Clinical and histopathological characteristics of patients with glomerulonephritis syndrome attending renal unit at Muhimbili National Hospital in Dar es Saalam, Tanzania.

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TITLECLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH GLOMERULONEPHRITIS SYNDROME ATTENDING RENAL UNIT AT MUHIMBILI NATIONAL HOSPITAL IN DAR ES SAALAM, TANZANIA.

By

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Dissertation submitted in (Partial) fulfillment of the requirements for the Degree of Master of Medicine in Internal Medicine of

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CERTIFICATION

The undersigned certifies that he has read and hereby recommends for acceptance by Muhimbili University of Health and Allied Sciences a dissertation titled: ***"Clinical and Histopathological characteristics of Patients with Glomerulonephritis Syndrome attending Renal Unit at Muhimbili National Hospital in Dar es Salaam, Tanzania'',*** in (partial) fulfillment of the requirements for the degree of Masters of Medicine (Internal Medicine) of Muhimbili University of Health and Allied Sciences.

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Date

DECLARATION AND COPYRIGHT

I, **Dr. Amira William Deng,** declare that this **dissertation** is my own original work and that it has not been, and will not be presented to any other University for a purpose of similar or any other degree award.

Signature…… **Date**……

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DEDICATION

I dedicate this dissertation to my beloved mother who nurtured and provided me with a good education foundation that brought me to where I am today.

ABSTRACT

Background: The histologic pattern of specific glomerulopathies and their related clinical presentation vary according to age, sex, race, socioeconomic status and geographic location. The underlying histopathological pattern of patients presenting with glomerulonephritis syndrome in Tanzania is virtually unknown.

Objectives: This study was set to determine different Biochemical and histopathological patterns of glomerulonephritis syndrome at Muhimbili National Hospital in Dar es Salaam Tanzania.

Patients and Methods: Descriptive hospital based case series, all adults from (18yrs and above) with proteinuria and hematuria who underwent renal biopsy from April 2017- December 2017 were consecutively recruited into this study.Patients infected with HIV, hepatitis B virus and hepatitis C virus were excluded due to resources constraints.

Results: 55% participants with glomerulopathies were enrolled for this study, but40 were eligible for percutaneous renal biopsy. Two-thirds of participants were female (67.5%) with mean age (±SD) of 32.7 (9.8) years. on clinical characteristics the most common symptoms were Edema 31(77.5%) and Foamy urine 31(77.5%) followed by oliguria 17(42.5%)**,** hypertension 14(35%) finally fever and other symptoms 5(12.5%).The commonest lesions were Focal segmental glomerulosclerosis (32.2%), followed by minimal Change disease (20.0%) and membranous nephropathy (17.5%). Membranoproliferative glomerulonephritis, IgA nephropathy and was (5.0%). Among others histologic findings including secondary glomerulopathiesrenal amyloidosis and Lupus nephritis were (5.0%) each, inconclusive findings (10.0%) and undetermined due to excessive fibrosis (1%).

Conclusion: Primary glomerulopathies in Tanzania occur more commonly among young age (≤ 40 years) .Female patients were common presented with glomerulonephritis syndrome, while secondary glomerulopathies were presented in both Gender. There is considerable heterogeneity in the histologic spectrum of glomerulopathies which is influenced by age and a gender factor, Focal segmental glomerulosclerosis was the leading cause of primary glomerulopathies in this study.

Recommendation: We recommend that kidney biopsying should be part of routine evaluation for patients with glomerulonephritis syndrome in our setting before giving corticosteroid and other adjuvant therapy .The findings from this study underscore the need to start and maintain the Tanzania Kidney Biopsy Registry that will be a great resource for future research on the causes and prevention of kidney diseases in Tanzania.

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LIST OF ABBREVIATIONS

ACEI	:	Angiotensin Converting Enzyme Inhibitors
ANA	:	Antinuclear Antibody
AZA	:	Azathioprine.
BUN	:	Blood Urea Nitrogen
CNS	:	Congenital Nephrotic Syndrome
CPO	:	Cyclophosphamide
CSA	:	Cyclosporine. A
CT	:	Computed Tomography
DMP	:	Diffuse Mesangial Proliferative
ESRD	:	End Stage Renal Disease
ESR	:	Erythrocyte Sedimentation Rate
FSGS	:	Focal Segmental Glomerulosclerosis
GFR	:	Glomerular Filtration Rate
GN	:	Glomerulonephritis
HDL	:	High Density Lipoproteins
IMN	:	Idiopathic Membranous Nephropathy
INS	:	Idiopathic Nephrotic syndrome
IVCPO	:	Intravenous Cyclophosphamide
LDL	:	Low Density Lipoproteins
MCNS	:	Mminimal Change Nephrotic Syndrome
MesPGN	:	Mesangioproliferative Glomerulonephritis
MGN	:	Membranous Glomerulonephritis
MMF	:	MycophenolateMofetil
MN	:	Membranous Nephropathy
MPGN	:	Membranoproliferative Glomerulonephritis
NS	:	Nephrotic Syndrome
RAA S	:	Rennin Angiotensin Aldosteron System.
RTX	:	Rituxima

DEFINITIONS OF KEY CONCEPTS

- **Glomerulonephritis**: inflammation/damage of the glomerular basement membrane resulting in altered function presented as nephrotic and/or nephritic syndrome.
- **Nephrotic syndrome:** was defined as proteinuria >3.5 g/day associated with hyperlipidemia, hypoalbuminemia and edema.
- **Nephritic Syndrome:** Clinical syndrome defined by: Haematuria/red cell casts, Hypertension, Oliguria, Uraemia and Proteinuria (<3g/24 hours).
- **Subnephrotic proteinuria**: Any amount of proteinuria less than 3.5g/day
- **Primary glomerulopathy** was defined as following histopathological diagnosis (*Focal Segmental Glomerulosclerosis, Minimal Change Disease, Membranous Nephropathy, Membranoproliferative glomerulonephritis and IGA nephropathy*).
- **Secondary glomerulopathy:** was defining as following histopathological diagnosis (included renal amyloidosis, lupus nephritis undetermined findings due to extensive fibrosis and inconclusive findings).
- **Chronic Kidney Disease**: was define as abnormalities of kidney structure or function, present for >3 months. Advanced Chronic Kidney Disease: define as stage4 and 5, determined by eGFR using MDRD equation.
- **Isolated hematuria:** Is urinary RBCs without other urine abnormalities (eg, proteinuria, casts).
- **Glomerulopathy** is a set of diseases affecting the glomeruli of the nephron which include inflammatory or no inflammatory processes.
- **Nephritis. :** acute or chronic inflammation of the kidney affecting the structure (as of the glomerulus or parenchyma) and caused by infection, a degenerative process, or vascular disease
- **Unexplained renal failure:** is define as Acute kidney injury due to unclear or unknown cause, account for about 10-20% of acute kidney injury.

1.0 INTRODUCTION

Glomerulonephritis is a group of diseases that injure the part of the kidney that filters blood (called glomeruli). Nephritis is also a general term used to describe a group of diseases that cause swelling and inflammation of the glomerulus. Nephritis is often used synonymously with glomerulonephritis. When the kidney is injured, it cannot get rid of wastes and excess fluid out of the body. There are many different types of nephritis vary from mild non-damaging to very serious problem causing kidney failure, nephritis can be acute or chronic. Factors such as age, characteristics of urine, accompanying hypertension and other factors can help to diagnosis different types glomerulonephritis syndrome. However most of the people with nephritis have at least one the following problems; swelling to face, feet, legs and hands, reduced kidney functions, blood in urine , protein in urine, high cholesterol , low albumin and sometimes high blood pressure are the most common clinical- biochemical characteristics . Recurrence rates of these underlying glomerulonephritis for patients who have undergone kidney transplantation remains high especially for FSGS, systemic lupus erythematosus (SLE), IgA nephropathy, amyloidosis, and membranoproliferative GN (especially type II) (1,5).

Glomerulonephritis (GN) remains an important cause of chronic kidney disease (CKD) and end stage renal disease (ESRD). It has been reported as the commonest cause in Australia and New Zealand, and as the third major cause of kidney disease in Europe and the United States comprising 12.4 and 15.4% of all progressive renal disease, respectively(6).International statistics GN remains much more common in regions such as Africa, Caribbean, India, Pakistan, Malaysia, Papua New Guinea, and South America. In Ethiopia, acute GN is second only to acute kidney injury that required dialysis, accounting for approximately 22% of cases(7).

There is a wide variation in the patterns of renal disease in different geographical areas but accurate and comprehensive statistics are lacking. Renal disease especially glomerular disease is more prevalent in Africa and seems to be of more severe form than that found in western countries. The most common mode of presentation is nephrotic syndrome. It is estimated that about 2-3 % of medical admissions in tropical countries are due to renal related complaints, majority being glomerulonephritis. Nephrotic syndrome account for 0.5% of hospital admissions in Zimbabwe, 0.2% in Kwa Zulu Natal South Africa and about 2.4% in Uganda and Nigeria(8).Other causes of GN are Focal Segmental Glomerulosclerosis, membranoproliferative

glomerulonephritis, Minimal Change Disease and Rapidly Progressive Glomerulonephritis (RPGN) accounted for 26.6%, 22.1%, 10.5% and 3.5% of cases respectively(5).Followed by lupus nephritis the commonest cause of secondary glomerulonephritis, accounting for 11.6% of cases. IgA nephropathy is uncommon but seen in only 4.7% of cases, around 3.3 % account for other cases(5,6).

Despite the fact that GN is common worldwide there are no reports of histopathological characteristics in our setting hence subjecting patients to empirical management based on clinical and biochemical findings. For effective GN management it's essential to establish the underlying histopathological characteristics in order to determine patient's management as well predicting the overall prognosis. Several prognostic factors have been evaluated as potentially important prognostic factors. Black patients are significantly more likely than others to develop renal insufficiency. Cellular crescents are the most predictive active pathological feature and interstitial fibrosis is the strongest chronic histological prognostic factor(5,8).

The definitive diagnosis of renal disease can only be established with the study of renal biopsy using light microscopy, immunohistochemistry (or even better using immunofluorescence) and electron microscopy. Histopathological diagnosis is the gold standard for the diagnosis of clinically suspected GN syndrome as GN accounts for 10-15% of glomerular diseases (6).Percutaneous renal biopsy (RB) is an invaluable diagnostic procedure in patients with renal disease. However the indications of RB and extent of its pathological evaluation vary from country to country and even from center to other center.

The prevalence of the biopsy-proven renal disease varies according to geographic region, socioeconomic conditions, race, age, demography and indications for renal biopsies. Some of the common indications for renal biopsies in most of studies include Nephrotic syndrome (NS), Acute Nephritic syndrome (ANS), Non-Nephrotic proteinuria(NNP)and acute renal failure of unknown etiology (ARF) (1,3,4,9).

Advances in imaging techniques and biopsy needles have optimized the tissue procurement and minimized the risk of complications associated with renal biopsy, making it an indispensable tool for diagnosis of GN syndrome. Globally there is a shift in the observed trend of the histological spectrum over the last few decades with a notable increase incidence of focal

segmental glomerulosclerosis (FSGS) and a declining incidence of minimal change disease (MCD) among adult population. Data from Indian CKD-Registry show that 13.8% of all causes for CKD is contributed by chronic glomerulonephritis underscoring the need and importance of kidney biopsying in detecting the causes of underlying kidney disease (1,3).

2.0 LITERATURE REVIEW

Several studies have demonstrated variability in social and demographical characteristics regarding nephritis syndrome as well as prognosis and outcome. Studies done in Canada, Italia and South Africa which explore the impact of gender in primary GN found that, one third of these patients were women at the time of the presentation. Moreover, the women tended to be 2 years younger but had better outcome than men in terms of both proteinuria and blood pressure control(10,11,12).A study done in the UK by Emily P et al which explored on the impact of social economy of primary GN patients in survival found out that those patients who are social economically deprived had more likelihood of death than those who are least deprived(13).

Several studies have described the histopathological characteristics of GN syndrome worldwide. In Asia studies (Japan, Pakistan and Hong Kong) found that the most common indications for renal biopsy was persistent proteinuria while the most frequently glomerular lesion was immunoglobulin A nephropathy, focal segmental glomerulosclerosis, Minimal-Change Disease (MCD), Membranous Nephropathy and Immunoglobulin M Nephropathy were the most common glomerular diseases that presented with nephrotic syndrome(14,15,16).

In a study done in Singapore which followed-up for three decades the global evolutionally trend of prevalence of primary GN has reported that most common form of GN is mesangial proliferative glomerulonephritis in the first decade but the trend shifted towards FSGS in the subsequent decades. A study done in South Korea found that MCD was the most common primary GN followed by IgAN, membranous GN (MGN) and membrano-proliferative GN (17). Further several studies done in the Middle East region (Saudi Arabia, Jordan, Egypt, Iran and Iraq) reported Mesangiocapillary Glomerulonephritis (MCGN) was the common primary GN followed by immunoglobulin A nephropathy (IgAN) and focal segmental glomerulosclerosis, minimal change disease, membranous glomerulonephritis and mesangioproliferative glomerulonephritis, whereas Lupus Nephritis was the leading cause for secondary glomerulonephritis (5,16,18,19,20).

Other studies found similar patterns, in India, Japan and South Africa whereby the most common indications for renal biopsies were nephrotic syndrome ,nephritic syndrome, renal failure of unknown etiology and asymptomatic haematuria of all the glomerulopathies,

membranous glomerulonephritis (MGN) was the commonest morphological pattern which followed by mesangioproliferative (MSGN) and membranoproliferative glomerulonephritis (MPGN)(11,21,22).Another study in South India in single center biopsy series found a notable increase incidence of focal segmental glomerulosclerosis (FSGS) with decrease incidence of minimal change disease(2,9).

In Africa, specifically in South Africa GN syndrome was studied and the pattern of this syndrome was more of the primary glomerulonephritis (GN) which included mesangiocapillary GN, (mesangioproliferative GN, membranous GN, crescentic and necrotizing focal and segmental glomerulosclerosis, post-infectious GN, minimal change disease, while IgA nephropathy and Lupus nephritis were the most frequent secondary glomerular disease and were also the most frequent cause of the nephrotic range proteinuria. Also another study done in South Africa which look upon outcome of patients who are poor found that poverty is associated with poor outcome(21,23).

A study among patients with nephrotic syndrome done in Africans and Indians of South Africa found membranoproliferative nephritis to be the most common histological patterns in both racial groups followed by membranous glomerulonephritis while minimal change disease was rare. In the East African region, In Kenyatta Hospital a study which explored histopathological characteristics of nephrotic patients found that the commonest histological lesions were mesangial proliferative glomerulonephritis, followed by minimal change nephropathy and focal segmental glomerulosclerosis(24).

Another study in Sudan found that the common histopathological characteristics were focal segmental membrano-proliferative followed by minimal change disease and the least common type were lupus nephritis and IgA nephropathy (25). In Nigeria, a histopathological review of renal biopsies found glomerulonephritis to be the most predominant disease followed by renal disease unknown etiology and the most common histological categories in adult population was focal segmental nephritis followed by membranous nephritis, minimal change disease was not common compare to other GN disease (3).

3.0 PROBLEM STATEMENT

Glomerulonephritis syndromes are common in Tanzania among patients attended in nephrology OPD and Wards but no studies have been done to report the histopathological characteristics. We treat GNs empirically (without tissue diagnosis**)** using oral corticosteroids and other adjuvant therapy, a practice that may expose patients to prolonged, inappropriate therapy and potential adverse effects. Percutaneous renal biopsy (RB) is an invaluable diagnostic procedure in patients with renal disease is also important in guiding type of treatment base on histopathological findings. As per kidney disease improving global outcome (KDIGO) guidelines for GN syndrome recommended all adults with glomerulonephritis syndrome must undergo for renal biopsy for treatment guiding**.** A study from Korea shows that among adult patients with GN syndrome, about 80% had primary GN whereas 20% had secondary GNs. This study aims at determining clinico-biochemical and histopathological characteristics of patients with glomerulonephritis syndrome.

4.0 STUDY RATIONALE

Due to sub-optimal rate of renal biopsying at MNH, treatment of patients with GN syndrome is still largely based on limited clinico- biochemical findings instead of histopathological evidence (as recommended by KDIGO). And the examples that are recommended by kidney disease improving global outcome guidelines for GN syndrome treatment are Prednisone, Cyclophosphamide, Azathioprine, MMF and etanercept can be used as adjunctive therapy.

This study aims at determining the biochemical and histopathological spectrum of GN syndrome. Findings from this study will establish the spectrum of underlying histopathological patterns among GN patients, guide clinicians to selecting appropriate treatment therapies and in the due course avert patients from potential adverse effects of prolonged corticosteroid therapies and other treatment modalities.

5.0 RESEARCH QUESTIONS

What are clinic biochemical and histopathological characteristics of patients with Glomerulonephritis syndrome?

6.0 OBJECTIVES

6.1 BROADOBJECTIVE

- To determine different clinical - biochemical and histopathological patterns of the patients with glomerulonephritis syndrome at Muhimbili National Hospital.

6.2 SPECIFICOBJECTIVES

- To describe the demographical characteristics of patients with GN syndrome at MNH.
- To describe clinical findings of patients with GN syndrome at MNH.
- To describe biochemical finding of patients with GN syndrome at MNH.
- To describe the histopathological findings from patients with GN syndrome at MNH.

7.0 METHODOLOGY

7.1 Study Design

Descriptive hospital based case series

7.2 Study Area

This study was conducted at MNH; a main referral hospital located at Eastern Zone of Tanzania in the capital city of Dar es Salaam. MNH receives referral patients from both public and private hospitals from all over the country. Patients with renal disorders enroll themselves to nephrology unit through EMD or OPD.

The nephrology unit runs an out-patient clinic on every Wednesday for CKD patients and Mondays for transplant screening, with an approximately 50 patients who are at different renal disease stages being attended per day.

The clinic also received as well prospective kidney donors for preliminary evaluation before referred for donation.

Staffing of the clinic and dialysis unit includes team of consultant physicians, nephrologists Nephrology fellows, internal medicine residents / registrars, nurses and nursing assistants. The clinic operates from 8 am to 2 pm.

7.3 Study Period April 2017 –December 2017 (8months).

7.4 Study Population

All adult patients (>18yrs) who were eligible for study.

7.5 Inclusion criteria (Documented diagnosis in patients files)

- Nephrotic syndrome
- Nephritic Syndrome
- Non-nephrotic proteinuria
- Isolated glomerular hematuria
- Unexplained renal failure

7.6 Exclusion criteria (Documented diagnosis in patients files)

- Age <18yrs.
- Bleeding diathesis
- Advanced kidney disease (Stage 4 and 5) eGFR using MDRD equation
- HIV/Hepatitis B and or C patients

7.7 Sampling Technique

It was a convenient sampling where all eligible underwent perctutaneous renal biopsy at MNH, principal investigator had to pass in wards one day before biopsy day to evaluated patients that were fit for renal biopsy and for the new OPD patients were recruited during clinic visit and all workups were done and biopsy Scheduled and patients were admitted to the ward one day before producer all the participants were counseled and the producer was clear explained and consent was taken.

7.8 Data Collection

Data was collected by using a questionnaire which included socio-demographic factors, Clinical findings as well as biochemical results and finally histopathological findings for patients with glomerulonephritis syndrome.

7.9 Study protocols/Procedures

This was descriptive hospital based case series. All eligible participants were underwent several assessments as follows:-

Questionnaire was used as data collection tool, Clinical examination (including vital signs, Anthropometric measurement and systemic examination) was conducted to all candidates and findings were recorded. Further information was gathered from the patients (on socio-demographic characteristics, what brought patient to the hospital, past medical and family social history and co- morbidities as well as indications for renal biopsy. All biochemical findings were recorded from the patients file or from computer system, these findings included: Bed side Urine dipstick test, Urinalysis, 24-hour urine collection for protein (Esbatch Test). Total cholesterol and serum Albumin. Renal Function test (serum Creatinine and BUN) Serum Electrolytes and Ions .Other laboratory test were done for fit candidates for renal biopsy bleeding profile Serology and hepatitis panel (HIV done by social worker nurse,

HBsAg, Hepatitis C virus, and complete blood count (CBC) C- reactive protein (CRP). KUB ultrasound was done to evaluate kidneys size for patients with nephritis in the wards as well as outpatient before biopsy obtained. All the above mentioned laboratory results was documented in patient file or recorded from Jeeva system before patient was taken to the producer room.

Renal Biopsy was the main procedure for this study all participants with indications for biopsy were subjected to:

- Patients were counseled, explained about the procedure and Consent was taken.
- To prepare the eligible participants for renal biopsy, all the above mentioned laboratory assessment were done and documented in patient files prior to the procedure and participants were interviewed and consented before biopsy taken .
- Renal biopsy was taken by using Bard Magnum Gun with core biopsy needle size 16.
- Renal biopsy was collected by nephrologists and biopsy core was examined and processed byhistopathologist/nephropathologist.
- Tissue biopsy were examined under light microscopy after staining with routine hematoxylin and Eosin.
- Histochemical stains (PAS, Trichrome stains).

The following equipment were used for Renal Biopsy:

Nonsterile Tray for Anaesthesia

- Nonsterile gloves
- Gel for ultrasound
- Probe sheath
- Povidone-iodine solution
- Lignocaine
- Zinc oxide plaster (7.5cm)
- Formalin container(s), 3% for the number of biopsies to be performed.

Sterile Tray for the Procedure

- Biopsy gun
- Sterile drapes
- Sterile gauze

- 1 Gallipot
- 1 Ten cc syringe

The procedure was performed as follow:-

- Check vital signs of the patient (BP, Oxygen saturation, pulse).
- Confirm that the patient blood test allow the procedure to be done this step was by sharing history and physical findings and all patients fit for needed to have IV line and urine catheter in place.
- Obtain a written consent from the patient.
- Prepare the renal biopsy tray, povidone and local anesthetic agent (lignocaine).
- Prepare sample collecting bottle as required, i.e. for LM and Fill the investigation form.
- Position the patient in prone position.
- Scrub.
- Wear sterile gloves.
- Clean the patients back at and around the marked site using povidone.
- Inject lignocaine via the mark on the skin site thru the whole required depth of skin
- Insert the biopsy needle at same marked site and take the biopsy.
- Remove the biopsy needle.
- Press firmly on biopsied site to stop any oozing /bleeding from the skin.
- Using a sterile wooden stick remove the tissue sample from the biopsy needle and put it in an appropriate sample collecting bottle.
- Dress the biopsied site with sterile gauze and secure with tight elastic plaster.
- Now put patient to lie and reassure the patient.
- Wipe the biopsy needle with povidone.
- Label the specimen and Send specimen bottles to the lab.

7.10 Data Analysis

Data was checked for completeness and each complete questionnaire was given a unique code. The complete questionnaires were entered into SPSS version 20 for analysis. Data were presented as proportions for categorical variables. The means was used to summarize continuous variables while categorical data were expressed as frequencies.

7.11 Ethical issues and clearance

The ethical clearance was obtained from Muhimbili University of Health and Allied Sciences (MUHAS) ethical review board. The permission was also asked from the head of the internal medicine At MNH.

The aim of the study was explained to the participants from whom consent form was sought. Confidentiality and maintenance of anonymity was ensured.

8.0. RESULTS

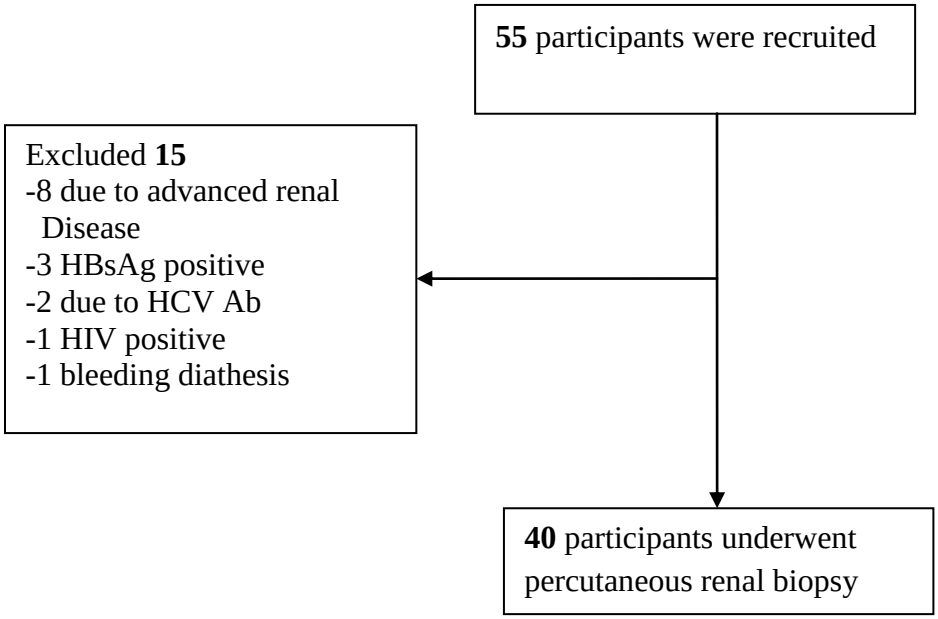


Figure 1.Recruitment flow chat

Table 1: The demographic characteristics of patients with glomerulopathy (N=40).

Characteristic	Levels	N (%)
Age in Years		
Age (Mean±SD)	32.5±10.40	
	≤40	34(85.0)
	>40	6(15.0)
Sex	Male	13(32.5)
	Female	27(67.5)
Education	No formal education	6(15.0)
	Primary school	17(42.5)
	Above primary school	17(42.5)
Marital Status	Single	14(35.0)
	Married	26(65.0)
Occupation	Unemployed	17(42.5)
	Employed	23(57.5)
Religion	Christian	29(72.5)
	Muslim	11(27.5)

A total of 40 patients participated in this study, about two-thirds (67.5%) were female. Their mean age was 32.±10.4, however majority (85%) of participants were below 40 years. About two thirds living with their partners (65%), most participants were educated and (57.5%) had formal employment as narrated in the Table above.

Table 2: History findings of the patients with Glomerulonephritis syndrome (N=40).

Variable	Levels	N (%)
Generalized Body swelling	Yes	31(77.5)
		9(22.5)
Facial puffiness		0(0.0)
	No	40(100.0)
Lower Limb swelling	Yes	9(22.5)
		31(77.5)
Red Urine		8(20.0)
	No	32(80.0)
Reduced urine amount		17(42.5)
	No	23(57.5)
Foamy urine	Yes	36(90.0)
		4(10.0)
Fever and other symptoms		5(12.5)
	No	35(87.5)
Ever have kidney disease		6(15.0)
	No	34(85.0)
	No	34(85.0)
Family member with similar diseases		3(7.5)
	No	37(92.5)
Ever diagnosed with diabetes		2(5.0)
	No	38(95.0)
Ever diagnosed with hypertension		14(35.0)
	No	26(65.0)
Indication for renal biopsy	Nephrotic syndrome	31(77.5)
	Nephritic syndrome	9(22.5)

In the history of the patients with GN syndrome most had generalized body swelling 31(77.5%) and Foamy urine 36 (90.0%). Nephrotic syndrome was the most indication for kidney biopsy 31(77.5%) as narrated in the Table above.

Table 3: Clinical assessment of patients with glomerulonephritis syndrome (N=40).

Variable	Levels	N (%)
Facial puffiness		2(5.0)
	No	38(95.0)
Lower Limbs edema only		9(22.5)
	No	31(77.5)
Anasarca	Yes	33(82.5)
		7(17.5)
Anemia		13(35.5)
	No	27(67.5)
Petechia,/ecchymosis/gum bleeding	Yes	1(2.5)
	No	39(97.5)
Calf tenderness		0(0.0)
	No	40(100.0)
Temperature	Normal	38(95.0)
		2(5.0)
Respiratory Rate	Normal	36(90.0)
		4(10.0)
Pulse Rate	Normal	30(93.8)
		2(25.0)
Blood Pressure	Normal	36(90.0)
		4(10.0)
Body Mass Index	Normal	19(47.5)
	Over weight	17(42.5)
	Obese	4(10.0)

During clinical assessment of the patients with glomerulopathies most common physical findings was Anasarca33 (82.5%), about 13(35.5%) had Anemia and 4(10.05) had high blood pressure and 17(53.1%) were overweight as depicted in table above.

Table 4: Biochemical findings of the patient with glomerulonephritis at MNH N=40

Variable	Levels	N (%)
Protein	2+	1(2.5)
	3+	34(85.0)
	4+	5 (12.5)
Nitrite	Negative	38(95.0)
	1+	1(2.5)
	2+	1(2.5)
Leucocytes	Negative	37(92.5)
	3+	3(7.5)
WBC	Negative	39(97.5)
		1(2.5)
RBC	Negative	26(65.0)
	2+	8(20.0)
	>3+	6(15.0)
Epithelial cells	Negative	37(92.5)
	1+	2(5.0)
Yeast Cell	Negative	40(100)
Hyaline casts	Negative	40(100)
Granular casts	Negative	38(95.0)
		2(5.0)
Ca oxalate casts	Negative	40(100)
Uric acid casts	Negative	40(100)
Ca phosphate	Negative	40(100)
Esbatch Test	Sub-nephrotic range	6(18.8)
	Nephrotic range	26(81.2)

On urine bedside test most of the participants had nephrotic range proteinuria nephrotic range 34(85.0%) as well on urine 24 hour test 26(81.2%) as in the table above.

Table 5: other laboratory findings of the patient with glomerulopathy at MNH N=40

Variable	Response	N (%)
Serum creatinine	Normal	22(55.0)
		18(45.0)
Serum BUN	Normal	31(77.5)
		8(20.0)
		1(2.5)
Serum Sodium	Normal	35(87.5)
		5(12.5)
Serum Potassium	Normal	36(90.0)
		2(5.0)
		2(5.0)
Serum Calcium	Normal	31(77.5)
		1(2.5)
		8(20.0)
Serum Phosphorus	Normal	40(100)
Serum Magnesium	Normal	39(97.5)
		1(2.5)
Total Cholesterol	High	39(97.5)
		1(2.5)
Serum Albumin	Low	40(100)
PT	Normal	39(97.5)
		1(2.5)
INR	Normal	40(100)
PTT	Normal	37(92.5)
		3(7.5)
White cell count	Normal	37(92.5)
		3(7.5)
Neutrophils (Ab)	Normal	36(90.0)
		3(7.5)
		1(2.5)
lymphocytes (Ab)	Normal	40(100)
Monocytes (Ab)	Normal	40(100)
Eosinophils (Ab)	Normal	40(100)
Basophils (Ab)	Normal	40(100)
Red blood cells	Normal	31(97.5)
		1(2.5)
Haematocrit	Normal	33(82.5)
		1(2.5)
		6(15.0)
Hemoglobin	Normal	28(70.0)
		12(30.0)
MCV	Normal	34(85.0)
		6(15.0)
MCH	Normal	37(92.5)
		3(7.5)
MCHC	Normal	37(92.5)
		3(7.5)
PLT Count	Normal	39(97.5)
		1(2.5)
CRP	Normal	38(95.0)
		2(5.0)

Most of the study participants had normal levels of BUN 31(77.5), about 18(54.0) had high levels of serum creatinine as well as high cholesterol 39(97.5), all 40 participants had low serum albumin (100.0) and 12(30.0) had low hemoglobin as depicted in table above.

Table 6: Histopathological findings of patients with GN syndrome at MNH N= 40

Variable	N (%)
Primary glomerulopathies	32(80.0)
FSGS	13(32.3)
MCD	8(20.0)
MN	7(17.5)
MPGN	2(5)
IgA	2(5)
Secondary glomerulopathies	8(20.0)
LN	2(5)
Other histologic findings	6 (15)

Among histopathological findings about 32(80%) were primary glomerulopathies commonest finding was Focal segmental glomerulosclerosis 13(32.2%) followed by Minimal-change disease 8(20.0%), Membranous nephropathy7 (17.5%) while secondaryglomerulopathies was 8(20.0) include LN 2(5.0%), other histologic findings (renal amyloidosis was about (4.0%), inconclusive findings (10.0%) and undetermined due to excessive fibrosis (1%). Others histologic findings* were renal amyloidosis was about (4.0%), inconclusive findings (10.0%) and undetermined due to excessive fibrosis (1%) as depicted in table above.

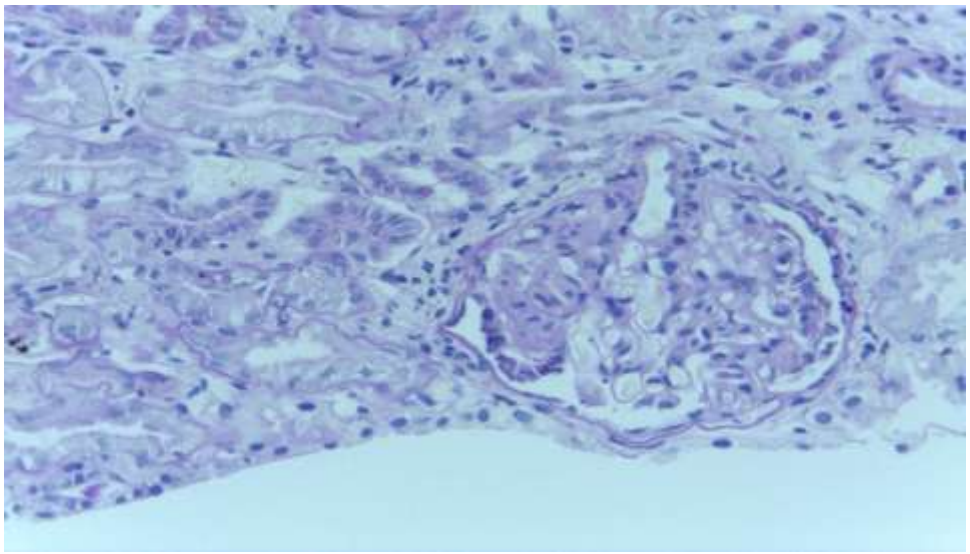
9.0 ILLUSTRATIONS

Case 1: 45 years old Male presented with generalized body swelling for 3/12 associated with Foamy urine and reduced urine amount. Denied history of HTN and DM.

Physical finding: Anasarca also had conjunctival pallor, on urine dipstick test he had 3+ protein and urine 24 hr for protein was 4.3 g/24hr. Indication for renal biopsy was nephrotic syndrome.

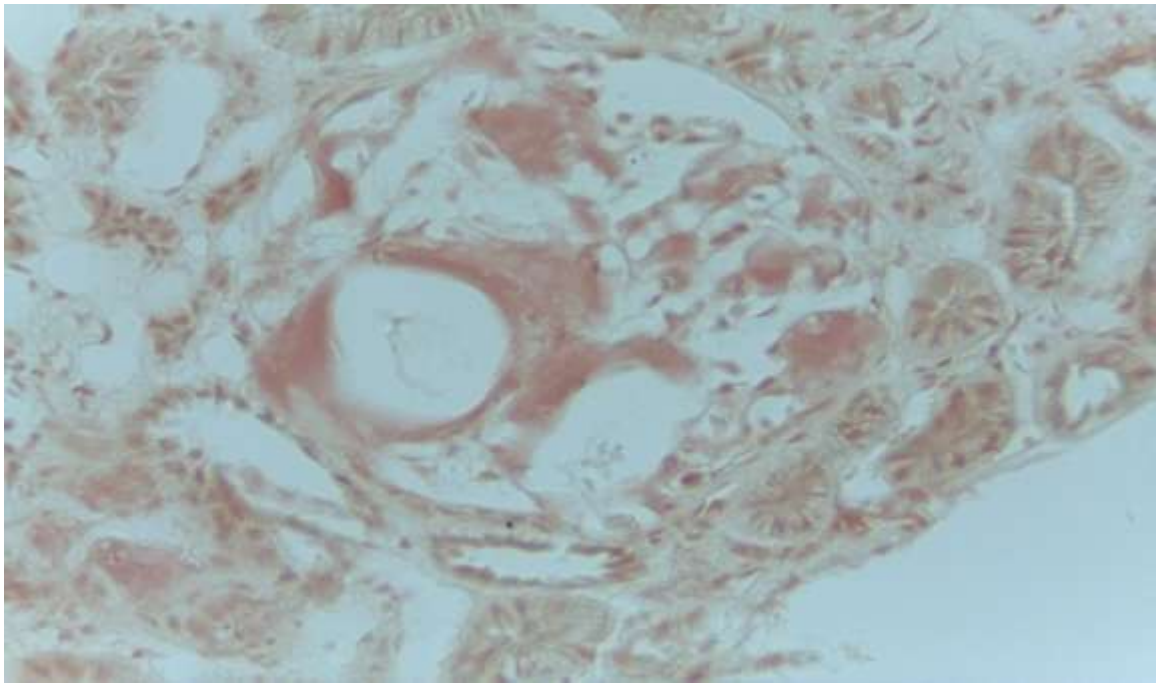
Histopathology finding was FSGS as shown in picture below HP

Number 6496/17LM H&E.



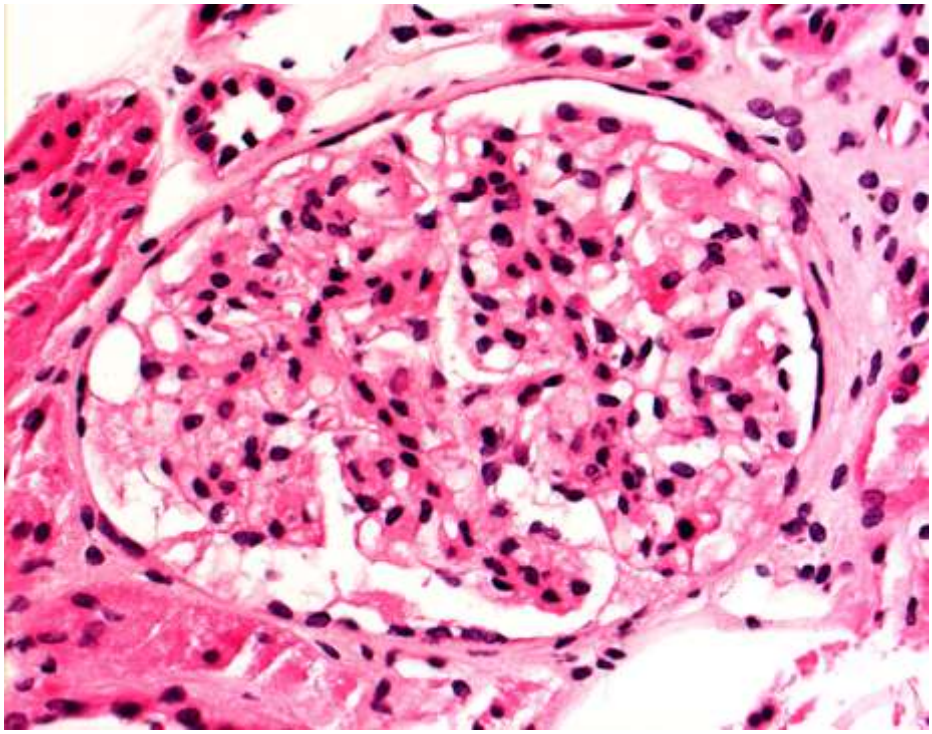
Section of kidney showing endocapillaryproliferation, tubules are moderately atrophic with vascular sclerosis being prominent.

Case 2:50 years old female from DSM ILALA district presented with generalized body swelling Foamy urine and for 2/12 associated with reduced urine amount known hypertensive for 3 yrs on medications. Physical finding : Anasarca , on urine dipstick test he had 4+ protein and urine 24 hr for protein was 10.3 g/24hur . Indication for renal biopsy was nephrotic syndrome. Histopathology results Amyloid associated glomerulonephritis asshown in slide below HP 7562/17 this was studied LM Congo red staining.



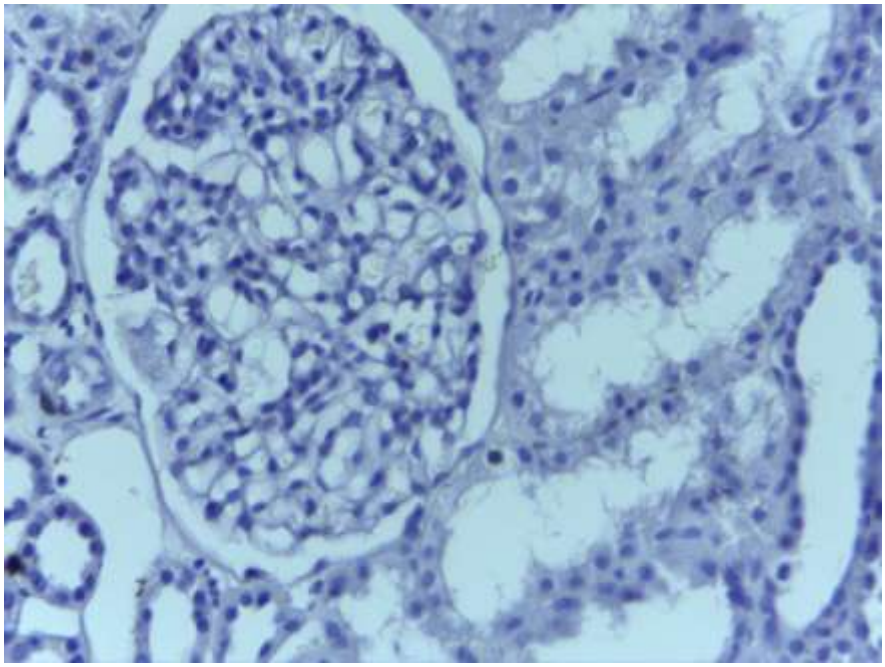
Congo Red showing orange deposites in mesangial area, vessels wall and intestitium**.**

Case 3: 26 years old female from presented with Foamy urine and red urine for 1/12 associated with reduced urine amount and newly diagnosed hypertensive on medications. Physical finding : bilateral lower limb edema , on urine dipstick test he had 4+ protein and5+ red blood cell , urine 24 hr for protein was 7.3 g/24hur , indication for renal biopsy was nephritic syndrome .Histopathology finding IgA nephropathy as shown in slide below HP 5239/17 this slide was studied by LM H&E .



In this picuter glomeruli showed both mesangeal hypercellularity and expansion.

Case 4: 21 years old female from presented with Foamy urine and generalized body swelling for 4/12. Physical finding Anasarca , Pale++ ,on urine dipstick test he had 4+ protein and 5+ red blood cell , urine 24 hr for protein was 5.3 g/24hr , indication for renal biopsy was nephrotic syndrome .Histopathology finding Minimal change disease as shown in slide below HP this slide was studied by LM H&E.



Section of kidney tissue showing glomeruli with very minimal menengial expansion.

9.0 DISCUSSION

In the present study conducted at Muhimbili National Hospital in Dar es Salaam Tanzania in patients with glomerulonephritis syndrome. Provides important information about demographics, clinical syndrome and the pattern of kidney diseases diagnosed by renal biopsy. In the history of the patients with glomerulopathies most had generalized body swelling 77.5%and Foamy urine 90.0%. Nephrotic syndrome was the most indication for kidney biopsy 77.5%. During clinical assessment of the patients with glomerulopathies most common physical findings was Anasarca 82.5%, about 35.5% had Anemia and 10.5% had high blood pressure and 53.1% were overweight. On urine bedside test most of the participants had nephrotic range proteinuria nephrotic range 85.0% as well on urine 24 hour test 81.2%. Most of the study participants had normal levels of BUN 77.5%, about 54.0% had high levels of serum creatinine as well as high cholesterol 39(97.5), all participants had low serum albumin100.0% and30.0% had low hemoglobin.

Among histopathological findings about 80% were primary glomerulopathies commonest finding was Focal segmental glomerulosclerosis 32.2% followed by Minimal-change disease20.0%, Membranousnephropathy17.5%, Membranoproliferative glomerulonephritis and IgA nephropathy was 5 % respectively.

While secondary glomerulopathies was 20.0% include LN 5.0%, other histologic findings renal amyloidosis was about4.0%, inconclusive findings 10.0% and undetermined due to excessive fibrosis 1%, based on age and gender most of the study participants were female 67.5% and mean age was 32.5±10.4,this findings were similar to studies done in Canada, Italian study, Sudan and South Africa in which female were more and the mean age falls within the range of these studies (32 - 33.7).Age wise distribution of glomerular disease seen in our study are similar to findings in the study by Narasimhan et al whereby glomerulopathies were common in young populations ≤40 years. Renal biopsies data from countries like Italy and Spain, and studies from Asian countries like China and Japan, had also reported similar age trends(26,12,27,17,14,28).

In this study nephrotic syndrome 75.0% was the most common indication for renal biopsy compared to nephritic in primary nephritis and most of the participants had nephrotic range proteinuria 81.2%, which was more in primary glomerulopathy. These findings aresimilar to several studies done in Middle East regions (Saudi Arabia, Jordan, Egypt, Iran and Iraq) as well in Africa regions specifically in South Africa, East Africa and West Africa (16,29,19,30,31,8,32,33,34,35).

In this study common presentation of the patients with glomerulonephritis syndrome were generalized body swelling 77.5% and Foamy urine 90.0% these findings were similar to that reported in many studies in African regions as well studies conducted in Spain ,UK and USA (36,27,37,38).

Focal segmental glomerulosclerosis was the common findings in this study32.2%.Results of several studies from Asia, Middle East regions and studies in Africa, had reported remarkably higher incidence of Focal segmental glomerulosclerosis in both African-American and whites populations making it the most common cause of primary glomerulopathy syndrome in their adult populations, which is similar to findings in this study (9,17,8,29,30,39,40,41). The incidences among Chinese and Japanese ranged from 20.7- 40.5 %, and up to 44.1% in the Italian registry. The only discrepancy was that most of the studies were reviews studies with good number of study participants(42,14,12).

Other studies done in USA ,UK and India showed that Focal segmental glomerulosclerosis to be 42 - 44.3% respectively (38,43,44).

Minimal-change disease comprised 20.0% of primary nephritis, these findings are similar to studies done in New York , Taiwan ROC , India, Brazil ,Iraq and Dakar in which minimal change disease ranged from 10-20% among young adults(7,16,45,46,41,47,40).However this findings do not agree with studies done in Sudan and Nigeria in which minimal change was not common as compared to other primary glomerulonephritis(36,48).

Membranous nephropathy was found in 17.5% of tissue finding in primary glomerulopathy. These findings are similar to several studies done in Middle East regions (Saudi Arabia, Jordan, Egypt, Iran and Iraq) as well as in Africa, specifically in South Africa and West Africa. Renal biopsy in Abuja Nigeria found membranous nephropathy to be the common histological findings(16,29,19,20,34,31,11).

The incidence of membranoproliferative glomerulonephritis in this study was5%, this findings was supported by studies which have same trend of low incidences, probably owing in better control of infections. The fact that we did not use electron microscopy (EM) which is better diagnostic tool for membranoproliferative glomerulonephritis, and this could explain the low incidence in this study (46,49).

In this study IgA nephropathy was found in 5%, following trend of a low prevalence reported by Indian studies (4.5%-14%). However IgA nephropathy was the common cause of primary glomerlopathy in countries like Singapore, Japan, and Hong Kong, Australia, Finland, and southern Europe in which IgA ranged from (20 to 40%) respectively (17,14,15,50,51,52,26). However in this study inability to do immunofluorescence studies and electron microscopy were also the contributing factor for low IgA nephropathy findings.

Secondary glomerulopathies was found in 20.0%, where by Lupus nephritis was about 5% while other findings were about 15.0%.Among other histologic findings were; renal amyloidosis 4.0%, inconclusive findings 10.0% and undetermined due to excessive fibrosis 1%. The findings for amyloidosis associate nephritis and lupus nephritis in the present study are similar to studies done in Zimbabwe and other regions (53,54,55,56). However studies in Hispanic population showed high incidence of SLE about 17.8 % as well as a study done in Peru Lima in which 30.2 % of study population had SLE(57,58).

10.0 STRENGTH OF STUDY

This was first local case series on clinical and histopathological characteristics, so the findings and recommendations will improve (d) treatment of the patients base on histopathological patterns rather than clinical / Lab characteristics.

11.0 LIMITATIONS OF THE STUDY

The main limitation of this study was inability to perform electron microscope and immunofluorescence studies due to non-availability of this facility at our center. Other limitations is the small sample size, this being a single center study and lack of data on renal biopsy as well quite number of the participants were excluded.

12.0 CONCLUSIONS

Primary glomerulopathies in Tanzania occur more commonly among young age (≤ 40 years) .Female patients were common presented with glomerulonephritis syndrome, while secondary glomerulopathies were presented in both Gender. There is considerable heterogeneity in the histologic spectrum of glomerulopathies which is influenced by age and a gender factor, Focal segmental glomerulosclerosis was the leading cause of primary glomerulopathies in this study.

13.0 RECOMMENDATION

We recommend that kidney biopsying should be part of routine evaluation for patients with glomerulonephritis syndrome in our setting. Further, the findings from this study underscore the need to start and maintain the Tanzania Kidney Biopsy Registry that will be a great resource for future research on the causes and prevention of kidney diseases in Tanzania

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APPENDICES

Appendix I: Questionnaire

Questionnaire; TO BE FILLED IN BY THE INVESTIGATOR OR ASSISTANT [MEDICAL PERSONEL] ONLY

i. Questionnaire Number……
ii. Date of interview…… Date of Procedure.....
iii. Patient's File Number……
iv. Patients /Next of kin Cell phone number……
v. Residence (District and Region).....
vi. Do you have a health insurance? Yes / No

SECTION1; Socio-demographic Characteristics.

1). Date of Birth…/…/…… (Age)…..
1. 18-27
2. 28-37
3. 38-47
4. 48-57
5. 58- 67
6. >68

2).Gender:
1. Male 2. Female

3) Marital status:
1. Single
2. Married/ cohabiting
3. Divorced/Widowed/ widower

4) Level of education:
1. No formal education
2. Primary education
3. Secondary education
4. Higher education

5i) Occupation:
1. Unemployed go to Qn 5ii)
2. Employed ; self employed /employee
3. Others (specify)……..

5ii) Who takes care of your daily living (food, Shelter, medication)?
1. Parents / guardian
2. spouse
3. Others;.....

6) Religion &believes:
1. Christian
2. Muslim
3. Others (specify)……..

SECTION2:
History & Examination findings

7) What brought you to the hospital?
1. Generalized body swelling
2. Facial Puffiness only
3. lower limb swelling only
4. Red urine
5. reduced urine amount
6. foamy urine
7. fever
8. Others.....

Past medical and family social history:

8) Have you ever been told that you have kidney disease?
1. Yes when .....months ago Go to Q.9
2. No

9) Were you given any medication?
1. Yes Go to Q5 for how long ....months
2. No

10) What kind of medication were you given?
1. Oral
2. Injectable

11) Is there any other family member with similar complain / disease
1. Yes who? .....
2. No

12) Have you ever been diagnosed with Diabetes mellitus
1. Yes how long .....months
2. No

13) Have you ever been diagnosed with Hypertension
1. Yes how long .....months
2. No

14) Indication for biopsy;.....

SECTION 3 Examination and biochemical findings

	Vitals	Measurement
15	Temp	
16	RR	
17	PR	
	BP1	BP2
18	AVE BP	

Anthropometric measurement

19	Weight (Kg)	
20	Height (cm)	
21	BMI kgm2	
22	MUAC	

Clinical assessment: √ the appropriate option.

23	Facial puffiness	
24	LL edema	
25	Anasarca	
26	Anemia (conjunctival/ palm pallor/ phantum	
27	Petechia/ ecchymosis / gum bleeding	
28	Calf tenderness	

Biochemical findings; Urine dipstick test:

	Tests	Circle the appropriate answer				
29	PH					
30	Urobilinogen	N	1+	2+	3+	
31	Glucoses	N	1+	2+	3+	
32	Billrubin	N	1+	2+	3+	
33	Ketones	N	1+	2+	3+	
34	Protein	N	1+	2+	3+	4+
35	Nitrite	N	1+	2+	3+	
36	Leukocytes	N	1+	2+	3+	
37	RBC	N	1+	2+	3+	
38	Macroscopic					
39	Protein	N	1+	2+	3+	4+
40	Glucose	N	1+	2+	3+	
41	Ketones	N	1+	2+	3+	
42	Blood	N	1+	2+	3+	
43	Nitrites	N	1+	2+	3+	
44	Leucocytes	N	1+	2+	3+	
45	Bilirubin	N	1+	2+	3+	
46	PH					
47	Specific gravity					
	Microscopy	Results				
48	WBC	N	P	Cells		
49	Rbc	N	1+	2+	3+	
50	Epithelial cells	N	1+	2+	3+	
51	Yeast	N		P		
52	Hyaline casts	N		P		
53	Granular casts	N		P		
54	Ca-oxalate	N		P		
55	Uric acid	N		P		
56	Ca-phosphate	N		P		
57	Parasite ID					
58	Esbatch test					

Other biochemical findings:

	Test	Results			
59	Serum Creatinine		N	H	L
60	BUN		N	H	L
61	Serum sodium		N	H	L
62	Serum potassium		N	H	L
63	Serum Calcium		N	H	L
64	Serum Phosphorus		N	H	L
65	Serum magnesium		N	H	L
66	Total cholesterol		N	H	L
67	Serum albumin		N	H	L
68	PT		N	H	L
69	INR		N	H	L
70	PTT		N	H	L
71	AST		N	H	L
72	ALT		N	H	L
73	HBsAg	N		P	
74	HcAb	N		P	
75	HIV 1 & 2	N		P	
	FBP	Results			
76	WBC		N	H	L
77	Neutrophils (Ab)		N	H	L
78	Lymphocytes (Ab)		N	H	L
79	Monocytes (Ab)		N	H	L
80	Eosinophils (Ab)		N	H	L
81	Basophils (Ab)		N	H	L
82	Red blood cells		N	H	L
83	Haematocrit		N	H	L
84	Haemoglobin		N	H	L
85	MCV		N	H	L
86	MCH		N	H	L
87	MCHC		N	H	L
88	PLT		N	H	L
89	CRP		N	H	L

Histopathology findings;

89) HP number:.....

90) Renal Biopsy findings

1. MCD
2. FSCGS
3. MN
4. IgAN
5. MPGN
6. LN
7. Others.....(specify)

Appendix II. Consent Form (English Version)

I am Dr. Amira William Deng a researcher from Muhimbili University of Health and Allied Sciences (MUHAS) I am conducting a study titled

'' CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH GLOMERULONEPHRITIS SYNDROME ATTENDING RENAL UNIT AT MUHIMBILI NATIONAL HOSPITAL IN DAR ES SAALAM, TANZANIA''

Participation in the study

You are kindly requested to be part of this study, if you accept to participate your particulars /information will be taken and used for the purpose of this study and this involve the following: taking your clinical records from clinical note which include examination findings and lab findings as well during your stay in the hospital your participation is completely voluntary and you may withdraw consent at any time in course of interview.

Confidentiality

You are strongly assured of the confidentiality of the information obtained that will only be used for the purpose of this research and anonymity will highly be observed when collecting data and compiling report. To assure you even your name will not be acquired to appear in the questionnaire.

Risks of participating

No anticipated or harm that may result from participating in this study. Your participation is absolutely voluntary and there is no penalty for refusing to participate. You are free to ask questions and you may stop to participate in this study at any time.

Contact person

The principle investigator, Dr. Deng (0684271832) is a key contact person with regard to any queries about this study.

If you have any question/concern about you rights as a participant you may contact Dr. Joyce Masalu Director Research and Publications Muhimbili University of Health and Allied Sciences (MUHAS) P. O. BOX 65001, Dar es salaam Tel; +255 754757577.

If you agree to participate in this study please sign this consent form.

I (initials)……. Have read and understand the contents of this form and I have been given satisfactory explanation with all my questions answered. I therefore consent to participate in this study

Signature of interviewee…… Date……

Signature of interviewer……Date ……

Appendix: III Consent Form (Swahili Version)

FOMU YA USHIRIKI

Mimi ni Dkt. Amira William Deng. Ni mtafiti kutoka chuo kikuu cha tiba na sayansi shirikishi MUHAS. Ninafanya utafiti kuhusu **"HALI ZA KIPATHOLOJIA NA NAMNA ZA WAGONJWA WA MARADHI YA VICHUJIO VYA NDANI YA FIGO, HAPA DAR ES SAALAM"**

Ushiriki wako katika utafiti

Tafadhali naomba ushiriki katika utafiti huu.

Endapo utashiriki, taarifa zako zote zitakazochukuliwa, zitatumika kwaajili ya utafiti huutu, na sivinginevyo.

Ushiriki utahusisha kuchukuliwa kwa taarifa na maelezo kutoka kwenye jalada lako la matibabu yanayohusu maradhi yako, vipimo na tiba, hususani kwa kipindi ulichokuwa umelazwa.

Ushiriki

Nakuhakikishia ya kwamba ushiriki wako ni siri. Hutotajwa jina lako popote. Sio wakati wa kukusanya taarifa, wala wakati wa kuandika ripoti. Zaidi ya hapo, hutahitajika kuandika jina lako hata kwenye dodoso.

Madhara katika kushiriki

Haitazamiwi kutokea madhara yoyote kwa kushiriki kwako. Ni hiari yako kushiriki na una haki ya kujitoa katika utafiti huu wakati wowote. Hutodhuriwa au kupata adhabu yoyote kwa kukataa kushiriki au kujiengua.

Kwa maelezo Zaidi wasiliana na:

Dkt. Amira Deng,Simu nambari 0684271832, Mtafiti mkuu.

Dkt. Paschal Ruggajo, Mhadhiri na msimamizi wa utafiti, MUHAS.

Kwa ufafanuzi Zaidi kuhusu haki zako kama mshiriki wa utafiti, wasiliana na:-

Dkt. Joyce Masalu

Mkurugenzi wa Utafiti

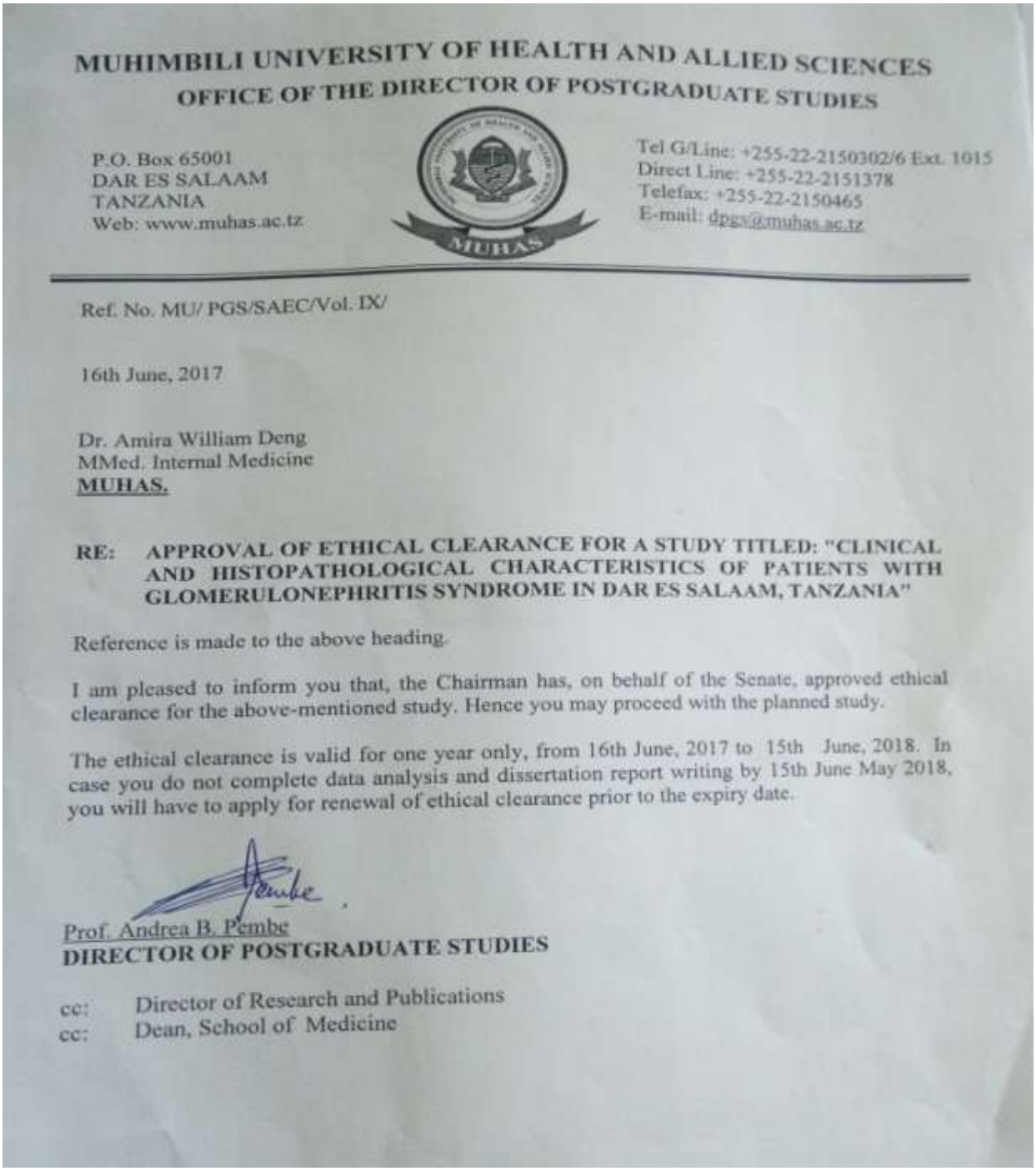
Chuo Kikuu cha MUHAS
S. L. P 65001, Dar es Salaam.
Simu nambari: +255 (0) 754757577.
Barua pepe: drp@muhas.ac.tz

Ikiwa umekubali kushiriki, tafadhalij aza na usaini hapa:

Mimi …… nimesoma/nimeelezewa yaliyomo kwenye fomu hii na nimeyaelewa. Nimekubali kushiriki katika utafiti huu.

Saini:……Tarehe:.....

Appendix: IV Ethical of Clearance



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Ref. No. MU/ PGS/SAEC/Vol. IX/

16th June, 2017

Dr. Amira William Deng
MMed. Internal Medicine
MUHAS.

RE: APPROVAL OF ETHICAL CLEARANCE FOR A STUDY TITLED: "CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH GLOMERULONEPHRITIS SYNDROME IN DAR ES SALAAM, TANZANIA"

Reference is made to the above heading.

I am pleased to inform you that, the Chairman has, on behalf of the Senate, approved ethical clearance for the above-mentioned study. Hence you may proceed with the planned study.

The ethical clearance is valid for one year only, from 16th June, 2017 to 15th June, 2018. In case you do not complete data analysis and dissertation report writing by 15th June May 2018, you will have to apply for renewal of ethical clearance prior to the expiry date.

Prof. Andrea B. Pembe
DIRECTOR OF POSTGRADUATE STUDIES

cc: Director of Research and Publications
cc: Dean, School of Medicine