Human Immunodeficiency Virus (HIV)-associated nephropathy among antiretroviral naïve adults with persistent proteinuria at the Moi Teaching and Referral Hospital (MTRH)

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Introduction

• The HIV pandemic disproportionately affects sub-Saharan Africa¹

• HIVAN - commonest cause of nephropathy among the HIV-infected²
  – Predilection for the black race³

Introduction ...

• HIVAN –
  • proteinuria
  • renal insufficiency -> end-stage renal disease
• Histology\(^3\) –
  • segmental glomerulosclerosis
  • glomerular collapse
  • tubular microcysts
  • interstitial fibrosis and inflammation

Introduction ...
Introduction ...
Global...

- Worldwide, data on HIVAN is scarce
- Varies between 1 and 10% of the HIV-infected population in different geographic locales\(^4\)

Global ...

- Males at higher risk; advanced HIV and low CD4 count\(^5\)

- However, HIVAN can manifest in earlier stages of HIV, even before seroconversion\(^6\)

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Africa ...

• SA, KZN: 615 patients, 6% proteinuria, HIVAN 83%\textsuperscript{7}

• SA, Soweto: 99 biopsies, 27% HIVAN, 21% HIVICK\textsuperscript{8}

• Ethiopian Israelis: no clinical evidence of HIVAN among a cohort of 176 patients\textsuperscript{9}

\textsuperscript{7} Han TM, Naicker S, Ramdial PK, Assounga AG. A cross-sectional study of HIV-seropositive patients with varying degrees of proteinuria in South Africa. \textit{Kidney Int.} Jun 2006;69(12):2243-2250


Kenya …

• KNH: 56 patients, 7(12.5%) UACR proteinuria >1 g/g – 5/6 on biopsy features of HIVAN

• AMPATH: 373 patients, 6.2% proteinuria

10 Koech E. Clinicopathological manifestations of kidney disease in HIV/AIDS patients with proteinuria at Kenyatta National Hospital. Nairobi, University of Nairobi; 2004

Main Objective

• To determine the prevalence of HIVAN among HIV-infected antiretroviral naïve adults with persistent proteinuria at MTRH
Secondary Objectives

• To determine the prevalence of persistent proteinuria among HIV-infected antiretroviral naïve adults at MTRH.

• To determine other histological variants of renal disease among HIV-infected antiretroviral naïve adults with persistent proteinuria.

• To estimate the prevalence of HIVAN among HIV-infected antiretroviral naïve adults at MTRH.
Methodology

- **Study design:** cross-sectional survey

- **Study site:** the AMPATH clinics at MTRH

- **Study population:**
  - All HIV-infected adults attending AMPATH who were not on antiretroviral treatment

- **Sampling:** convenient sampling
Methodology ...

• Inclusion Criteria
  – HIV-1 infected, antiretroviral naïve
  – Aged 14 years and above
  – Persistent proteinuria
  – Consent given by patient or parent/guardian for those under 18
Methodology ...

• **Exclusion Criteria**
  
  – Previous or current use of antiretroviral drugs
  
  – Evidence of urinary tract infection, concurrent febrile illness, diabetes, hypertension, heart disease or other known causes of chronic kidney disease
  
  – Transient proteinuria
  
  – Contraindications for renal biopsy
  
  – Documented end-stage renal disease (ESRD)
Figure 1. Recruitment Schema

1. HIV infected
   - 14 years
   - ARV naïve

2. ?UTI, fever, DM, HTN, HD, CKD cause
   - NO
   - Urinalysis
   - YES
   - Exclude

   - NO
   - Repeat Urinalysis
     - ≥2 weeks
     - YES
     - Ultrasound
     - Contra indication?
       - YES
       - Exclude
       - NO
       - RENAL BIOPSY
     - NO
     - Exclude
Results

• Data was collected between December 2010 and May 2011
Figure 2: Flow diagram of screening and recruitment

Ineligible (11):
- 2 UTI
- 3 febrile
- 2 high glucose
- 3 hypertension
- 1 heart disease

Total screened: 534

Day 1 negative (438)
- Lost follow-up (32)

Day 1 positive (85)
- Day 14+ negative (21)
- Day 14+ positive (32)
- Lost follow-up (3)
- Withdrew consent (2)
- BIOPSIED (27)

Spot proteinurina

Persistent proteinurina
## Screened

### Table 1: Screened subjects, proteinuria

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screened (eligible)</td>
<td>523</td>
<td></td>
</tr>
<tr>
<td>Spot proteinuria</td>
<td>85</td>
<td>16.3%</td>
</tr>
<tr>
<td>Persistent proteinuria</td>
<td>32</td>
<td>9.8%</td>
</tr>
</tbody>
</table>
## Biopsied: Clinical

### Table 2: Biopsied subjects, clinical findings

<table>
<thead>
<tr>
<th>Clinical Findings</th>
<th>Number (range)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsied</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Age, mean (range) in years</td>
<td>36.6 (23 - 65)</td>
<td></td>
</tr>
<tr>
<td>Sex, Females</td>
<td>17/27</td>
<td>63.0%</td>
</tr>
<tr>
<td>Black race</td>
<td>27/27</td>
<td>100%</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>6/27</td>
<td>22.2%</td>
</tr>
<tr>
<td>Family history of kidney disease</td>
<td>1/27</td>
<td>3.7%</td>
</tr>
<tr>
<td>Abnormal physical exam</td>
<td>4/27</td>
<td>14.8%</td>
</tr>
</tbody>
</table>
Figure 3: Age distribution, grouped

Age groups

Age groups in years

Frequency

15-24
25-34
35-44
45-55
>55
# Biopsied: Labs

## Table 3: Biopsied subjects, Labs

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Number (range)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 cell counts, mean (range) cells/μL</td>
<td>340.7 (3 - 1060)</td>
<td></td>
</tr>
<tr>
<td>&gt;&gt; CD4 cell count &lt; 200 cells/μL</td>
<td>9/27</td>
<td>33.3%</td>
</tr>
<tr>
<td>Creatinine clearance &lt; 60 ml/min</td>
<td>1/26</td>
<td>3.8%</td>
</tr>
<tr>
<td>UACR, mean (range) mg/g</td>
<td>384.2 (5 - 1384)</td>
<td></td>
</tr>
<tr>
<td>&gt;&gt; UACR &gt; 1 g/g</td>
<td>2/26</td>
<td>7.7%</td>
</tr>
</tbody>
</table>
Figure 4: Primary diagnosis

- AIN: 41%
- Non specific nephritis: 33%
- Arteriosclerosis: 7.4%
- FSGS: 3.7%
- Pyelitis: 3.7%
- Papillary sickling: 3.7%
- APIGN: 3.7%
- CIN: 3.7%
Figure 5: AIN with periglomerular inflammation PAS x400
Figure 6: Arteriosclerosis H&E x400
Figure 8: Papillary necrosis and sickling H&E x200
Figure 9: Sickled vasa recta
Trichrome x600
Figure 10: CIN Trichrome x200
Figure 11: AGN H&E x400
Figure 12: AGN and AIN H&E x200
## Inferential Statistics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>$p$</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.757</td>
</tr>
<tr>
<td>Sex</td>
<td>0.885</td>
</tr>
<tr>
<td>Tribe</td>
<td>0.823</td>
</tr>
<tr>
<td>UACR</td>
<td>0.679</td>
</tr>
<tr>
<td>CD4</td>
<td>0.450</td>
</tr>
</tbody>
</table>
Discussion

- Demographics:
  - 63% of study subjects were female
    - national statistics, HIV F>M\textsuperscript{12}
    - AMPATH study, 67.9% F
    - SA study 71% F, France 71.5% M
  - younger age group(36.6y - 35.8y F, 38y M)
    - National peak 30-34y F, 40-44y M
    - AMPATH study 35.0y
    - SA study 32y, France 34y

Discussion ...

• Clinical:
  – 78% reported no symptoms
    • Outpatients on follow-up
    • Excluded fever, htn, DM, HD
    • SA 98%
  – Only 3.7% reported a family history of kidney disease
    • AMPATH study 6.9%
Discussion ...

- Clinical:
  - 85.2% had a normal physical exam
    - Only minor skin and mucosal findings
    - None had features of KD
    - KD rarely presents with overt symptoms
    - SA 90%
Discussion ...

• Labs:
  – the mean CD4 of the subjects was 340 cells/μL
    • AMPATH study 391 cells/μL
    • SA study 264±46 cells/μL
  – 92% of the subjects had normal renal function
    • eGFR 103.8 ± 84
    • AMPATH study 11.5% abnormal
    • SA study mean 77±35 ml/min
Discussion ...

- Labs:
  - spot proteinuria rate of 16.3%
    - AMPATH study 6.2%
    - SA study 6.2%
    - Rwandan women 8.7%
  - UACR on average 384.2 mg/g
    - 92% had 24-hour proteinuria <1 g/g
    - SA 6±6 g/24hr
Discussion ...

- Histology:
  - no HIVAN in this sample
  - KNH- 5/6 suggestive of HIVAN
  - Uganda - 0.3% HIVAN /299
  - SA, KZN - 83%
  - SA, Soweto - 27% HIVAN, 21% HIVICK
  - SA, Wits – 5% HIVAN, 40% HIVICK, 45% other
  - Nigeria – 7/10 features of HIVAN
Discussion ...

• Histology:
  – most common histological diagnosis was acute interstitial nephritis (AIN)
    • SA 10%
    • Johns Hopkins 11%
    • Possibly infections associated with HIV
    • ?herbal meds
Conclusions

• HIVAN among HIV-infected antiretroviral naïve adults with persistent proteinuria at MTRH very low

• Estimated persistent proteinuria 9.8%

• Commonest histological diagnosis is AIN

• probably a very low prevalence of HIVAN among all HIV-infected antiretroviral naïve adults at MTRH
Recommendations

• Routine use of urinary microscopic examination and dipstick analysis

• Biopsy may not be imperative in HIV-infected patients with low levels of proteinuria

• Further studies to ascertain the cause of AIN and non-specific renal inflammation
Study Limitations

• Couldn’t elucidate on the causes of the diagnoses seen at biopsy
• Renal pathology light microscopy only
• Losses to follow up
• Limited number of subjects with heavy proteinuria
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