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An evaluation of clinical and biochemical features and outcomes of patients with mesangiocapillary glomerulonephritis in people with HIV compared to HIV negative patients at a tertiary hospital, in Cape Town, South Africa.

University of Cape Town
Faculty of Health Sciences
For the fulfilment of the degree of
Master of Medicine (MMed) in Internal Medicine

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Declaration

I, Shaheed Salim Sorathia hereby declare that this research is completely my own (except where acknowledgements indicate otherwise). No part of it has ever been published in any format or submitted for another degree in this or any other university. I empower the University of Cape Town to reproduce for the purpose of research either the whole or any portion of my work in a manner that suits the institution. I intend to submit the results of my research in a published format to a journal of my choice at a later date.

Signed on this 31st August 2022, at Century City, Cape Town.

Signature Signed by candidate

Acknowledgements & Contributions

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The format of the thesis is in the published/publication-ready format to be published in Kidney International.

This was presented as a poster presentation at the 2021 UCT Department of Medicine Annual Research Symposium achieving Best Clinical Poster and was also presented at the SA Renal Congress 2022.

Supervisor Declaration

I, Professor Nicola Wearne do declare that this thesis meets all requirements to be included in for planned publication and that:

- The journal accepting the paper is accredited by the Department of Higher Education and training or it has been approved by the UCT Health Sciences Specialist Training committee
- The candidate, Shaheed Salim Sorathia is the first author of the paper
- The candidate contributed the most to the paper
- The candidate developed the protocol and wrote the paper under supervision
- The candidate was involved in the analysis, presentation and interpretation of results
- The other authors and their contributions to the paper are stated
- The above statements will be included in the declaration page of the dissertation.

Signed on this 31st day of August 2022, at Groote Schuur Hospital, Cape Town.

Signed by candidate

Prof. Nicola Wearne

List of Tables and Figures

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Abbreviations

ANA – Antinuclear Antibody

ART – Anti Retroviral Therapy

CKD – Chronic kidney disease

dsDNA – double stranded DNA

eGFR – Estimated Glomerular Filtration Rate

ESKD – End Stage Kidney disease

GN – Glomerulonephritis

Hb – Haemoglobin

HIV – Human Immunodeficiency Virus

HMIC – High-and middle-income countries

HIVAN – HIV associated nephropathy

HIVICK – HIV associated immune complex kidney disease

ICGN – Immune complex glomerulonephritis

IQR – Interquartile range

KRT – Kidney replacement therapy

LMIC – Low- and middle-income countries

MCGN – Mesangiocapillary Glomerulonephritis

PWH – People with HIV

RPGN – Rapidly progressive glomerulonephritis

uPCR – Urine protein creatinine ratio

VDRL – Venereal disease research laboratory test

VL – Viral Load

Abstract

An evaluation of clinical and biochemical features and outcomes of patients with mesangiocapillary glomerulonephritis in people living with HIV compared to HIV negative patients at a tertiary hospital, in Cape Town, South Africa.

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Background & Aim

Mesangiocapillary glomerulonephritis (MCGN) is a common histological pattern of glomerular injury in developing countries. South Africa has the highest proportion of people living with HIV (PWH) and the co-existence of MCGN and HIV may affect kidney prognosis. The aim of this study was to compare the clinical and biochemical features between PWH and HIV-negative individuals with a diagnosis of MCGN and to review kidney function and survival.

Materials and Methods

A retrospective study was conducted in patients with a biopsy diagnosis of MCGN between January 2010 and December 2017. The following data were collected: age, sex, use of illicit drugs, date of initiation of antiretroviral therapy (ART), blood pressure, presence of oedema, need for kidney replacement therapy, HIV status, CD4 and viral load. Secondary causes were excluded.

Kidney outcomes [(serum creatinine, estimated glomerular filtration rate (eGFR), urine protein creatinine ratio (uPCR)] were assessed at 6, 12 and 24 months post biopsy. The composite outcome was defined as a 40% decline in eGFR, progression to end stage kidney disease or death.

Results:

The study included 116 participants: 27 (23%) were PWH, 89 (77%) were HIV-negative. The median age was 33 years. There were more males in the HIV-negative group [63/89 (71%)].

Oedema was more common in HIV-negative patients [66/86 (77%), p=0.011]. Haemoglobin and albumin were lower in PWH [9.1g/dL vs 11.2 g/dL (p=0.053) and 20 g/L vs 27 g/L, (p=0.053), respectively].

Baseline creatinine, eGFR and uPCR were not different between the groups. However, at 6 and 12 months the creatinine was higher in PWH: 137 µmol/L compared to 97 µmol/L (p=0.028) and 125 µmol/L compared to 87 µmol/L(p=0.023), respectively. uPCR was higher in PWH at 6 and 12 months: 0.63 g/mmol vs 0.075 g/mmol, (p=0.002) and 0.28 g/mmol vs 0.028 g/mmol, (p=0.022), respectively.

The composite endpoint was not different between the two groups in the first three years of follow-up.

Conclusions:

MCGN has a poor prognosis irrespective of HIV status. Despite no differences in creatinine and uPCR at the time of biopsy, PWH had a higher uPCR, and creatinine at 6 and 12 months. HIV status did not affect survival.

Key Words: *mesangiocapillary glomerulonephritis, HIV status, South Africa*

Introduction

Mesangiocapillary glomerulonephritis (MCGN) also known as membranoproliferative glomerulonephritis (MPGN), is a histological pattern of glomerular injury. It is characterized by mesangial hypercellularity, increased mesangial matrix, and thickening of glomerular capillary walls. This is due to subendothelial deposition of immune complexes, and/or complement factors, cellular entrapment, with resultant new basement membrane formation.[1,2,3]

MCGN is the most common cause of nephrotic syndrome found in kidney biopsy series in lower middle income countries (LMIC), especially in Africa and carries a poor prognosis.[1,2,4] The clinical presentation and course of MCGN are extremely variable – ranging from benign and slowly progressive to rapidly progressive. Thus, patients can present with asymptomatic hematuria and proteinuria, acute nephritic syndrome, nephrotic syndrome or even a Rapidly progressive glomerulonephritis (RPGN).[6] A systematic review on the epidemiology of histologically proven glomerular diseases in Africa reported a prevalence of idiopathic MCGN of 12%.[5] In South Africa, two retrospective studies from two tertiary hospitals in Cape Town showed that the prevalence of primary MCGN accounted for 20% of all primary glomerulonephritides. MCGN was also reported as the most common biopsy confirmed glomerulonephritis (GN) in Cape Town and also found to carry a poor outcome.[2,4] Poor prognosis was defined by doubling of serum creatinine and progression to end stage kidney disease (ESKD).[3,4]

The high prevalence of MCGN seen in African cohorts differs from high [HIC] and upper-middle incomes countries[UMIC], where IgA nephropathy is the most common primary GN, particularly on the Asian subcontinent, while MCGN is currently on a downward trend.[6,7-10] It is postulated that a combination of genetic, ethnic, environmental and population screening contribute to IgA nephropathy being more common in HIC and UMIC. For example, in Asia, routine urinalyses are performed for school children, and kidney biopsies are performed for patients with asymptomatic hematuria, thereby raising the reported prevalence of the disease.[11] However, a report from Romania [UMIC], demonstrated that MCGN was the most frequent primary GN accounting for 29% of all primary GNs reported between 1995-2003.Therefore, emphasizing the ongoing worldwide concern. Importantly the prevalence of MCGN declined in this study with improvement in income, sanitation, social and medical infrastructure.[12]

Recently, there has been a change in the classification of MCGN from a previous morphological classification to now being classified based on immune complex deposition. The immunofluorescence pattern separates MCGN into three categories: 1. an immune complex group with both C3 and IgG present, 2. only C3 present, and 3. pauci-immune group.[3,13] Crescentic GN is a histological manifestation of severe glomerular damage characterized by rapid loss of kidney function, and the histological presence of glomerular crescents (>50%). Crescents, especially small and focal, have been reported in about 10% of patients with MCGN.[14] However, in a report from India, in the setting of HIV associated MCGN, crescentic GN was rarely seen.[15]

It is estimated that 7.8 million people are living with HIV (PWH) in South Africa with a prevalence of 19%.[16] HIV is a major cause of kidney disease in Africa.[17-19] Less than 50% of infected individuals are receiving antiretroviral therapy (ART).[14-16] Classic HIV associated nephropathy (HIVAN) has been well studied in PWH, however, less is understood regarding immune complex disease in this cohort. The term HIVICK (HIV associated immune complex kidney disease) was previously used to describe this spectrum of disease, however due to lack of clarity of causality the group has rather been termed "immune complex disease in the setting of HIV".[5,20] Almost every form of immune complex-mediated GN (ICGN) has been identified on kidney biopsy in PWH.[14] This heterogenous group includes MCGN, postinfectious GN, membranous GN a "lupus-like" GN and IgA nephropathy. An unusual ultrastructural appearance of subepithelial deposits, or "ball in cup" lesion, has also been described in South Africa, but is rarely observed in other settings.[21]

A reduction of classical HIVAN has been reported, however the incidence of the individual GNs in the setting of HIV has not been clearly described. The reduction of HIVAN is attributed to the introduction of ART suppressing viral replication in the kidney. ICGN appears to be more predominant since the introduction of ART, however this could be proportional to the reduction in HIVAN.[22]

The aim of this study was to compare PWH and HIV-negative cohorts with a histological diagnosis of MCGN. The primary objective was to compare clinical and biochemical features between the two groups. The secondary objective was to compare the composite of kidney

survival and mortality up to three years, and kidney function [creatinine, estimated glomerular filtration rate (eGFR), and urine protein creatinine ratio (uPCR)] at 6, 12, and 24 months between the two cohorts.

Methods

This was a retrospective review of all patients with a histological diagnosis of MCGN on kidney biopsy between 2010 and 2017, performed at Groote Schuur Hospital, in Cape Town, South Africa. The inclusion criteria were an age greater than 18 years and a diagnosis of MCGN based on a histological pattern of glomerular injury. Exclusion criteria included a secondary cause of MCGN based on a combination of clinical and laboratory data (including C3 on IF), however HIV was not considered a secondary cause for the purpose of this study. The study received ethical approval from the University of Cape Town human research ethics committee (HREC 431/2021). MCGN was defined as mesangial hypercellularity, increased mesangial matrix, and thickening of glomerular capillary walls due to subendothelial deposition of immune complexes, and/or complement factors, cellular entrapment, and new basement membrane formation.[23]

Data were collected from written and electronic records. Demographic data (e.g. age and sex) and clinical data (blood pressure, oedema, a drug history including timing of ART initiation in relation to biopsy and illicit drug use as well as self-reported incarceration in prison) were documented. Biochemical data were collected from the National Health Laboratory Service (NHLS). These included kidney parameters, i.e. serum creatinine (µmol/L), eGFR

(ml/min/1.73m^2) using CKD Epi[24] and uPCR (g/mmol) at 6, 12 and 24 months. HIV status at the time of biopsy was recorded as well as CD4 count (cells/mm^3) and viral load (copies/ml). Additional laboratory investigations included albumin(g/L), cholesterol (mmol/L) and haemoglobin (g/dL). Secondary causes were investigated, including serology for Hepatitis B & C, C3, C4, ANA, dsDNA, VDRL.

Outcome data were collected. Kidney outcomes assessed were creatinine and eGFR at 6, 12 and 24 months. Deterioration of kidney function was defined as a decline in eGFR of 40% or more over the study period or doubling of serum creatinine. Progression was defined as developing end stage kidney disease (ESKD) (stage 5) or transition to kidney replacement therapy (KRT). uPCR was recorded at baseline, 6, 12 and 24 months after biopsy. Survival analysis was assessed for the composite outcome of death, eGFR decline of >40% ± doubling of serum creatinine up to three years. Lost to follow was defined as no further Clinicom (clinic visits) past the two year follow-up period. Death was based on medical records.

Statistics

Continuous data were assessed for normality. Non-normally distributed data were reported as medians with interquartile ranges (IQR). Categorical data were reported as proportions. Mann-Whitney U test or student t-test were used to compare continuous variables and either the Chi-squared or Fisher's exact test was used to compare categorical variables, dependent on the sample size. A p value of less than 0.05 was considered statistically significant. Outcome data were analyzed using Kaplan Meier curves, comparing those with and without HIV at biopsy. A

sub-analysis was performed on PWH based on viral load suppression at biopsy to determine differences in kidney function and uPCR.

Results

Table 1 describes the baseline characteristics of 116 patients with biopsy proven MCGN at the time of kidney biopsy in PWH compared to HIV-negative patients during the period of January 2010 and December 2017. There were 27 PWH (23%), 75 were male (64%), and the majority of patients in the HIV-negative cohort (70%) were male (p=0.02). The median age of all patients included was 33 years.

Oedema was more common in the HIV-negative cohort (66/86), accounting for 77% of patients (p<0.011), as compared to 48% in PWH. There was no difference in the use of illicit substances between the groups, however numbers were too small to make a meaningful comparison. The haemoglobin was lower in the cohort of PWH (9.1 g/dL vs 11.2 g/dL) and approached statistical significance (p=0.053). Serum albumin was also lower in the PWH 20 g/L vs 27 g/L and approached statistical significance (p =0.053). In the cohort of PWH, 17/27 (63%) patients were on ART at the time of biopsy. Of those who had a viral load performed, 14/27 (52%) only seven were virally suppressed. Out of 26 patients with CD4 counts at the time of biopsy, the median CD4 count was 445 cells/mm^3 with an IQR (39-1524 cells/mm^3). Of those on ART, the median CD4 was 380 cells/mm^3, with an IQR (277-721 cells/mm^3) while those not on ART had a median CD4 of 383 cells/mm^3 with an IQR (149-410 cells/mm^3).

Baseline creatinine, eGFR and uPCR were not statistically different between the groups. Table 2 demonstrates kidney function and uPCR at baseline and at 6, 12, and 24 months. There were no differences at baseline, however differences in creatinine levels, eGFR and uPCR were noted at the first (0-6 month) and second (6-12 month) period following kidney biopsy and were both clinically and statistically significant, figure 1. At 6 months, serum creatinine was higher in PWH [137 (87;258) µmol/L compared to 97 (77.2; 137.5) µmol/L in the HIV-negative cohort] and at 12 months in PWH [125 µmol/L compared to 87 µmol/L in the HIV-negative cohort]. Correspondingly, the eGFR was lower in PWH 43.5 ml/min/1.73m^2 vs 86.5 ml/min/1.73m^2 at 6 months, and 49 ml/min/1.73m^2 vs 86 ml/min/1.73m^2 at 12 months. The difference in uPCR was found to be statistically significant in PWH at 6 and 12 months compared to the HIV-negative cohort: 0.63 g/mmol vs 0.075 g/mmol, and 0.28 g/mmol vs 0.028 g/mmol respectively. Meaningful analyses at 24 months were limited due to the number of individuals lost to follow up, however of the data available, the findings were: In PWH the follow up serum creatinine at 6 months was 26/27 (96%) and this declined to 11/27 (41%) at 2 years. The follow up of proteinuria at 6 months was 14/27(52%), and this declined to 4/27 (15%) at 2 years.

In HIV negative patients, the follow up serum creatinine at 6 months was 61/89 (%) and this declined to 21/89 (24%). The follow up of proteinuria at 6 months was 46/89 (52%) and this declined to 16/89 (18%) at 2 years.

Overall, the composite endpoint was not different between the two groups in the first three years following kidney biopsy, figure 2. Survival ranged from 60-70% and the proportion with the composite outcome was 10/26 (38%) in PWH, and 21/89 (24%) in the HIV-negative cohort.

In PWH, there was no difference noted in creatinine, or eGFR at any time period based on ART. However, there was a statistically significant difference in uPCR at the time of biopsy in PWH on ART (p=0.020). These differences may be underestimated as the follow up data are too limited to be analyzed.

Discussion

In this retrospective study looking at differences in clinical, laboratory and kidney outcomes of biopsy proven MCGN in PWH and HIV-negative cohorts, some pertinent findings were seen. There were more males in the HIV-negative cohort and the median age of patients in both cohorts was young at 33 years. Oedema was more common in the HIV-negative cohort but serum albumin was lower in PWH. Despite kidney outcomes showing no difference, serum creatinine and uPCR were higher in the first year following biopsy in PWH.

In a large kidney biopsy series of 192 PWH from Cape Town, there were 58 (30%) patients who had a type of ICGN. MCGN comprised the largest group, with 13/58 (22%) cases.[21] To the best of our knowledge, there has only been one previous study comparing clinical and biochemical profiles and outcomes in PWH and HIV-negative patients with MCGN. This earlier study found that in the HIV-negative cohort, there was more hypertension (48%) vs 35% in PWH, 35% had substance use or had been incarcerated, while PWH were younger (33.5 years), predominantly of Black race, had more oedema (90%), lower albumin at 20 g/L, and a higher creatinine at the time of biopsy (354 µmol/L).[25] These results are very similar to what we have observed in our study.

Despite relatively limited published data, MCGN has been found to be common in LMICs and has historically been shown to carry a poor prognosis.[25] Current literature is summarized in Table 3, which describes the proportion of MCGN observed in biopsy series, those with HIV, kidney outcomes and the predictors thereof. Locally, two different retrospective studies have been performed in the two main tertiary hospitals in Cape Town. Both studies demonstrated that MCGN is a common glomerular histological diagnosis in the Western Cape, more common in males, and carries a poor prognosis.[3,4] This is in contrast to a Mexican study of 133 MCGN patients, that found the prevalence of MCGN was lower at 3.6%, and more commonly found in women (60% of their cohort).[26] The high prevalence of MCGN in the Western Cape has not been replicated in other areas of South Africa. Bloemfontein and Johannesburg report that FSGS was the most common primary GN found in their biopsy series.[27,29]

Both previous studies in Cape Town concluded that MCGN remains the most common biopsy proven GN, with a 20% prevalence. There was a predominance of males (75%), oedema was common, albumin was low and the majority were hypertensive, with only 20% reporting substance use or incarceration.[2,3,4] The poor prognostic indicators include: lower eGFR at presentation, Black African race and presence of interstitial fibrosis on histology.[3] Kidney outcomes were poor with 81% of those with MCGN developing doubling of creatinine, progressing to ESKD or dying within 5 years.[4] The clinical findings in these studies were similar to our study in that we found 96% had oedema, the median albumin was 26 g/L and 27% reached the composite outcome within the follow-up period. The poor prognosis of MCGN has been demonstrated elsewhere. In Tunisia the presence of MCGN was associated with kidney

failure at the time of diagnosis and significantly correlated with death or ESKD in 43% of patients.[30] Kidney outcomes in patients with MCGN, irrespective of HIV status, have been shown to have a poor prognosis due to late presentation and advanced kidney failure at presentation.[25] However, ART has been shown to improve survival in these patients.[21,25] In PWH, our study demonstrated that there was no difference in creatinine and outcomes based on the use of ART at biopsy. However, there were only 27 PWH and 17 were on ART at the time of biopsy, 7 of which were virally suppressed. This limits the value of analysing the differences based on the use of ART. Furthermore, ART use was not reported in the follow up period. However due to the active ART rollout program in South Africa, these patients may have been initiated shortly after biopsy, limiting meaningful analysis based on ART at biopsy. Inusah *et al.*, report that 60% of their PWH cohort were on ART at biopsy but the majority of the remaining PWH were initiated during the index presentation by referral centers.[25] Nevertheless, a recent study in Cape Town demonstrated that there was no difference between PWH and HIV-negative patients in doubling of creatinine or ESKD and the severity of kidney failure but the quantity of proteinuria at the time of biopsy was greater in PWH.[25] Our study demonstrated similar uPCR results, table 2.

Data from Cape Town have suggested that the use of illicit substances is associated with MCGN and chronic kidney disease (CKD), where MCGN was found in 58% of biopsies performed in those taking methamphetamines (tik).[31] There was also a significant proportion who were found to have hypertensive nephrosclerosis on biopsy. It is hypothesized that the association of substance abuse with MCGN could be due to chronic antigenemia from chronic infections

through sharing of drugs and injectables, tattoo ink, and close physical contact.[31] In this biopsy series that described the association of tik use and MCGN only 1 individual was found to be HIV positive. Our study, performed 10 years later, reports an equal proportion of drug use. However, there was underreporting of methamphetamine use noted in PWH; only 11/27 (41%) had documentation of whether or not they were using illicit substances.

We recognize that this study has a number of limitations. As this was a retrospective study, it limited the type of data that could be collected and analyzed during this period. Secondly, missing data, particularly in the post biopsy follow up period resulted in limited monitoring of progression of uPCR affecting the accuracy of the final statistical analysis. Furthermore, many patients were lost to follow-up during the post biopsy period, which could have affected the final data on kidney outcomes in the two cohorts. Thirdly, the small number of patients included in this study may have contributed to the minimal differences in clinical and biochemical outcomes between the two cohorts.

Conclusions

Overall MCGN has a poor prognosis, and often detected on biopsy in PWH, although causality cannot be ascribed. HIV status does not appear to affect survival, even though there is a higher creatinine and uPCR detected in the first year of follow-up. Similarly, the use of ART does not demonstrate difference in outcomes. Prospective data are warranted in order to evaluate treatment options particularly in the setting of limited KRT.

Disclosure Statement

The Authors have declared that no competing or conflicts of interests exist.

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Appendices

ETHICS APPROVAL:

Ethical approval was obtained from the Human Research Ethics Committee of the University of Cape Town. HREC 431/2021. Attached.

CONSENT FOR PUBLICATION – to be published in Kidney International.

AVILABILITY OF DATA & MATERIAL:

Data sets are available from the corresponding author on reasonable request.

COMPETING INTERESTS:

The authors declare they have no competing interests.

FUNDING:

This study required no funding.

AUTHOR CONTRIBUTIONS:

NW provided the research idea. NW, EJ and SS provided the study design. SS wrote the proposal under the guidance of NW. SS performed data collection. NW and EJ were involved in data analysis and interpretation. SS, NW and EJ were involved in the manuscript preparation and writing of the paper. Each author contributed important intellectual content during manuscript writing and accepts accountability for the overall work.

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UNIVERSITY OF CAPE TOWN
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Human Research Ethics Committee

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13 July 2021

HREC REF: 431/2021

Prof N Wearne
Division of Nephrology
E-13 NGSH
Email: Nicola.wearne@uct.ac.za
Student: shaheed.sorathia@gmail.com

Dear Prof Wearne

PROJECT TITLE: AN EVALUATION OF CLINICAL, BIOCHEMICAL, RENAL HISTOLOGY AND OUTCOMES OF PATIENTS WITH MESANGIOCAPILLARY GLOMERULONEPHRITIS (MCGN) IN HIV POSITIVE COMPARED TO HIV NEGATIVE PATIENTS AT A TERTIARY HOSPITAL, IN CAPE TOWN, SOUTH AFRICA-MASTERS' CANDIDATE-DR SHAHEED SORATHIA

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020 & 06 July 2020.

Approval is granted for one year until the 30 July 2022.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Dr Shaheed Sorathia will also be involved in this study.

Please quote the HREC REF 431/2021 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator must obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN

CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
NHREC-registration number: REC-210208-007
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2020), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES

FHS017: Annual Progress Report / Renewal

Record Reviews/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30-7-23
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee		ate Signed	6/7/2022

Note: Please note that incomplete submissions will not be reviewed.
Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za.

Please clarify your plan for research-related activities during COVID-19 lockdown

HUMAN RESEARCH ETHICS COMMITTEE
04 JUL 2022
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	17/6/22		
HREC REF Number	431/2021	Current Ethics Approval was granted until	July 31 2022
Protocol title	PROJECT TITLE: AN EVALUATION OF CLINICAL, BIOCHEMICAL, RENAL HISTOLOGY AND OUTCOMES OF PATIENTS WITH MESANGIOCAPILLARY GLOMERULONEPHRITIS (MCGN) IN HIV POSITIVE COMPARED TO HIV NEGATIVE PATIENTS AT A TERTIARY HOSPITAL, IN CAPE TOWN, SOUTH AFRICA-MASTERS' CANDIDATE-DR SHAHEED SORATHIA		
Principal Investigator	Prof N. Wearne		
Department / Office Internal Mail Address	Division of Nephrology E-13 NGSH		
1.1 Does this protocol receive US Federal funding?		☐ Yes	☑ No

2. Protocol status (tick ☐)

☐	Research-related activities are ongoing
☑	Data collection is complete, data analysis only
Please indicate (in the block below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository.	

3. Protocol summary

Total number of records or specimens collected, reviewed or stored since the original approval		116
Total number of records or specimens collected, reviewed or stored since last progress report		—
Have any research-related outputs (e.g. publications, abstracts, conference presentations) resulted from this research? If yes, please list and attach with this report.	☐ Yes	☐ No

4. Signature

Signature of PI	Nicola Wearne	Date	22-6-2022

(Note: Please complete the Closure form (FHS019) if the study is completed within the approval period)

List of Tables and Figures

Table 1: Baseline characteristics of patients undergoing kidney biopsy.

Characteristics at biopsy	Total N=116	HIV – N=89	PWH N=27	P value
Age (median, IQR)	116	29 (24.5;42.5)	32 (29;36)	0.776
Gender (males, n, %)	116	63 (70.8)	12 (44.4)	0.020
Oedema (n, %)	111	33 (76.7)	78 (48)	0.011
Dialysis (n, %)	9	6/45 (13.3)	3/26 (11.5)	0.685
Substance use (n, %)	33	30/89 (33.7)	3/11 (27.3)	1.000
Systolic BP (median, IQR)	116	130 (124;142)	128 (115;150)	0.555
Diastolic BP (median, IQR)	116	80 (70;90)	80 (70;90)	0.293
Creatinine (median, IQR)	116	149 (101;317)	146 (109;424)	0.588
eGFR (median, IQR)	116	49.5 (22;86)	38 (12;55)	0.119
uPCR (median, IQR)	116	0.48 (0.30;0.90)	0.70 (0.29;1.20)	0.265
Cholesterol (median, IQR)	116	5.1 (4.0;6.0)	5.0 (3.8;6.3)	0.879
Albumin (median, IQR)	116	27 (22;32)	20 (17;24)	0.053
Hemoglobin (median, IQR)	116	11.2 (9.3; 12.4)	9.1 (7.9;12.4)	0.053
Low C3 (n, %)	82	37 (56.9)	6/16 (37.5)	0.263
Low C4 (n, %)	79	7/63 (11.1)	0/17 (0)	0.336

eGFR – estimated glomerular filtration rate; UPCR – urine protein creatinine ratio; IQR – interquartile range, BP – blood pressure, HIV - human immunodeficiency virus

Table 2: Follow up data at various intervals during the follow up period

Clinical Parameter	HIV Status	Baseline	0 – 6 months	6-12 months	12-24 months
Creatinine	PWH	146 (109;424)	137(87;258)	125 (100;479)	100 (68;132)
	On ART	136 (107.5;452)	137 (92.7;398)	159 (103.7;512)	112 (68;412)
	Not on ART	179 (108.7;400.5)	139 (84;241.2)	108 (87;970.5)	90 (60.75;102.7)
	HIV -	149 (101.2;317.5)	97 (77.2; 137.5)	87 (73;125)	90(74.5;142)
	P value (PWH vs HIV-)	0.588	0.028	0.023	0.796
eGFR	PWH	38 (12;55)	43.5 920.2;85.7)	49 (9;88)	83(53;121)
	On ART	45 (11;55.5)	41.5 (15.2;80.5)	37.5 (8.5;80)	60 (11;114)
	Not on ART	34 (15.2;56.7)	45 (24;93.7)	88 (16;100)	119 (85;153)
	HIV -	49.5 (22;86.2)	86.5 (36.7;117.2)	86 (53;113)	83(39.5;135)
	P value (PWH vs HIV-)	0.119	0.016	0.053	0.813
UPCR	PWH	0.70 (0.29;1.2)	0.63(0.22;1.2)	0.28(0.06;0.61)	0.25(0.06;0.76)
	On ART	1.0 (0.40;1.4)*	0.64 (0.3;1.6)	0.3 (0.04;0.8)	0.5 (0.12)
	Not on ART	0.44 (0.20;0.71)	0.46(0.06;0.9)	0.09 (0.07)	0.22 (0.05)
	HIV -	0.48 (0.30;0.9)	0.075 (0.020;0.45)	0.028 (0.01;0.28)	0.087(0.085;0.33)
	P value (PWH vs HIV-)	0.265	0.002	0.022	0.277

UPCR – urine protein creatinine ratio; PWH – people with HIV, eGFR – estimated glomerular filtration rate, PWH – people with HIV, HIV – Human immunodeficiency virus.
**UPCR – p=0.020*

Figure 1: Creatinine at baseline and at follow-up points

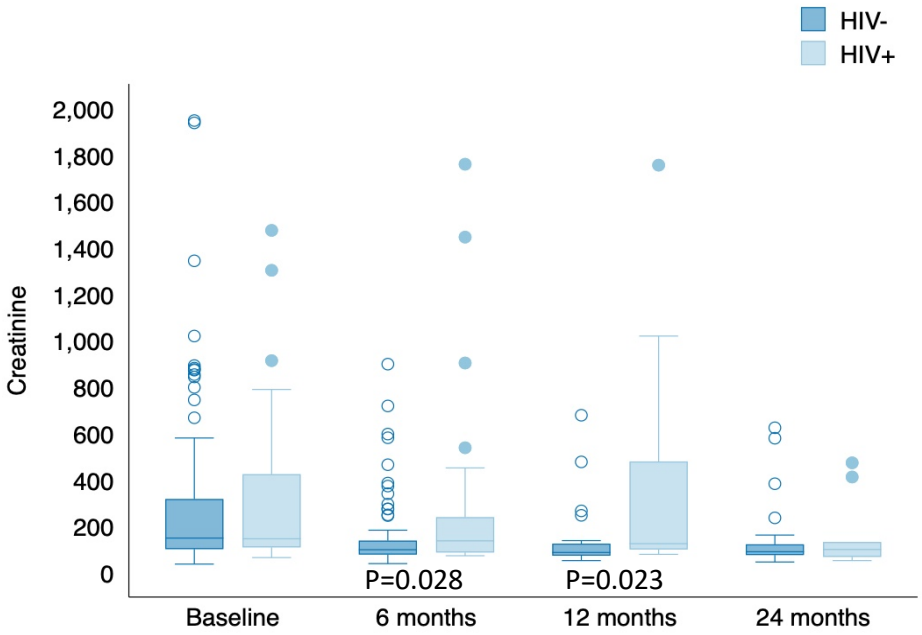
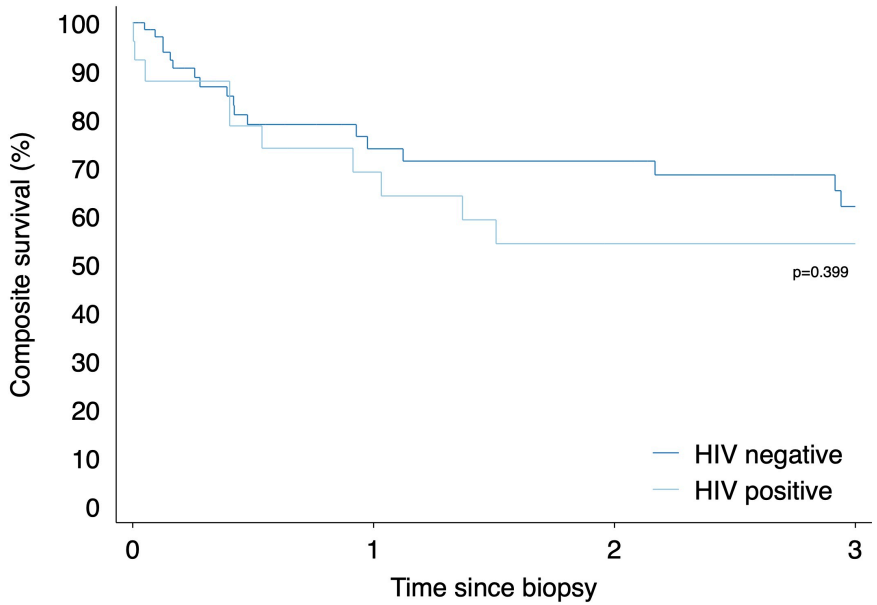


Figure 2: Kaplan Meier comparing composite outcome



Number at risk				
HIVSTATUS = 0	89	29	27	19
HIVSTATUS = 1	26	14	10	10

Table 3: Illustrating studies conducted showing prevalence of MCGN in LMIC & UMIC

Region		Period	Total biopsies conducted / No. of MCGN patients recruited*	Prevalence of MCGN on biopsy (%)	Proportion that reaching the composite outcome#	Predictors of outcomes at biopsy	Median survival (months)
Systematic Review & Meta-analysis							
South & West Africa[1,]		1984-2004	12,093	11.8%	NR	N/A	N/A
Retrospective							
Timisoara[9]	Romania	1995-2004	635	29.4%	N/A	N/A	N/A
Cape Town [2]	South Africa	2000-2009	1753	20.4%	N/A	N/A	N/A
Johannesburg[27]	South Africa	2001-2010	1495	18%	N/A	N/A	N/A
Johannesburg[28]	South Africa	1982-2011	1848	18.1%	N/A	N/A	N/A
Cape Town[25]		2000-2016	79*	100%	30.4%	Advanced kidney failure, proteinuria	N/A
Cape Town[17]	South Africa	1995-2017	2888	32.3%	N/A	N/A	N/A
Bloemfontein[29]		1997-2006	1216	14.9%	N/A	N/A	N/A
Cape Town[4]	South Africa	2000 -2016	70*	100%	68.6%	Creatinine >200 µmol/L, interstitial fibrosis, >50% crescents	N/A
Cape Town[3]	South Africa	2000-2011	79*	100%	34%	Black Race, low eGFR, interstitial fibrosis,	38.7
Mexico City[26]	Mexico	2011-2016	133	3.3%	N/A	N/A	N/A
Sfax[30]	Tunisia**	1996-2011	118	6.2%	43.5%	Kidney failure, hypertension, crescents and interstitial fibrosis	84

** Total number of MCGN patients recruited. MCGN – mesangiocapillary glomerulonephritis. # Composite outcome – doubling of creatinine, or ESKD. NR not reported. N/A not applicable.** All are UMIC except Tunisia which is a middle income country.*

Citation

Sorathia SS, Wearne N, Jones ESW, Davidson B. (2022). An evaluation of clinical, biochemical and outcomes of patients with mesangiocapillary glomerulonephritis in people with HIV compared to HIV negative patients at a tertiary hospital, in Cape Town, South Africa **.** (*MMed thesis*). University of Cape Town & Groote Schuur Hospital, Cape Town, South Africa.

Mini-Citation

Sorathia SS, et al. (2022). An evaluation of clinical, biochemical and outcomes of patients with mesangiocapillary glomerulonephritis in people with HIV compared to HIV negative patients at a tertiary hospital, in Cape Town, South Africa **.** University of Cape Town. Cape Town, South Africa.