajazwa kwenye fomu.Baada ya hapo ,mtoto atatolewa mili lita mbili ya damu ili kupima kiwango ya lipid nap rotini kwa damu.pia utapewa chupa ya kuwaka mili lita tano ya mkoja ili kupima protein kwa mkojo

Wakati utakaotumika

utahitaji dakika kumi na tano tu kukuuliza maswali nakujaza fomu halafu mtoto kutolewa vipimo vya damu na mkojo.

Usiri

Matokeo ya utafiti huu yatawekwa siri wala hayatapatiwa mtu yeyote asiyehusika na utafiti huu. Zaidi ya hayo badala ya jina la mtoto, numbari zitatumiwa kutambulisha watoto hawa. Matokeo yatazungumziwa na idara ya afya ya watoto pekee.

Haki ya kutoshiriki

Kushiriki utafiti huu ni kwa kujitolea na iwapo hungependa kushiriki, uamuzi wako utaheshimiwa na pia hautathiri kwa njia yoyote matibabu yako. Bali utaendelea kupokea matibabu na huduma ya hospitali hii kama hapo awali.

Pendekezo hili limeangaliwa na kuidhinishwa na Idara ya afya ya watoto ya Chuo kikuu cha Nairobi na kamiti ya maadili ya utafiti katika hospitali ya Kenyatta inayohakikisha kuwa haki za wanaoshiriki utafiti wowote inchini,zinazingatiwa **.** Iwapo utakuwa na swali lolote kumbuka una uhuru kuuliza.

SEHEMU YA II: Shahada ya Idhini

Nambari Maalum:_____

Nimesoma maaelezo yote ya utafiti huu au nimesomewa maaelezo haya na nimekuwa na fursa ya kuuliza maswali .Maswali yangu yamejibiwa kadri na matarajio yangu kwa njia ya kuridhisha.Kwahio kama mzazi/ mlezi wa : _____ ningependa kupeana idhini yangu na pia kujitolea kushiriki kwa utafiti huu .

Jina la mshiriki: _____ Mtafiti mkuu: Dkt Ummulkheir Hassan

Sihihi la mshiriki: _____ sahihi ya mtafiti mkuu: _____

Tarehe: _____ Tarehe: _____

Kwa maelezo zaidi hata baada ya utafiti huu una uhuru wakuwasiliana na watu wafuatao kupitia anwani na numbari za simu silizoandikwa hapa chini.

Jina: Dkt Ummulkheir Hassan (Mtafiti mkuu)
Numba ya simu: 0724087388
Barua pepe: umulkheirhassan.uh@gmail.com

Dkt: Dkt Daniel Njai
Namba ya simu: 0722682929
Barua pepe: drdanielnjai@yahoo.com

Jina: Dkt Bashir Admani
Namba ya simu: 0721967818
Barua pepe: pedbashir@yahoo.com

Kenyatta National Hospital/University of Nairobi Ethics and Research Committee

College of Health Sciences
P. O. Box 19676 00202 Nairobi
Simu. (254-020) 2726300-9 Ext 44355
Barua pepe: uonknh_erc@uonbi.ac.ke

APPENDIX 4: ASSENT FORM

HYPERLIPIDERMIA AMONG CHILDREN ON FOLLOW UP FOR IDIOPATHIC NEPHROTIC SYNDROME AT KNH

Informed Assent Form for _____

This informed assent form is for children above 7 years of age who attend the Paediatric nephrology Clinics Kenyatta National hospital and who we are inviting to participate in research to study hyperlipidemia among children on follow up for idiopathic nephrotic syndrome

The principal investigator is Ummulkheir Hassan under supervision from Dr Bashir Admani and Dr Daniel Njai on a study looking at hyperlipidemia among children on follow up for idiopathic nephrotic syndrome, a study done under the department of Paediatrics and Child Health in the University of Nairobi.

This Informed Assent Form has two parts:

- **Information Sheet (gives you information about the study)**
- **Certificate of Assent (this is where you sign if you agree to participate)**

You will be given a copy of the full Informed Assent Form

Part I: Information Sheet

My name is Ummulkheir Hassan and I am a doctor at Kenyatta National Hospital. I am interested in doing a research in children with nephrotic syndrome that might help the children with this condition live a better life. We want to know the risk factors associated with hyperlipidemia among children with idiopathic nephrotic syndrome.

I am going to give you information and invite you to be part of a research study. You can choose whether or not you want to participate. We have discussed this research with your parent(s)/guardian and they know that we are also asking you for your agreement. If you are going to participate in the research, your parent(s)/guardian also have to agree. But if you do not wish to take part in the research, you do not have to, even if your parents have agreed.

You may discuss anything in this form with your parents or friends or anyone else you feel comfortable talking to. You can decide whether to participate or not after you have talked it over. You do not have to decide immediately.

There may be some words you don't understand or things that you want me to explain more about because you are interested or concerned. Please ask me to stop at any time and I will take time to explain.

Purpose: Why are you doing this research?

We want to improve the management and follow up of children with nephrotic syndrome

Choice of participants: Why are you asking me?

We want to get some information from children with nephrotic syndrome

Participation is voluntary: Do I have to do this?

You don't have to be in this research if you don't want to be. It's up to you. If you decide not to be in the research, its okay and nothing changes. This is still your clinic, everything stays the same as before.

I have checked with the child and they understand that participation is voluntary _____ (signature)

Procedures: What is going to happen to me?

If you allow us we are going to ask you some questions and take a small sample of blood and urine for analysis.

I have checked with the child and they understand the procedures _____ (signature)

Risks: Is this bad or dangerous for me?

You will not be in any harm when you take part in this research

I have checked with the child and they understand the risks and discomforts ____ (signature)

Benefits: Is there anything good that happens to me?

Nothing might happen to you, but the information you give us might help us improve follow of children at the nephrology clinic

I have checked with the child and they understand the benefits_____ (Signature)

Reimbursements: Do I get anything for being in the research?

Unfortunately there will be no gifts if you choose to participate in the study.

Confidentiality: Is everybody going to know about this?

We will not tell other people that you are in this research and we won't share information about you to anyone who does not work in the research study.

Information about you that will be collected from the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone.

Sharing the Findings: Will you tell me the results?

When we are finished with the research we will not contact you personally to give you the results but you can come find out about the research at the Department of Paediatrics, University of Nairobi. We will be telling more people, scientists and others, about the research and what we found. We will do this by writing and sharing reports.

Right to Refuse or Withdraw: Can I choose not to be in the research? Can I change my mind?

You do not have to be in this research. No one will be mad or disappointed with you if you say no. It's your choice. You can think about it and tell us later if you want. You can say "yes" now and change your mind later and it will still be okay.

Who to Contact: Who can I talk to or ask questions to?

You can ask me questions now or later. I have written a number and address where you can reach us or, if you are nearby, you can come and see us. If you want to talk to someone else that you know like your teacher or doctor or auntie, that's okay too.

If you choose to be part of this research I will also give you a copy of this paper to keep for yourself. You can ask your parents to look after it if you want.

You can ask me any more questions about any part of the research study, if you wish to. Do you have any questions?

PART II: Certificate of Assent **Serial Number:**

_____

I understand that this research is about hyperlipidemia among children on follow up for nephrotic syndrome .I will be asked questions, examined and blood and urine sample taken for analysis if I choose to participate in the research.

I have read this information (or had the information read to me) I have had my questions answered and know that I can ask questions later if I have them.

I agree to take part in the research.

OR

I do not wish to take part in the research and I have <u>NOT</u> signed the assent below._____ (initialed by child/minor)

<u>Only if child assents:</u>

Print name of child _____

Signature of child: _____

Date: _____

If illiterate:

I have witnessed the accurate reading of the assent form to the child, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness (not a parent) _____ AND Thumb print of participant

Signature of witness _____

Date _____

I have accurately read or witnessed the accurate reading of the assent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given assent freely.

Name of researcher: DR Ummulkheir Hassan
Signature of researcher_____
Date_____

Statement by the researcher/person taking consent
I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the child understands the purpose and procedure of the study
I confirm that the child was given an opportunity to ask questions about the study, and all the questions asked by him/her have been answered correctly and to the best of my ability.
I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this assent form has been provided to the participant.
Name of Researcher: DR Ummulkheir Hassan
Signature of Researcher _____
Date _____

Copy provided to the participant _____ (initialed by researcher)

Parent/Guardian has signed an informed consent: Yes_____ No_____

Who to Contact

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following:

Name: Dr Ummulkheir Hassan (Primary Researcher)

Mobile Number: 0724087388

Email: umulkheirhassan.uh@gmail.com

Name: Dr Bashir Admani

Mobile Number: 0721967818

Email: pedbashir@yahoo.com

Name: Dr Daniel Njai

Mobile Number: 0722682929

Email: drdanielnjai@yahoo.com

Kenyatta National Hospital/University of Nairobi Ethics and Research Committee

College of Health Sciences

P. O. Box 19676 00202 Nairobi

Tel. (254-020) 2726300-9 Ext 44355

E-mail: uonknh_erc@uonbi.ac.ke

APPENDIX 5: FIVE: QUESTIONNAIRE

Serial number …….

Date …….

Patient's demographics

Age (months/yrs.): ……..

Gender: Male ( ) Female ( )

Vital signs

Blood pressure: mmHg systolic…….

Diastolic……

Height (cm): ……..

Weight (kg): …….

BMI (kg/M^2): …….

Past medical history

When the diagnosis of idiopathic nephrotic syndrome was made…….. (Month, year)

Number of retreatment /relapse due to nephrotic syndrome in a year or past 6monthes since diagnosis…….……..……..

Current treatment (indicate the exact drug)…….

Laboratory results

Urine protein creatinine ratio (mg/mmol)…….

Serum albumin (g/L)……

Serum lipid profile: Total Cholesterol (mg/dl)……

Triglyceride (mg/dl)……

Low Density Lipoprotein (mg/dl)……

High Density Lipoprotein (mg/dl)……..

APPENDIX 6: BUGDET

Category	Remarks	Units	Unit Cost (KShs)	Total (KShs)
Proposal Development	Printing drafts	200 pages	5	1000
	Proposal Copies	6 copies	500	3,000
Data Collection	Printing questionnaire	70	5	350
	Printing consent	70	5	350
	Research assistant	4monthes	8000	32000
	Lipid profile	66 participants	2500	165000
	Urine protein creatinine ratio	66 participants	1000	66000
	Snack	66	100	6600
Data Analysis	Statistician	1		25,000
	Printing drafts	500pages	5	2500
	Printing Thesis	6 copies	800	4,800
	Posters	1		2,000
Contingency (15%)				36390
TOTAL				**344990**