CLINICAL AND HISTOPATHOLOGICAL PATTERNS OF GLOMERULONEPHRITIDES AMONG PATIENTS AT MOI TEACHING AND REFERRAL HOSPITAL IN ELDORET, KENYA

Maritim Peter Kipyegon Kirui

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DECLARATION

Student's Declaration

This thesis is my original work and has not been presented for a degree in any other University. No part of this thesis may be reproduced without prior permission of the author or Moi University.

 Maritim, Peter Kipyegon

SM/PGM/03/2013

Sign: …………………………................... **Date**: ……………

Declaration by Academic supervisors

This thesis has been submitted with our approval as the University supervisors.

Prof. Owino Ong'or Willis, MBChB, MMed, MPH

Associate Professor of Medicine, Department of Medicine

Moi University School of Medicine

Sign: …………………………................... Date: ……………

Dr. Mathew Koech, MBChB, MMed, cert. Nephrol (S.A) Phys. FISN.

Consultant Physician

Moi Teaching and Referral Hospital

Sign: …………………………................... Date: ……………

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

CKD	Chronic Kidney disease
DM	Diabetes mellitus
ESRD	End stage Renal disease
FSGS	Focal Segmetal Glomerulosclerosis
GBM	Glomerular Basement Membrane
GN	Glomerulonephritis
IF	Immunoflorescence
KDIGO	Kidney Disease; Improving Global Outcome
MCD	Minimal Change Disease
MPGN	Membranoproliferative Glomerulonephritis
MTRH	Moi Teaching and Referral Hospital
MUSOM	Moi University School of Medicine
RRT	Renal replacement therapy
SSA	Sub-Saharan Africa
WHO	World Health Organization

ABSTRACT

Background: End stage renal disease (ESRD) affects 3.2 million people globally. The prevalence of ESRD in Kenya is 16 per 1 million populations. Glomerulonephritides (GN) are the leading causes of ESRD globally. In resource limited settings (RLS) histological diagnoses are rare, and treatment is often empiric. As such, limited data exist on types of GN in RSL.

Objective: To describe the clinical and histopathological patterns of GN at Moi Teaching and Referral Hospital (MTRH).

Methods: This cross sectional study conducted at the MTRH renal and adult medical wards enrolled consecutive participants ≥15 years with nephritis or nephrosis (symptoms and signs of GN including hematuria, body swelling, reduced urine output and hypertension). Demography (age, gender, body mass index) clinical (history& physical examination) and laboratory (cholesterol, albumin, creatinine, complementC3, antinuclear antibody, anti-streptolysin-O titers, complete blood count and urinalysis) data were collected. Renal biopsies were conducted and tissues subjected to histopathological diagnosis by light microscopy. All data were collected using a structured questionnaire, keyed into Microsoft Excel® database and analysed using STATA version 13®. Descriptive statistics were summarized in tables and graphs and correlations were done using Pearson's Chi Square test.

Results: Of the 42 participants who had a renal biopsy conducted 24(57.8%) were female, median age was 35 years (IQR: 24, 45) and majority (86.3%) had hematuria. Nephrosis and nephritis accounted for 46.7% of the clinical presentations each. Three (6.7%) of the cases were indeterminate. Based on renal histopathology results the most common patterns were: Focal Segmental Glomerulosclerosis (FSGS – 23.8%); Lupus Nephritis (LN – 19.0%); Minimal Change Disease (MCD – 11.9%); and Membrano-proliferative glomerulonephritis (MPGN – 9.5%). There was no relationship between the type of clinical syndrome and the histological pattern (p = 0.129).

Conclusion: The most common GN at MTRH on histological diagnosis is FSGS.

Recommendation: Empiric treatment of patients with GN based on clinical presentation should be discouraged since no significant association was established between clinical and histological findings

CHAPTER ONE: INTRODUCTION

1.1 Background information

Primary glomerulonephritis (GN) remains the leading cause of end‑stage renal disease (ESRD) in many developing countries(Barsoum, 2002) and is presumed to be responsible for 52% of patients with ESRD in Africa(Arogundade, Sanusi, Hassan, & Akinsola, 2011; Okpechi, 2012) In Sudan, the overall prevalence of treated ESRD is 106 patients per million population, among these the incidence of primary GN is under diagnosed and reported as 5.5%; whereas in more than 40%, the primary kidney disease leading to ESRD is undetermined, the patients being late presenters with established ESRD. GN remains the most probable underlying etiology in this group labeled as having ESRD of uncertain etiology.(Elamin S, 2010)

Focal segmental glomerulosclerosis (FSGS) is the leading of glomerular disease worldwide. In India a five decade analysis of glomerular diseases causing nephrotic syndrome found out that FSGS was most common pattern.{Rathi, 2014).

1.2 Problem statement

Glomerulonephritis is linked to the upsurge in incidence and prevalence of chronic kidney disease (CKD) in both developed and developing nations.(Arogundade & Barsoum, 2008)

There are no studies looking at the clinical presentation of GN at MTRH.

The last documented pattern of GN was done over 2 decades ago (McLigeyo, 1994). Thus no current data is available on the trend of GN patterns.

1.3 Study justification

Glomerulonephritis in SSA and Kenya in general is not well elaborated and described in terms of clinical and histopathological patterns.

The study will provide data on the clinical and histological patterns of GN that is scarce.

1.4 Research question

What are the clinical and histopathological patterns of glomerulonephritis in patients seen at MTRH?

1.5 Objectives

1.5.1 Main objective
To determine the clinical and histopathological patterns of glomerulonephritis in patients seen at MTRH.

1.5.2 Specific objectives
1. To describe the clinical patterns and presentation of glomerulonephritis (GN) as seen at MTRH.

2. To find out the histopathological patterns of GN encountered at MTRH.

3. To correlate the association of clinical presentations and histopathological patterns of GN.

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology

Endstage renal disease (ESRD) affects 3.2 million people globally. The prevalence of ESRD in Kenya is 16 per 1 million population. Glomerulonephritides (GN) are the leading causes of ESRD globally.

Studies have shown that renal disease, especially glomerular disease, which commonly presents as nephritic syndrome, is more prevalent in Africa and more severe in blacks than whites.(Naicker, 2003) It is estimated that 2-3% of all medical admissions in tropical countries are due to renal related complaints, the majority being glomerulonephritis.(Naicker, 2003) In Nigeria, glomerulonephritis accounts for 5.9% of the aetiology of renal failure and as high as 40% of cases of death due to chronic kidney disease (CKD)(Ojo, Akinsola, Nwosu, & Odesanmi, 1992). Locally a study done by Mcgligeyo found that the prevalence of GN was 25%(McLigeyo, 1994).

GN in acute nature or chronicity has an impact in the disease burden of a nation and a region at large. SSA contains approximately 70% of the least developed countries of the world, which have huge debt burdens and poor governmental policies with an estimated population of about 800 million, predominantly rural (65%), most of the countries have a gross domestic product per capita of less than $1,500, and about half the population lives on less than $1 per day; management of CKD is not just difficult, but impracticable.(Department,of, the United Nations Secretariat, & Prospects, 2006) This extreme poverty, the increasing prevalence of non-communicable diseases such as hypertension and diabetes mellitus, and

the ever increasing prevalence of communicable or infectious diseases—exemplified by the scourge of human immunodeficiency virus/acquired immunodeficiency syndrome and hepatitis B virus infection—has led to a phenomenal increase in the incidence and prevalence of CKD in SSA. The overall life expectancy in SSA has decreased significantly in the last 10 years and now averages 46.3 and 44.8 years for women and men, respectively.(Arogundade & Barsoum, 2008) Kenya in 2006 had a life expectancy of 48.9 years but currently in 2010 it rose to 57.9 years as per the 2014 world population review.

It is estimated that 2% to 3% of medical admissions in tropical countries are for renal-related symptoms, with the majority being the glomerulonephritides.(Arogundade & Barsoum, 2008).

2.2 Etiology and risk factors

The etiologic agents of GN can be classified as infectious and non-infectious agents. GN in the tropics is presumed to be caused by infections which often than not are untreated or treated when already too late. Tailored to specific regions, any prevalent infection in this set up is most often" implicated for the GN "(Mathieson, 2006). Examples of infectious agents include, group A beta-hemolytic streptococcus- serotype 12 and 49, hepatitis B viral and malaria.

Non infectious agents can either be as a result of primary renal diseases or systemic diseases. Examples of primary renal diseases include Membranoproliferative

Glomerulonephritis (MPGN) and idiopathic FSGS. The most common systemic cause of GN is sylstemic lupus erythromatosus (SLE)

Trying to understand etiology of GN has led to proposition of there being genetic predisposition or a secondary trigger, the former being referred to as 'first hit' and the later as 'second hit' which is mediated by a pathogenic immune response and the mediators of tissue injury. (Couser & Johnson, 2014)

Genetic risk factors may vary one individual to the other. Different glomerular diseases also show varied genetic predisposition, for example patients with genetic variants in apolipoproteinL1 (APOL1) are predisposed to kidney diseases. Two APOL1 risk alleles have been indentified in subjects of black decent and it is now known to predispose one to FSGS. There is also a strong genome linkage between primary Membranous Nephropathy and HLA DR, as well as single nucleotide polymorphisms in PLA2R genes (Jeffrey et al, 2015).

2.2 Pathogenesis

Infectious agents either in acute or chronicity lead to various mechanisms that cause GN and it is also now known that infection also play a role in triggering autoimmunity. Autobodies associated with chronic infection include cryoglobulins (IgM antibodies directed against IgG), rheumatoid factors, antinuclear antibodies, and even antineutrophil cytoplasmic antibodies (ANCAs). It has been noted that several factors play a role on the transition from

an initial immune response to an exogenous agent into an autoimmune response. Infections trigger an immune response after gaining entry into circulation through local infection (such as skin or sinus). The first immune response is innate which can contain the infection, but if the infection persists, adaptive immune response takes effect with resultant T and B cells that are antigen specific. Autoimmunity usually does not occur as a result of deletion of self-reactive T cells through central tolerance. Loss of self tolerance leads to autoimmunity. The major mechanisms of development of autoimmunity are: abnormalities of immune regulation, generalized activation of preexisting autoreactive T and B cells (adjuvant or bystander effects, epitope conformational changes, epitope spreading, antigen and antibody complementarity.{Couser, 2014). The end result is tissue injury of the glomeruli with resultant pathological findings

2.4 Clinical features

There are various clinical presentations that are synonymous with renal diseases. The most common presentations are hematuria, body swelling, oliguria and anuria. Laboratory evaluation shows presence of protein in urine or deranged renal function. Renal diseases are mostly asymptomatic only to present in late stages of the illness; these patients are mostly discovered during screening exercises.

The most common clinical syndromes that patient present with are either nephritic or nephrotic syndromes. In a study done in Sudan among adult patients, the varying presentation of glomerular diseases was shown to be nephrotic syndrome 46.5%,

unexplained renal failure 33.8%, asymptomatic urinary abnormalities 8.5%, nephritic syndrome 7%and non-nephrotic proteinuria 4.2%.(Nadium, Abdelwahab, Ibrahim, & Shigidi, 2013) A similar study on the spectrum of glomerular diseases in Iraq revealed presentation of acute kidney failure in 5.2%, nephrotic syndrome75.9%, proteinuria62.1%, hematuria10.3%, SLE 3.4%, nephritic syndrome 10.3%, anemia 17.2% hypertension 32.8% and CKD 17.2%.(Al-Saegh & Assad, 2013)

2.5 Renal biopsy and complication

Renal diseases are mostly diagnosed by clinical acumen(Elamin S, 2010). The accurate diagnosis of GN is by performing a renal biopsy. This procedure is not only important in diagnosis but also in planning for specific treatment. It is established that since the use of ultrasound guided biopsy, there has been much understanding of pathology and pathogenesis of glomerular diseases and thus improving the overall outcome of this diseases when treated with accurate diagnosis.(etal, 2011) The safety of the procedure has been shown to be good and less complications occurring. A retrospective study in South Africa showed that of the 112 patients who underwent native kidney biopsies minor complications only occurred in 25.8% and no major complication occurred. (K.M etal, 2011)

Similarly a study in Sudan adult patients who were biopsied were found to have minimal complication, eight out of 83 patients developed non-life threatening complications (9.6%). They were mainly pain at puncture site in four patients (4.8%), massive hematuria in three

patients (3.6%), and in one more patient(1.2%) the procedure was complicated by severe pain together with massive hematuria. Most patients, 75 out of 83 (90.4%), underwent the procedure without complications. Two patients (2.4%) required blood transfusions due to massive bleeding. None of the patients required further surgical or radiologic interventions and no mortality was observed following kidney biopsies.(Nadium et al., 2013)

There are various indications of renal biopsies, in several studies the most common indications were: unexplained renal failure, nephrotic syndrome, unexplained renal failure of transplanted kidney, worsening of renal function, isolated non-nephrotic proteinuria or hematuria, renal masses and connective tissue diseases.(Nadium et al., 2013)

2.6 Patterns of Glomerulonephritides

Outcomes of renal biopsies have been shown to vary as the pattern of renal diseases do vary according to geographical factors and socioeconomic circumstances.(Naicker, 2003)

IgA nephropathy (IgAN) is the predominant glomerular disease seen across Europe, whereas in Africa, it is not common.(Okpechi, 2012) The most frequently described glomerular disease in Africa is mesangiocapillary glomerulonephritis (MCGN).(Okpechi, 2012) The difference in the prevalence of glomerular disease seen in Africa and Europe may depend on several factors including genetic, socio-economic and demographic influences. Different exposure to infections (hygiene hypothesis) and patterns of T-helper 1 and T-helper 2 responses may also contribute significantly to observed differences.(Okpechi, 2012)

A study in Iraq had Nephrotic syndrome as its predominant clinical presentation (75.9%). Focal segmental glomerulosclerosis (FSGS) was the commonest GN at (29.3%) followed by minimal change disease (20.7%) and membranous glomerulonephritis (13.8%). (Al-Saegh & Assad, 2013)

Senegal also had a study on patterns of renal diseases that are proven by biopsies amongst 133 patients and Lupus nephritis was the most common in 48(36.1%) with a female preponderance, focal segmental glomerulosclerosis (FSGS) 26(19.5%), followed by membranous glemerulopathy (MGN) 13 (9.8%), and mesangial proliferative glomerulonephritis 6 (4.5%). IgA nephropathy and acute proliferative glomerulonephritis each accounted for 4(3.0%). Membranoproliferative glomerulonephritis accounted for 3 (2.3%). Focal proliferative and cresentic glomerulonephritis each accounted for 2(1.5%). Vasculitis was not common and there was no report of anti-GBM disease.(Al Riyami, Al Shaaili, Al Bulushi, Al Dhahli, & Date, 2013)

 Accurate diagnosis and treatment of GN is important in ultimately reducing the prevalence CKD/ESRD. As noted by Biruck D. Yirsaw in a letter to the editor of *Annals of African Medicine,* he lamented that the prevalence of CKD particularly ESRD patient population is on rise worldwide, and that it remains under diagnosed and under-treated since in its early stages the disease is often asymptomatic, making individuals with the disease and also their healthcare providers unaware of its silence yet threatening presence.(Yirsaw, April-June, 2012)

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Study setting

The study was conducted at the Moi Teaching and Referral Hospital (MTRH) medical wards and renal outpatient clinic. MTRH serves as the teaching hospital for Moi University School of Medicine (MUSOM) and is the second largest tertiary referral center in Kenya. It serves a population of 16 million people (40% of Kenya's population) in western Kenya and is the primary care site for the 300,000 urban population of Eldoret town. The hospital has a total bed capacity of 720 with 140 beds in two adult general medical wards and has a renal clinic that patients who do not require admissions are treated and followed up from.

3.2 Study Population

The study population was patients attending the MTRH renal clinic and/or admitted at the hospital with glomerulonephritis.

3.3 Eligibility Criteria

3.3.1 Inclusion criteria

1. Patients of the age of 15 years and above.

2. Patients with nephritic syndrome.

3. Patients with nephrotic syndrome.

4. Patients with symptomatic proteinuria and or hematuria not meeting the nephritic or nephrotic   syndrome.

3.3.2 Exclusion criteria

1. Patients who have transplanted kidneys

2. Patient with renal tumors or suspected genitourinary abnormality

3. Patients with urinary obstruction.

5. Patients with shrunken kidneys/small kidneys (<8cm)

6. Patients with polycystic kidneys.

7. Patients with solitary kidney or any acquired or congenital malformation of the kidneys.

3.4 Study design

A descriptive study design

3.5 Sample size

This was a census done over one year period seeking to recruit all patients encountered with

Glomerulonephritis.

3.6 Sampling technique

Patients from the study population were screened for Glomerulonephritis during the study
duration and those who met inclusion criteria were recruited

3.7 Data variables

3.7.1 Primary outcome variables

Nephritic syndrome: This is a syndrome characterized by abrupt macroscopic hematuria,

oliguria , acute renal failure, manifested by edema and hypertension. Urinary protein varies

widely in this syndrome and is generally less than 3g of protein per day.(Hricik et al., 1998)

Nephrotic syndrome: Patients with the nephrotic syndrome present with"heavy"

proteinuria (protein excretion, >3 g per day), hypoalbuminemia, edema, and varying degrees

of hyperlipidemia and lipiduria.(Hricik et al., 1998)

3.7.2 Other data variables that were collected

1. Creatinine levels

2. Albumin levels

3. Cholesterol levels

4. Complete Blood count

5. HIV rapid diagnostic test

6. Complement C3 level

7. Anti nuclear antibody

8. Antistreptolysin-O- titer

3.8 Study procedure

The study was done at MTRH renal clinic and patients admitted in the medical general wards. Recruitment of participants into the study was done in the triage room, the waiting bay as they waited to see the clinicians and in the medical wards. The purpose of the study and potential benefits was explained to the participants individually in a language that they understood and all their questions answered. Those who met the inclusion criteria and consented to participate in the study were enrolled after signing informed consent forms.

The informed consent acquisition process entailed:

1. Introduction of the researcher seeking consent to the patient(APPENDIX II)

2. A brief description of the study in summary

3. Explanation to the patient why he/she required the renal biopsy(patient individualized indication for biopsy)

4. The whole biopsy procedure from preparation before, during, and after the biopsy was explained as in appendix V

5. If the patient assented/consented to participate, he/she was requested to sign the consent form in the presence of a witness and the researcher assistant.

The study procedure is summarized as shown in figure 1:

14

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┌─────────────────────────────────────────────────┐
│   Patients suspected to have GN in Renal clinic/ward │
└─────────────────────────────────────────────────┘
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┌─────────────────────────────────────────────────┐
│   Examined, medical records -KUB, co morbidities, │
│            ascertain GN of each patient.          │
└─────────────────────────────────────────────────┘
```

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┌──────────────────────────────────────┐        ┌──────────────┐
│ Those who met inclusion criteria & gave informed │   │  EXCLUDED    │
│   consent had questionnaire filled and │        └──────────────┘
└──────────────────────────────────────┘
```

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┌──────────────────────────────────────┐
│   Lab work: C3, ASOT, ANA, Cr,         │
│   Alb, Chol, Hb, PLT, BT, INR, U/A     │
│            drawn for analysis          │
└──────────────────────────────────────┘
```

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┌──────────────────────────────────────┐
│   Ultrasound-guided kidney biopsy      │
│               done by PI               │
└──────────────────────────────────────┘
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┌──────────────────────────────────────┐
│                Histology               │
└──────────────────────────────────────┘
```
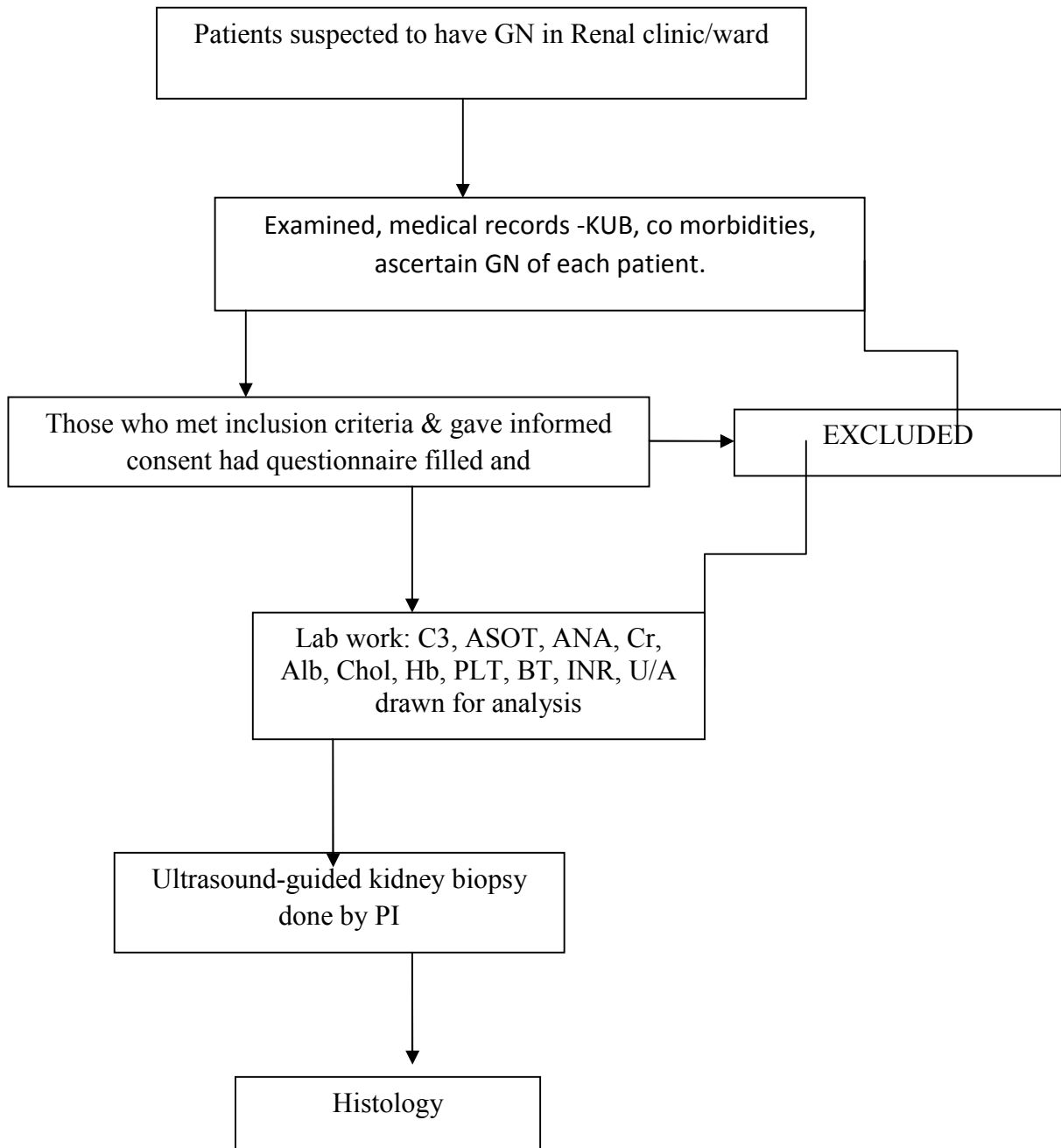
Figure 1: Algorithm of the study procedure

The patient was also told the measures that were taken to ensure the safety and the confidentiality of the data they gave. It was also emphasized that their participation in the study was voluntary. If they decided not to participate it would not affect the health care services they were going to receive. They were also free to decline to answer any particular question they did not wish to answer for any reason. The informed consent forms are attached in Appendix II & III. Participants were first taken through the study questionnaire (Appendix I). Subsequently they had their anthropometric measurements (body weight – Appendix XI) and blood pressure taken (Appendix IX). All participants had urine collected for urinalysis using urine dip-stick (Appendix IV) and then underwent a native kidney biopsy (Appendix V) and sample taken for light microscopy (hematoxylin and eosin, periodic acid Schiff, silver methenamine and Jones methenamine silver). Patients recruited from the clinic were also scheduled for kidney biopsy as outpatient and thereafter they were observed at the observation room for 24 hours to monitor any post-procedure complication. The cost incurred for this stay was paid from the research budget allocation. The patient did not incur this cost. In case of any complication that arose from the procedure, the cost of admission, medical intervention and any other expense as a result of this complication were settled by the principal investigator.

The results from the study were availed to the primary care doctor to assist in the patients' management. Patients enrolled in the ward were further advised on the importance of outpatient follow-up on discharge at the hospitals' renal clinic.

3.9 Data collection

Clinical and laboratory data were collected through interviewer administered questionnaire and examination of medical and laboratory files/reports respectively. The research assistant, who had undergone International Review Board training (IRB), facilitated the consent acquisition. The data was then transferred to a database.

3.10 Data management

A clinical assessment questionnaire was used to collect study participants' demographic, socioeconomic and clinical data. Anthropometric and laboratory measurements were recorded on a pro-forma.

Data was dually entered into Epidata software (copyright by EpiData Association 2000-2014) and validated. Simple descriptive statistics, including frequencies, proportions and means were used to summarize the dataset

3.11 Ethical considerations

1. Ethics review and approval was sought from the Moi Teaching and Referral Hospital/Moi University School of Medicine Institutional Research and Ethics Committee(IREC)

2. Permission was sought from the management of MTRH to conduct the study.

3. Informed consent was obtained from every participant before participating in the study.

4. Participation into the study was voluntary and recruited patients were free to withdraw from the study any time as the study progressed.

5. Patients who declined to be enrolled were not discriminated against and they received treatment as routinely provided.

6. All patient information was kept confidential with only the study results of participants being shared with the attending clinician.

7. No payment was made to the participants.

8. The clinician directly managing the patient did not take part in recruitment or consenting and therefore minimized coercion.

3.12 Dissemination of results

The results of the study were disseminated through a written thesis and an oral defense convened by the school of medicine. The results shall also be published in a peer reviewed journal.

CHAPTER FOUR: RESEARCH FINDINGS

4.1 Recruitment and enrolment.

A total of 87 patients were encountered for recriutment:24 from the medical wards and 21 from the renal clinic during the study period. Of all the patients screened: 42 patients did not meet the inclusion criteria (27 had shrunken kidneys, 10 had obstructive uropathy, 2 had polycystic kidney diseases, 1 had transplanted kidney and 2 had solitary kidneys). 45 patients were enrolled in the study with only 42 consenting for kidney biopsy after 3 declined to consent. The results of the 42 patients were included in the final analysis.

The recruitment schema is shown in Figure 2:

8 | 87 patients were screened and 45 recruited -21 renal clinic, 24 ward

↓

45 medical records examined- KUB, co morbidities, ascertain GN

↓

45 met inclusion criteria & 45 questionnaire filled
45 gave informed consent for participation

↓

45 Lab work: C3, ASOT, ANA, Cr, Alb, Chol, Hb, PLT, BT, INR, U/A done → 3 declined biopsy & excluded

↓

42 ultrasound guided kidney biopsy done by the PI

↓

42 histological results by LM obtained

From renal pathologist Lancet → Results relayed to pt & primary physician

Figure 2: Recruitment schema

4.2 Demographics

The median age was 35 (IQR: 24-45) years with a minimum and a maximum of 15 and 84 year respectively. Females represented 57.8% of the participants.

4.3 Clinical characteristics

More than half, 27 (60.0%) had bloody/cola coloured urine. Thirty five, 77.8%, had reduced urine output. More than 90% had facial swelling.

Four, 8.9%, had been treated for recurrent sore throat, and another 6 (13.3%) had been treated for chronic wounds/boils. More than half, 23 (51.1%) had been treated for hypertension and another 22.2% had been treated for diabetes mellitus.

Seventeen, 37.8%, had used NSAIDS, and another 33.3% had used traditional herbs in the recent past.

Only one participant reported family history of kidney disease and the member who was affected was the aunt.

Physical examination revealed that 15 (36.6%) had anasarca, 20 (48.8%) had edema, 3 (7.3%) had pallor. The clinical characteristics are summarized in table 1 and figure 3:

Table 1: Clinical Characteristics

Variable	n(%)
Symptoms	N=45
Bloody/cola coloured urine	27 (60.0%)
Reduced urine output	35 (77.8%)
Increased urine output	1 (2.2%)
Pain on urination	4 (8.9%)
Frequent urination	13 (28.9%)
Facial swelling	42 (93.3%)
Leg swelling	43 (95.6%)
Difficulty in breathing	14 (31.1%)
Bloody diarrhea	2 (4.45)
Treated for any of the following	
Recurrent sore throat	4 (8.9%)
Chronic wounds/boils	6 (13.3%)
Hypertension	23 (51.1%)
Diabetes Mellitus	10 (22.2%)
Drugs used recently	
Traditional medical herbs	15 (33.3%)
NSAIDS	17 (37.8%)
Others: Steroids	1 (2.2%)
Family history of kidney disease	1 (2.2%)
General & systemic examination	
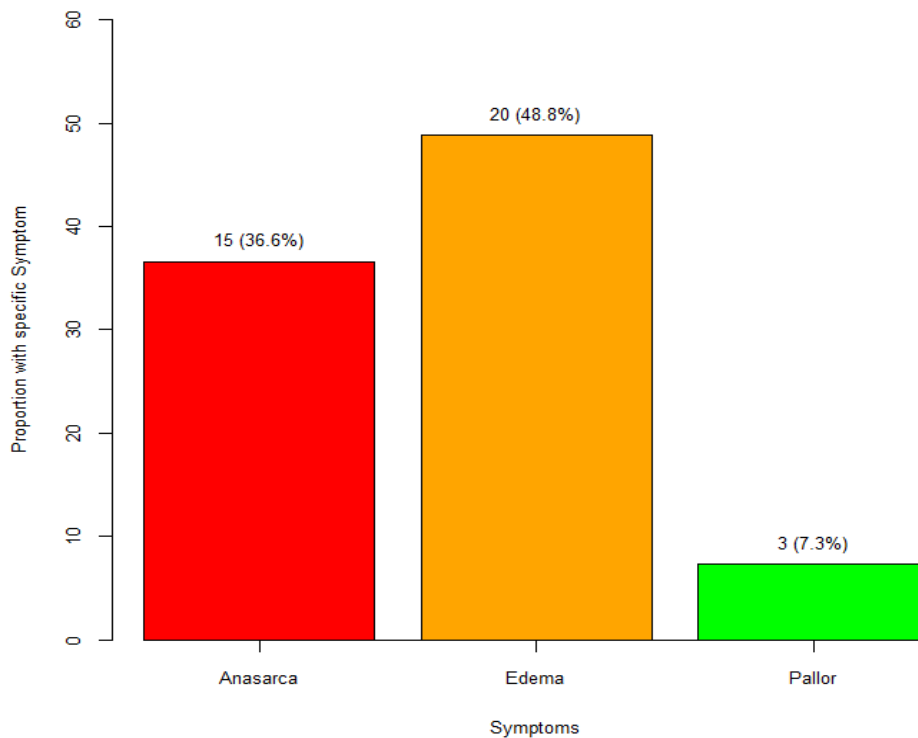
Figure 3: Distribution of participants by General Examination

Median SBP, and DBP were 130.0 (IQR: 120.0, 140.0), and 80.0 (IQR: 74.0, 90.0) respectively. Twelve, 26.7%, were hypertensive, SBP>140 and/or DBP>90 (Table 2).

Median BMI was 24.6 (IQR: 22.4, 29.2) kg/m^2 with 21 (47.7%) who were either overweight or obese. Cardiovascular examination revealed that 2 (4.4%) had abnormal functionality with systolic murmur that was reported in one of the participants. All the participants had normal nervous system (Table 2).

Table 2: Clinical vital and systemic characteristics

Variable		
Continuous variables		**Median (IQR)**
SBP (mm Hg)		130.0 (120.0, 140.0)
DBP (mm Hg)		80.0 (74.0, 90.0)
‡BMI (Kgs/m^2)		24.6 (22.4, 29.2)
Categorical variables		**n (%)**
BP>140 /90		12 (26.7%)
Ascites		14 (31.1%)
Organomegally		2 (4.4%)
Respiratory(Edema&Effusion)		4 (8.9%)
Abnormal cardiovascular functionality		2 (4.4%)

†n = 43; ‡n = 44.

4.4 Laboratory findings

Normal WBC count was recorded in 27 (60.0%) participants, 10 (22.2%) had leucopenia, and 8 (17.8%) had leukocytosis. Over seventy percent (70.5%) were anemic and 2 (4.6%) had polycythemia. Thirty six (80.0%) had normal platelets levels and 7 (15.6%) had either thrombocytopenia.

Total cholesterol among 22 (48.9%) participants were above >5.2 mol/L. Low albumin was documented in 25 (55.6%) of the participants.

Analysis of the other laboratory results is summarized in table 3:

Table 3: laboratory findings

Test	N= 45	Nephrotic	Nephritic
Low C3	10(22.2%)	6(60%)	4(40%)
ANA positive	9(20.0%)	8(88.9%)	1(11.1%)
ASOT positive	5(10.9%)	4(80%)	1(20.0%)
eGFR-CKD EPI >60 ml/min	22(48.9%)	15(68.2%)	7(31.8%)
eGFR-CKD EPI <60ml/min	23(51.1%)	7(30.4%)	16(69.5%)
Hematuria	38(86.3%)	28(73.7%)	10(26.3%)
High cholesterol	22(48.9%)	19(86.4%)	3(13.6%)
Low Albumin	25(55.6%)	18(72.0%)	7(28.0%)
Proteinuria Nephrotic Range	22(48.8%)	22(48.8%)	-
Proteinuria Non Nephrotic range	23(51.2%)	-	23(51.2%)

Majority of patients with low C3 6(60.0%), positive ANA (88.8%) and positive ASOT 4(80.0%) had nephrotic syndrome on presentation. Similarly a high proportion of patients

with nephrotic syndrome had hematuria 28(73.7%), high cholesterol 19(86.4%) and low albumin 18(72.0%). CKD with eGFR of < 60 ml/min on presentation was found to be high in nephritic syndrome at 16 (69.5%).

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4.5 Syndromic Presentation

The overall syndrome presentation was equal between the nephrotic and nephritic syndrome at 21(46.7%) with 3(6.7%) being indeterminate this is shown in table 4:

Table 4: syndromic presentation

Nephrotic	Nephritic	Indeterminate	
21(46.7%)	21(46.7%)	3(6.7%)	N=45

4.7 Histology

Histology results showed that majority of the participants (23.8%) had FSGS. End stage kidney disease (ESRD) was found in 2 (4.8%) of the participants. Five (11.9%) of the participants had MCD, and 1 (2.4%) had malignant hypertension. Table 5 shows the histological patterns.

Table 5: Histology

Histology		n (%)
FSGS		10 (23.8%)
Lupus Nephretis(LN)		
LN III	1(2.4%)	
LN IV	3(7.1%)	8(19%)
LN V	4(9.5%)	
MCD		5 (11.9%)
MPGN		4 (9.5%)
ATN		2(4.8%)
ESRD		2 (4.8%)
Idiopathic membranous		2 (4.8%)
Membranous		2 (4.8%)
Mesongioproliferative		2 (4.8%)
Malignant hypertension		1(2.4%)
PIAGN		1 (2.4%)
Pyelonephritis		1 (2.4%)
Renal vasculitis		1 (2.4%)

4.7 Clinical Syndrome and Histology Association

There was no significance in any correlation between syndromic presentation and histology (p-0.129). Most patients with nephrotic syndrome 70% had FSGS on histology, LN nephritis had equal presentation of nephrotic and nephritic presentation 37.5%. This is shown in table 6:

Table 6: clinical and histology association

Histology	Nephrotic	Nephritic	Indeterminate	P – value
FSGS	7(70%)	3(30%)	0(0%)	
LN	3(37.5%)	3(37.5%)	2(25%)	
MCD	3(60%)	2(40%)	0(0%)	0.129
MPGN	0(0%)	4(100%)	0(0%)	
Others	5(33.3)	9(60%)	1(6.7%)	

Chapter Five: Discussion

Renal biopsies enabled the diagnosis of glomerulonephritis among the 45 patients that would have been impossible. The age of participants was comparable to studies done around the region, with a median age of 35 (IQR: 24, 45) years compared to a Sudanese adult study with ages of 34.6 ± 18 years. The difference with the Sudanese study is that they had more male participants at 54.9% compared to our predominant female population of 28(62.2%). (Nadium et al., 2013)

There are various modes of presentation of glomerular diseases; they may be symptomatic or asymptomatic. Those who are symptomatic often seek medical attention early as compared to the asymptomatic patients who present late. This varied presentation of GN has been illustrated in various studies and there is no one specific symptom that is pathognomonic for GN. The most frequent presentation was hematuria 86.3%. Iraq had less of hematuria 10.3% on presentation. (Al-Saegh & Assad, 2013). Patients presenting with proteinuria were analyzed as to whether it is of nephrotic range or not. The study had nephrotic range proteinura of 48.8%, in Sudan nephrotic range proteinuria was at 46.5%(Nadium, 2013)and in Iraq, nephrotic proteinuria was at 75.9%.(Al-Saegh & Assad, 2013).

In terms of syndromic presentation our study had equal representation of nephritic and nephrotic syndromes. A patient presenting with high cholesterol, low abumin and varying degrees of hematuria will most likely have nephrotic syndrome as demonstrated by the study.(Hricik, 1998). Syndromic presentation has been shown to vary depending on the

study population, for example a study done in Sudan among adult patients with GN, nephrotic syndrome represented 46.5%, nephritic syndrome 7%, unexplained renal failure 33.8%, asymptomatic urinary abnormalities 8.5%.(Nadium, Abdelwahab, Ibrahim, & Shigidi, 2013)The results differ from these studies due to varied clinical presentation and the various clinical approach including referral system in these countries.

Late presentation was shown by the finding of histological patterns that suggest disease chronicity. These chronic disorders include Chronic interstisial nephritis (CIN) 2(4.9%), ESRD 1(2.4%) and chronic glomerulonephritis 1(2.4%). The explanation to this late presentation could be attributed to the health seeking behavior of these patients which is shown by the 34.2% that had used a non specified amount of herbal medication and self medication of NSAIDS for quite some time before presentation. This may have resulted to direct or indirect kidney injury. Secondly existence of premorbid non communicable diseases contribute to the chronicity on presentation, these patients had hypertension and diabetes mellitus. A study done in Ghana revealed almost similar results in the hypertension diabetes groups, it found out that the prevalence of CKD in patients with hypertension to be 22 % and in patients with diabetes of 27 %.(EK, 2015)

The histological pattern with the highest proportion was focal segmental glomerulosclerosis (FSGS) 23.8%, lupus nephritis 19% (M:F 1:7) followed by minimal change disease(MCD) 11.9%. This is comparable to a study done in Sudan in the year 2011 on 83 patients which revealed that FSGS was diagnosed in 29.6% of patients, followed by membrano-proliferative glomerulonephritis (MPGN) in 26.8% and minimal change disease in 16.9% the same results was similar to another study done on 86 renal patients showing FSGS as the

most common cause of primary GN. Still in the same region of Africa, Egypt found out that in primary GN, FSGS was the most common glomerular disease accounting for 21% of cases. Similarly FSGS and MPGN were reported by the Saudi renal registry as the leading causes of primary GN. Patients of African descent in developed countries have been found to have a higher prevalence of FSGS. This is echoed from a report in the United States that the incidence of FSGS patients reaching ESRD has increased by 11-folds during the past two decades.(Nadium et al.2013). There has been identification of APOL1 gene among patients of African descent with high prevalence of FSGS (Jeffrey et al, 2015). Lack of uniform diagnostic work up for patients, especially renal biopsy with accurate tissue diagnosis may explain some of the discrepancies. The existence of unmatched socio-economic status across the African continent may be influencing the overall distribution of disease as this would result in inadequate definitive diagnosis of GN. Lack of skilled clinicians to perform the biopsy also results in paucity of data.

Patients with lupus nephritis (LN) were 8(19%) and the study was able to demonstrate the various classification of LN amongst these patients. Female preponderance of LN was at a ratio of 1:7 and the most likely explanation would be estrogen that predisposes one to autoimmune diseases.(Schwartzman, 2012). Patients found to have lupus were also found to have low C3 6(60%) and most of them presented as nephrotic syndrome, this is due to compliment cascade activation with resultant consumptiom of C3. Nephrotic syndrome in these group of patients is due to disease process that is more proliferative as it worsens with histological patterns favoring nephrotic syndrome. (Schwartzman, 2012). Senagal had prevalence of LN at 36.1%. (Al Riyami, 2013.)

Among the 9 patients with DM, 3(33.3%) had FSGS, 2(22%) had LN and 1(11%) MCD. This demonstrated that DM patients are at risk of having GN like the other population. The most likely explanation for the LN patients having DM was the long term use of steroids. Other studies have demonstrated MCD and MPGN amongst patients with diabetes mellitus (Kvender, 2001). These findings suggest that all patients with DM presenting with GN should have renal biopsies done for tissue diagnosis.

The 3 HIV patients recruited had AIN, TDF associated toxicity and FSGS-Non-HIVAN. The patient with the TDF toxicity had exposure of the drug for 8 weeks and on biopsy revealed karyomegally that is diagnostic for TDF associated toxicity. This was similar to findings from a study on patients exposed to TDF.(Herlitz, 2010). The FSGS NON HIVAN, though found in one patient, was not found to be prevalent amongst patients who had proteinuria in HIV. This study was done on the same study population at MTRH/AMPATH by Koech KM, 2012 in a thesis study that did not find HIVAN prevalent amongst his study population.

We could not make much correlation of the clinical and histological presentation since there was much overlap in presentation and having a study population that could not allow inference to be made regarding the general population. But of note is that the LN group had varied distribution on presentation as nephrotic or nephritic: nephrotic 37.5%, nephritic 37.5%, and indeterminate 25%. Incongruence between the presentation and histology amongst the patients who had lupus nephritis has been demonstrated, Bihl, 2006.

Study limitation

Inability to perform immunohistochemistry and electron microscopy on the renal specimen, limited to tissue diagnosis to light microscopy.

Chapter Six: Conclusion And Recommendation

6.1 Conclusion

The most common clinical presentation of GN was oliguria 35(77.8%) and hematuria 38(86.3%).

The histopathological pattern of GN with the highest proportion was FSGS in MTRH.

There was no association between the clinical presentation and the histological findings of GN amongst our study population.

6.2 Recommendation

Empiric treatment of patients with GN based on clinical presentation should be discouraged since no significant association was established between clinical and histological findings.

Renal biopsy still remains the best way of making definitive diagnosis of GN even in circumstances of low socioeconomic status.

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APPENDICES

Appendix I – Questionnaire and Data collection form

CLINICAL AND HISTOPATHOLOGICAL PATTERNS OF GLOMERULONEPHRITIS

AMONG PATIENTS SEEN AT MOI TEACHING AND REFERRAL HOSPITAL IN

ELDORET, KENYA

Instructions

1. To be filled by investigator/research assistant once the client consents to the study.
2. Please fill all sections.
3. If the response is a date and the participant does not remember the exact put the approximate year if still cannot remember the year write **00/0000**
4. Please write legibly and clearly.
5. Follow the instructions in each of the sections.

Study Number __ __/__ __ __

Date (MUST FILL): dd/mm/year __ __/__ __/__ __ __ __

AMRS # (MUST FILL!)   __ __ __ __ __ __ __ __ __ __

Participant name _____

Mobile phone # _____

Home phone # _____

BIODATA

a. Date of birth: __ __/__ __/__ __ __ __ **(dd/mm/year)**
b. If date of birth unknown, age at last birthday: __ __ __ years
c. Gender (**Tick appropriate response**)
    ☐ Male   ☐Female

<u>HISTORY</u>
Do you have any of these symptoms?

Bloody/cola colored urine	Yes	☐	No	☐
Reduced urine output	Yes	☐	No	☐
Increased urine output	Yes	☐	No	☐
Pain on urination	Yes	☐	No	☐
Frequent urination	Yes	☐	No	☐
Facial swelling	Yes	☐	No	☐
Leg swelling	Yes	☐	No	☐
Difficulty in breathing	Yes	☐	No	☐
Bloody diarrhea	Yes	☐	No	☐

Have you been treated recently for any of these illnesses?

Recurrent sore throat	Yes	☐	No	☐
Chronic wound/Boils	Yes	☐	No	☐
Hypertension/ D.M	DM	☐	HPTN	☐

Have you used any of these drugs recently or for a long duration?

Traditional medicinal herbs	Yes	☐	No	☐

NSAIDS ☐   Others ☐

Is there anyone in your family with kidney diseases?

Yes ☐   No ☐   if yes how are you related to him/her?_____

PHYSICAL EXAMINATION

Stable ☐   Fair ☐   Sick ☐

Pallor ☐   Edema ☐   Anasarca ☐

Vitals signs:

BP……/…….mmhg   P.R………..b/m   RR……………b/m

Temp………………C.   SPO2……………%…

Height…………..cm   **Weight**……………Kg

Abdomen:

Ascites   Yes ☐   No ☐

Masses   Yes ☐   No ☐

Organomegally   Yes ☐ ☐   No ☐

Renal Bruit   Yes ☐   No ☐

Renal Angle tenderness Yes ☐   No ☐

Respiratory:

☐   ☐

	Normal	Abnormal

Pulmonary Edema   Yes ☐   No ☐

Stony Dullness   Yes ☐   No ☐

Cardiovascular Exam

Normal ☐   Abnormal   …………………☐…………………

Nervous System Examination

Normal ☐   Abnormal   ……………☐……………………

Laboratory results

	Test	Results	Remark
1	CBC	WBC…………… Hb……………… Platelets…………	
2	Creatinine level	(mmol/l)……………… GFR	
3	Total Cholesterol level		
4	Compliment 3 levels		
5	ANA titers		
6	ASOT titers		
7	Albumin		
8	Urinalysis	Blood …………….. Protein …………… Leucocytes………… Microscopy…………………………. ……………………………………… ………………………………………	
9	INR		
10 11	Bleeding time HIV		

Appendix II: Consent Form – English

<u>**CONSENT FOR PARTICIPATION**</u>

My name is……………………….(research assistant's name). Dr Martim Peter is a registered medical doctor with the Kenya medical and dentist board and currently persuing his masters degree in medicine at Moi University.

His study is about clinical and histopathological patterns of kidney diseases called glomerulonephritis. I would like to request your participation in this study because you fit the study's inclusion protocol.

The study is about kidney diseases called glomerulonephritis which manifest as body swelling, dark urine colour or reduced or no urine at all and may also cause high blood preasure. If this disease is not treated it may result to total kidney failure.

The diagnosis of these diseases can only be done through kidney biopsy(removal of kidney tissue) Before biopsy procedure is done ,your weight, height and blood pressure will be taken. Your Urine and blood sample will also be taken for determination of your creatinine, cholesterol levels, ASOT titers, C3 levels and ANA levels. You will also be screened for any bleeding tendencies before a renal biopsy is performed on you. The removed kidney tissue will be taken to a laboratory for tissue diagnosis of your current kidney ailment. The procedure will have minimal pain but use of pain numbing drugs will be used. The importance of this study to you is that definite and accurate diagnosis is made of your disease and definitive treatment shall be promptly instituted. The study will provide us with the understanding of the types of kidney diseases common in our set up in order to be prepared in treating them, including their long term complication. The study shall not cost you anything on your participation.

The results of the study will be stored in a database that is password protected and only accessible by those conducting the study. No one will be able to identify you or your results.

Should the data be published, no individual information will be disclosed. Your participation in this study is voluntary. If you decide to participate, you can change your mind later and quit the study before the end of the study. If you decide not to participate, or if you quit the study, it will not affect health care services you receive. By signing this document, you are voluntarily agreeing to participate. You are free to decline to answer any particular question you do not wish to answer for any reason.

If you have any questions about the study, please contact Dr. Maritim Peter, Moi Teaching and Referral Hospital. The Institutional Review and Ethics Committee of Moi University and Moi Teaching & Referral Hospital has reviewed and approved our request to conduct this study.

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18 YEARS AND ABOVE

I have read this informed consent and authorization form. ALL OF MY QUESTIONS HAVE BEEN SATISFACTORILY ANSWERED, AND I WANT TO TAKE PART IN

THIS RESEARCH STUDY. By signing below, I give my permission to participate in this research study and for the described uses and release of information.

Signature of the participant

_____**Date**_____

Signatureofwitness(nurse/researchassistant) __

Date_____.....

BELOW 18 YEARS

I have read this informed consent and authorization form. ALL OF MY

QUESTIONS HAVE BEEN SATISFACTORILY ANSWERED, AND I

WANT TO TAKE PART IN

THIS RESEARCH STUDY. By signing below, I give my permission to

participate in this research study and for the described uses and release of

information.

Signature parent/guardian

Date_____**..............................**

Signature of Witness_____**Date……………………………**

Appendix III: Consent Form – Kiswahili

<u>**IDHINI YA KUHUSISHWA**</u>

Jina langu ni…………………..(jina la mtafiti msaidizi), utafiti huu unaendeshwa na Daktari Maritim Peter ambaye analesheni ya utibabu wa watu. Yeye ni daktari mwanafunzi kwa shahada ya upili wa utibabu kwenye chuo kikuu cha Moi

Utafiti wake unahusu ungojwa wa figo. Magojwa haya yanajulikana kupitia kutolewa kwa kipande cha nyama ya figo kisha kupimwa kwenye maabara husika. Nigependa kuchukuwa fursa huu kukuomba kuhusishwa kwenye utafiti huu.

Magojwa haya ya figo hujulikana ambapo mgojwa anafura mwili, anakojowa mkojo nyekundu ama kupungua au kukosa mkojo, wengineo wata pata shinikizo la damu kwenda juu. Magojwa haya yasipotibiwa yaweza kupooza figo kabisa.

Kabla ya kutolewa kipande cha nyama kwenye figo,utapimwa uzito wako, urefu na kipimo cha shinikizo la damu. Kisha sampuli ya mkojo na damu utachukuliwa ili kuweza kupima vipimo vya figo na chembechembe vya mafuta mwilini. Utaweza kuchunguzwa pia kama kuna kasoro kwenye ndamu kuganda kabla ya kutolewa kipande cha nyama kwenye fingo kwa uwezo wa kipima picha. Vipande vyanyama vitakao tolewa kwa figo, zitachukuliwa kwenye maabara kwa ajili ya tishu utambuzi wa maradhi kwenye figo. Dawa ya kupunguza maumivi utatumiwa wakati wa kufanya utaratibu huu. Umuhimu wa somo hili ni kwamba utatuwezasha kutambua kwa uhakika na usahihi ugonjwa wako na matibabu sahihi kuanzishwa bila kupoteza wakati. Utafiti huu itatuwezasha kuelewa aina ya magonjwa ya figo ambazo zina patikana katika eneo letu ili ituwezashe kuwa tayari kuyatibu hayo

magojwa. Utafiti huu hautakugharimu malipo yoyote.

Matokeo ya utafiti huu yatawekwa kisiri kwenye mpangilio iliyo na ulinzi kamilifu na ambao unaweza kufikiwa na watafiti peke yao. Hamna yeyote mwingine atakayeweza kufikia matokeo ya vipimo yako. Ikiwa matokeo yatachapishwa, habari zozote za kibinafsi hazitachapishwa. Uhusishwaji wako kwenye utafiti huu ni wa hiari. Ukipenda kushirikishwa ni kwa hiari wako na unaweza kubadili nia baadaye na kujiondoa kabla ya utafiti kumalizika. Ikiwa hungependa kushirikishwa ama kujiondoa, matibabu yako utakayopokea hautaadhiriwa kwa njia lolote. Kwa kutia sahihi hati hii ni kwamba unaidhini kushirikishwa kwa hiari yako. Pia una uhuru wa kutojibu swali lolote utakalopenda kutojibu kwa sababu yoyote ile.

Kwa maswali yoyote juu ya utafiti huu, tafadhali wasiliana na Dkt. Maritim Peter au Kamati ya Maadili ya Tathmini na Utafiti ya Chuo Kikuu cha Moi na Hospitali ya Rufaa na Mafunzo ya Moi imeweza kuidhinisha ombi letu la kuendeleza utafiti huu.

MIAKA KUMI NA NANE NA JUU
Nimesoma na kuelewa hati hii ya idhini ya hiari na kutoa ridhaa. MASWALI YANGU YOTE YAMEJIBIWA KWA NJIA INAYORIDHISHA. Kwa kutia sahihi hapa, naidhinisha kuhusishwa kwangu kwenye utafiti huu pamoja na kuchapishwa na kutumiwa kwa matokeo yake.

Sahihi ya mshiriki _____ **Tarehe**_____
Sahihi ya mshahidi(muuguzi/mzaidizi)_____ **Tarehe**_____

MIAKA KUMI NA NANE NA CHINI
Nimesoma na kuelewa hati hii ya idhini ya hiari na kutoa ridhaa. MASWALI YANGU YOTE YAMEJIBIWA KWA NJIA INAYORIDHISHA. Kwa kutia sahihi hapa, naidhinisha kuhusishwa kwangu kwenye utafiti huu pamoja na kuchapishwa na kutumiwa kwa matokeo yake.

Sahihi ya Mzaazi/Msimamizi _____ **Tarehe**_____.........
Sahihi ya mshahidi(muuguzi/mzaidizi)_____ **Tarehe**_____.........

Appendix IV: Urinalysis

1. **Dipstick urinalysis**

A Uristix® strip (**Siemens Healthcare Diagnostics, 1717 Deerfield Road, Deerfield, IL 60015-0778, USA**) is briefly immersed in the urine specimen, covering all reagent areas.

The edge of the Uristix® strip is run against the rim of the urine container to remove excess urine. The strip is held in a horizontal position. The strip measures proteinuria based on 'protein error of pH indicators' principle. This principle states that at constant pH the development of any green color is due to the presence of protein. The result ranges from yellow for negative results to yellow green to green blue for positives. The test pad contains a pH dye indicator using bromphenol blue. Due to the negative charge of albumin, if protein (albumin) is present in urine, the pH increases, and a positive test result occurs.

The reactions are read visually. The strip test area is compared to that on the Uristix® color chart. This will be read after 60 seconds. The color at the center of the pad is compared to the corresponding color chart on the bottle label. 2 observers will read the color and a third person acts as a tie-breaker if there is disagreement.

The results are recorded, and the strip is discarded.Normal and abnormal controls will be run daily to ensure validity of results.

Appendix V: Renal biopsy procedure

Renal biopsy will be performed on patients as the main diagnostic procedure on those who meet the inclusion criteria. The procedure is done under ultrasound guidance at an interventional radiologists' room.

The following is an overview of the procedure

1. Signed informed consent.

2. Laboratory investigation pre-procedure- Complete blood count, platelets >50000/mm3. Coagulation profile: INR<1.5, normal prothrobin time(PT)/partial thromboplastin time(PTT)

3. The procedure is always done on a patient who is in a prone position with a pillow placed under the patients' abdomen to reduce the lumbar loidosis and one on the chest to improve patients breathing.

4. The patient may or may not be sedated and midozalam is the drug of choice if need be. Lignocaine 1-2% is used as a local anaesthesia that is infiltrated on the skin surface, tissues and to the renal capsule.

5. With help of a surgical blade a stab knick is made on the intended entry point to ease penetration of the biopsy needle.

6. Using a gauge 16-18 needle, the kidney is biopsied under ultrasound guidance at its inferior pole. Two core specimens shall be collected.

7. After each biopsy, pressure is applied over the entry site for up to 5 minutes to act as tampornade for any possible active bleeding.

8. Ultrasound re-examination of the kidney is done to detect any hematoma post-procedure

9. Dressing and adhesive is applied over the biopsy site.

Post-procedure care plan

1. The patient is advised bed rest mostly supine for 18-24 hours.
2. Blood pressure monitoring is done as follows:
    - Every 15 mins for one hour.
    - Every 30 mins for one hour
    - Every 1 hour for four hours then
    - 4 hourly for the next 24 hours
3. Hematocrit to be checked 6-8 hours after procedure and thereafter at 18-24 hours
4. Patients' urine shall be collected in a clear container to examine any gross hematuria.
5. Analgesics shall be prescribed.

Anticipated complications shall be documented.

Appendix VI: Procedure for drawing venous blood

Venous blood will be drawn for fasting lipid profile. The procedure will be explained to the participant and verbal consent obtained. Universal safety procedures shall be observed. Venous blood draw will be from the median cubital vein (in the antecubital fossa) of the less dominant upper limb.

Below is an overview of the steps that will be followed:

1. Arm is selected and a tourniquet is placed on the arm above the draw site. The median cubital vein is selected.
2. Site is cleansed with a sterile alcohol/methylated spirit preparation pad.
3. A needle is inserted into the vein and the collection tube is engaged.
4. Two milliliters of blood is collected into a Vacutainer (plain) blood collection bottle.
5. Tourniquet is removed once the quantity of blood desired has been obtained.
6. A small gauze pad and Band-aid are placed on the venous blood draw site.
7. The blood collection tube is labeled with the patient's information.
8. Blood collection tubes batched until five samples obtained before being taken to the laboratory for analysis.

Appendix VII : Procedure for testing total cholesterol

CHOLESTEROL liquicolor CHOD-PAP-Method Enzymatic Colometric Test for cholesterol with Lipid Clearing Factor (LCF)

Method

The cholesterol is determined after enzymatic hydrolysis and oxidation. The indicator quinoneimine is formed from hydrogen peroxide and 4-aminophenazone in the presence of phenol and peroxidase.

Appendix VIII: Procedure for determining serum creatinine

Blood in plain Vacutainer$^®$ bottles are taken immediately to the lab. Serum may be stored for up to one day at 2 to 25°C, up to seven days at 4 to 8°C and up to six months at -20 to -80°C.

The bottle is set onto a centrifuge and spun at 3000 rpm for 3 minutes to separate the serum from the cells. The supernatant (serum) is carefully suctioned using a micropipette and transferred to a sample cup.

The sample cups are systematically set on a rack that goes onto a Cobas Integra$^®$ 400 plus analyzer (**Roche Diagnostics, 9115 Hague Road, PO Box 50457, Indianapolis, IN 46250-0457**). This is an autoanalyzer that uses the Jaffe reaction to quantify creatinine; creatinine reacts with picric acid in the presence of an alkaline pH to produce a yellow-red complex that has a maximum absorbance at 512nm. The rate of dye formation is proportional to the level of creatinine in the sample. The analyzer reads out this absorbance and based on its software it calculates the serum creatinine. It prints out the result on paper.

The result is reported in μmol/L alongside reference serum creatinine levels.

Quality control checks are run daily.

Appendix IX: Procedure for measuring Blood pressure

Blood pressure will be taken using an Omron M2 compact upper arm blood pressure (BP) monitor (Omron Healthcare, Inc., 1200 Lakeside Drive, Bannockburn, Illinois 60015). The patients will be required to have had at least 15 minutes rest in a quiet place and in a relaxed sitting position with no tight fitting clothing on the upper arm, or any thick clothing such as a sweater.

Below is an overview of the steps that will be followed:

1. Participant will be seated upright with the back straight and right arm placed on the table so that the cuff will be on the same level as the heart.
2. Cuff will be wrapped on the arm so that the bottom of the cuff will be at least 1cm above the elbow. The cuff will then be fastened snugly.
3. Start button will then be pressed and the cuff will automatically inflate to take the blood pressure reading.
4. Blood pressure and pulse rate results will be displayed on the on the screen of the machine.
5. Blood pressure readings will be recorded on the pro-forma.
6. Should an error occur during the process, the cuff will be deflated and the process repeated.
7. High blood pressure readings (Systolic BP >140mmHg and Diastolic BP >90mmHg) will be confirmed manually using a mercury sphygmomanometer.

Appendix X: CKD Epi calculator for GFR estimation

The CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation was developed in an effort to create a formula more precise than the MDRD formula, especially when actual GFR is > 60 mL/min per 1.73 m^2. It is as a result of pooled data from multiple studies to develop and validate this new equation.. The CKD-EPI equation performs better than the MDRD (Modification of Diet in Renal Disease Study) equation, especially at higher GFR, with less bias and greater accuracy.

The CKD-EPI equation, expressed as a single equation, is:

GFR = 141 X min(Scr/κ,1)$^{\alpha}$ X max(Scr/κ,1)$^{-1.209}$ X 0.993^{Age} X 1.018 [if female] X 1.159 [if black]

Where Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, α is − 0.329 for females and −0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1.(Levey & Stevens, 2010; Levey et al., 2009)

Appendix XI: Procedure for measuring weight

The weight of participants will be taken to help calculate the body mass index (BMI), which is the weight relative to the height. The weight will be measured with a scientific floor Scale (SECA)

Below are the steps that will be followed in measuring weight:

1. The scale will be placed on a firm, flat surface.

2. Participant will be asked to remove their footwear (shoes, slippers, sandals, etc).

3. The participant will be asked to step onto scale with one foot on each side of the scale.

4. Participant will be asked to: stand still, face forward, place arms on the side and□wait until they will be asked to step off.

5. The weight in kilograms will be recorded on the participant's pro-forma.

6. The participant will be asked to step off the scale.

Appendix XII: MTRH Approval Letter

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke

P. O. Box 3
ELDORET

Ref: ELD/MTRH/R.6/VOL.II/2008
Dr.Peter K.Maritim,
Moi University,
College of Health Sciences,
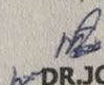School of Medicine.
P.O. Box 4606-30100,
ELDORET-KENYA.

16th September, 2014

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:

"Clinical and Histopathological Patterns of Glomerulonephritis among Patients seen at Moi Teaching and Referral Hospital in Eldoret, Kenya".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR.JOHN KIBOSIA
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

CC   -   Deputy Director (CS)

          -    Chief Nurse

          -    HOD,HRISM

INSTITUTIONAL RESEARCH &
ETHICS COMMITTEE

1 6 SEP 2014

APPROVED
P. O. Box 4606-30100 ELDORET

Appendix XII: IREC Approval Letter

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
16th September, 2014

Reference: IREC/2014/182
Approval Number: 0001266

Dr. Peter K. Maritim,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Maritim,

RE: FORMAL APPROVAL

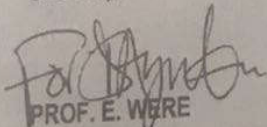The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Clinical and Histopathological Patterns of Glomerulonephritis among Patients seen at Moi Teaching and Referral Hospital in Eldoret, Kenya."

Your proposal has been granted a Formal Approval Number: *FAN: IREC 1266* on 16th September, 2014. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 15th September, 2015. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

INSTITUTIONAL RESEARCH &
ETHICS COMMITTEE
1 6 SEP 2014
APPROVED
P.O. Box 4606-30100 ELDORET

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc   Director - MTRH   Dean - SOP   Dean - SOM
     Principal - CHS   Dean - SON   Dean - SOD