HIV Case-Based Scenarios in Renal Health
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Case 1: 28 Year Old White Male

HIV dx 4 months ago

Past Medical History: Depression

Medications: Sertraline 50mg daily

Baseline Labs:
- CD4+: 280 cells/µL
- HIV VL: 275,000 copies/mL
- Serum Cr: 1.1 mg/dL
- eGFR: 97 ml/min/1.73m²
- Urinalysis: no proteinuria

HIV Genotype: No resistance

The patient is interested in a single-tablet regimen

Screening & Monitoring
Assess GFR using serum creatinine
- baseline every 6 months (AII)

- BUN, Urinalysis
- baseline every 6 months (AIII)

- For patient on Tenofovir-based regimen
  - Baseline
  - 1 month after initiation of treatment
  - Every 4 months


Case 1: Continued

- The patient was started on Tenofovir/Emtricitabine/Elvitegravir/Cobicistat

- The patient missed his 4 week follow up due to back pain.

- Patient went to Urgent Care for evaluation.
  - Ibuprofen 800mg three times daily
  - Cyclobenzaprine 10mg three times daily

Laboratory Studies:
- Serum Cr: 2.2 mg/dL
- eGFR: 48ml/min/1.73m²
- Urinalysis: 2+ blood

Case 1: Continued

- Returns to HIV provider 7 weeks after starting ART.

- Nauseated, fatigued, on-going, intermittent back pain with radiation to flank.

- Afebrile; Vitals Stable

Is the patient’s current renal function of concern?

A. No, this is an expected side effect of his ART regimen.
B. No, the patient most likely has nephrolithiasis and this is typical presentation.
C. Yes, this is most likely due to nephrotoxicity from his ART.
D. Yes, although exact cause is difficult to discern.
What additional interventions would be appropriate?

A. Order an abdominal CT with contrast  
B. Order non-contrast CT  
C. Hydrate the patient and treat empirically for nephrolithiasis  
D. Check lactic acid for possible lactic acidosis

Non-steroidal Anti-Inflammatory Drugs

Assess for use of NSAIDS in patients with declining renal function.

Use of NSAIDS may exacerbate kidney disease.

Case 1: Continued

- The patient was found to have a large, partially obstructing, renal stone.

Case 1: Continued

The most appropriate next step would be:

A. Temporarily discontinue ART  
B. Stop NSAID and use alternate analgesia  
C. Continue ART with no dose reduction  
D. Switch to an alternate ART regimen
Elvitegravir/Cobicistat/Tenofovir/Emtricitabine

**Dose:**
- 1 tablet daily (separate ≥ 2 hours with antacids)

**With Renal Impairment**
- Do not initiate if CrCl < 70 mL/min
- Discontinue if CrCl < 50 mL/min

**Common Adverse Events (≥ 5%)**
- Nausea, diarrhea, abnormal dreams, headache, and fatigue

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**Case 1: Follow-up**

- The patient had all ART discontinued temporarily.
- Stone passed and repeat labs returned to baseline.
- The patient opted for alternate ART and remains undetectable, with normal renal function.

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**Case 2:**
**51 Year Old Black Male**

**Past Medical History**
- HIV dx 10 years ago
- Diabetes dx 3 years ago
- Tobacco Use

**Medications**
- Metformin 1000mg BID
- Tenofovir/Emtricitabine/Efavirenz
- Aspirin 81mg daily

**Physical Exam**
- BP: 138/80 mmHg
- BMI: 29 kg/m²

**Laboratory Studies:**
- CD4+: 560 cells/µL
- HIV VL: < 20 copies/mL
- HgA1C: 8.4%
- Cr: 1.0 mg/dL
- eGFR: 95 mL/min/1.73m²
- Random Microalbumin: 62mcg/mg

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**Case 2: Continued**

<table>
<thead>
<tr>
<th></th>
<th>June 2012</th>
<th>September 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>132/82 mmHg</td>
<td>130/80 mmHg</td>
</tr>
<tr>
<td>HgA1C</td>
<td>8.1%</td>
<td>8.5%</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>1.1 mg/dL</td>
<td>0.9 mg/dL</td>
</tr>
<tr>
<td>eGFR</td>
<td>86 mL/min/1.73m²</td>
<td>108 mL/min/1.73m²</td>
</tr>
<tr>
<td>Urine Albumin</td>
<td>68 mcg/mg</td>
<td>54 mcg/mg</td>
</tr>
</tbody>
</table>

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**What is an appropriate intervention at this time?**

A. Switch the patient’s Tenofovir/Emtricitabine to Abacavir/Lamivudine
B. Add an additional oral hypoglycemic
C. Have the patient stop smoking
D. Start an ACE/ARB

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**Risk Factors for Kidney Disease in the HIV Positive Population**

![Risk Factors Diagram](image-url)
Management of Co-Morbid Conditions

- Clinicians should treat hyperglycemia, dyslipidemia, anemia, and hypertension in HIV-infected patients with kidney disease according to standard guidelines for non-HIV-infected patients (AI)


Recommendations: Nephropathy

- To reduce risk or slow the progression of nephropathy
  - Optimize glucose control (A)
  - Optimize blood pressure control (A)

ADA. VI. Prevention, Management of Complications. Diabetes Care 2012;35(suppl 1):S34.

Stages of Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min per 1.73 m² body surface area)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage* with normal or increased GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage* with mildly decreased GFR</td>
<td>60–89</td>
</tr>
<tr>
<td>3</td>
<td>Moderately decreased GFR</td>
<td>30–59</td>
</tr>
<tr>
<td>4</td>
<td>Severely decreased GFR</td>
<td>15–29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>

GFR = glomerular filtration rate
*Kidney damage defined as abnormalities on pathologic, urine, blood, or imaging tests.


Definitions of Abnormalities in Albumin Excretion

<table>
<thead>
<tr>
<th>Category</th>
<th>Spot collection (µg/mg creatinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;30</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>30-299</td>
</tr>
<tr>
<td>Macroalbuminuria (clinical)</td>
<td>≥300</td>
</tr>
</tbody>
</table>

ADA. VI. Prevention, Management of Complications. Diabetes Care 2012;35(suppl 1):S34. Table 12.

Use of ACE/ARBs

- HIV-infected, normotensive patients with kidney disease should receive ACE/ARB according to standard guidelines for non-HIV-infected patients (AI)


Recommendations: Nephropathy Treatment

- Patients with micro- or macroalbuminuria
  - Use ACE or ARB (A)
  - If one class is not tolerated, other class should be substituted (E)

- Reduction of protein intake may improve measures of renal function (urine albumin excretion rate, GFR) (B)
  - To 0.8–1.0 g x kg body wt⁻¹ x day⁻¹ in those with diabetes, earlier stages of CKD
  - To 0.8 g x kg body wt⁻¹ x day⁻¹ in later stages of CKD

ADA. VI. Prevention, Management of Complications. Diabetes Care 2012;35(suppl 1):S34.
Recommendations: Nephropathy Treatment

- When ACE, ARBs or diuretics are used, monitor serum creatinine and potassium for increased creatinine and hyperkalemia (E)
- Continued monitoring of urine albumin excretion to assess response to therapy and progression of disease is reasonable (E)
- When eGFR is <60 mL x min/1.73 m², evaluate and manage potential complications of CKD (E)

Management of CKD in Diabetes

<table>
<thead>
<tr>
<th>GFR (mL/min/1.73 m²)</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>Yearly measurement of creatinine, urinary albumin excretion, potassium</td>
</tr>
<tr>
<td>45-60</td>
<td>Referral to nephrology if possibility for nondiabetic kidney disease exists</td>
</tr>
<tr>
<td></td>
<td>Consider dose adjustment of medications</td>
</tr>
<tr>
<td></td>
<td>Monitor eGFR every 6 months</td>
</tr>
<tr>
<td></td>
<td>Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, parathyroid hormone at least yearly</td>
</tr>
<tr>
<td>30-44</td>
<td>Assure vitamin D sufficiency</td>
</tr>
<tr>
<td></td>
<td>Consider bone density testing</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Referral for dietary counseling</td>
</tr>
</tbody>
</table>

Management: Guidelines

- Patients with low-grade proteinuria and slightly decreased GFR, should receive ART if not receiving it and ACE/ARB
- Consider nephrologist when patients are approaching ESRD and require special interventions of hyperparathyroidism, anemia, hemodialysis vascular access, peritoneal dialysis, and/or kidney transplant options. (AII)

Case 2: Follow-up

- Patient added glyburide to metformin
- Therapeutic lifestyle modification
- Smoking cessation
- Losartan 50 mg daily
- Repeat HgA1C: 7.2% after 3 months
- Urine albumin: 35 mcg/mL

Case 3: 51 Year Old White Male

**Past Medical History:**
HIV diagnosed 15 years ago

**Laboratory Data**
- CD4+: 536 cell/µL
- HIV VL: < 20 copies/ml
- Cr: 1.63 mg/dL
- eGFR: 48 mL/min/1.73m²
- UA: negative

**Medications:**
- Tenofovir/Emtricitabine/
- Atazanavir/r

**Physical Exam:**
- BP: 110/70 BMI: 24
Case 3: Laboratory Data

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Cr (mg/dL)</td>
<td>1.63</td>
<td>1.44</td>
<td>1.43</td>
<td>1.31</td>
<td>1.29</td>
</tr>
<tr>
<td>eGFR ml/min/1.73m2</td>
<td>48</td>
<td>59</td>
<td>57</td>
<td>63</td>
<td>65</td>
</tr>
<tr>
<td>Urine Protein</td>
<td>negative</td>
<td>negative</td>
<td>negative</td>
<td>negative</td>
<td>negative</td>
</tr>
</tbody>
</table>

What is the best next step?

A. Continue Tenofovir/Emtricitabine + Atazanavir/ritonavir and repeat labs
B. Switch to Abacavir/Lamivudine+ Atazanavir/ritonavir
C. Switch to Abacavir/Lamivudine+ Atazanavir
D. Add ACE/ARB

Repeat Labs

- Serum Creatinine: 1.39 mg/dL
- eGFR: 59 mL/min/1.73m2
- Urine Albumin: 6 μg/mg

ART & Renal Function

- Several antiretrovirals have been associated with renal effects including:
  - Tenofovir
  - Atazanavir
  - Lopinavir
  - Indinavir


ART exposure and rates of progression to a confirmed eGFR of ≤70 mL/min from ≥90 mL/min

Abacavir vs Tenofovir on Renal Function

Recovery of Renal Function Following Tenofovir Discontinuation

- N=710 on Tenofovir
- N=29 (4%) stopped d/t renal dysfunction
- 96% White Median Age: 56 years old 79% on PI 81% < 50 copies/ml Median Tenofovir exposure: 30 months (14-42)


Factors Associated with Recovery

<table>
<thead>
<tr>
<th></th>
<th>&gt;20 mL min 1.173^2</th>
<th>&lt;20 mL min 1.173^2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid Decline</td>
<td>1.9 (0.8-2.7)</td>
<td>0.7 (0.2-1.2)</td>
<td>0.009</td>
</tr>
<tr>
<td>PI therapy</td>
<td>100%</td>
<td>54%</td>
<td>0.02</td>
</tr>
<tr>
<td>Duration on Tenofovir</td>
<td>21 months (11-41)</td>
<td>40 months (21-51)</td>
<td>0.08</td>
</tr>
</tbody>
</table>


Screening & Diagnostic Evaluation

- For patients with DM and no proteinuria
  - assess for microalbuminuria annually (AI)
- For Patients with borderline GFR (AIi)
  - Urinalysis
  - Quantification of urinary protein excretion
  - Renal sonogram
  - Careful Physical Examination


Case 3: Follow-up

- HLA-B*5701: negative
- Opted to switch to Abacavir/Lamivudine + Raltegravir
- Follow-up ongoing.

Case 4: 43 Year Old Puerto Rican Male

**Past Medical History**
- HIV
- Hypertension

**Medications**
- Abacavir/Lamivudine with Lopinavir/ritonavir
- Telmisartan

**Laboratory Data**
- CD4+: 280 cells/µL
- HIV VL: < 20 copies/mL
- Serum Cr: 2.5 mg/dL
eGFR: 28 mL/min/1.73m2

**Physical Exam**
- 150/90 mmHg
- BMI: 23 kg/m2
What would be the most appropriate steps to take now?

A. Stop ART
B. Obtain renal sonogram
C. Consult Nephrologist
D. Dose reduce Abacavir/Lamivudine to every other day

Dosing in Renal Impairment

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir + Lamivudine Fixed Dose</td>
<td>Not Recommended Ccr &lt; 30 mL/min</td>
</tr>
<tr>
<td>Abacavir</td>
<td>No Dose Adjustment</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Ccr: 30-49 mL/min 150mg daily</td>
</tr>
<tr>
<td></td>
<td>Ccr: 15-19 mL/min 150mg x 1, then 100mg daily</td>
</tr>
<tr>
<td></td>
<td>Ccr: 5.1-14 mL/min 50mg x 1, then 25mg daily</td>
</tr>
<tr>
<td></td>
<td>Ccr &lt; 5 mL/min 25mg daily</td>
</tr>
<tr>
<td>Tenofovir + Entecavir</td>
<td>Fixed Dose</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Ccr: 30-49 mL/min 1 tab every 48 hours</td>
</tr>
<tr>
<td></td>
<td>Ccr: 10-19 mL/min Adjust dose based on each drug</td>
</tr>
<tr>
<td>Entecavir</td>
<td>Ccr: 5-9 mL/min 300mg every 48 hours</td>
</tr>
<tr>
<td></td>
<td>Ccr: 3-5 mL/min 300mg every 72 hours</td>
</tr>
<tr>
<td></td>
<td>Ccr &lt; 3 mL/min 200mg every 96 hours</td>
</tr>
</tbody>
</table>

D:A:D Study: Predictors of Advanced Chronic Kidney Disease in HIV

- D:A:D patients with ≥3 estimated GFR measurements (2007-2011; n=35,192)
  - Median follow-up: 6.2 years
- Advanced CKD/ESRD
  - Prevalence: 0.4%
  - Incidence rate: 0.67/1000 pt-yrs
- Switching ART increased as eGFR declined
- Neither current or recent use of ART was associated with advanced CKD/ESRD
  - No association with individual ARVs

Refer for Renal Consult (AII)

- Diagnosis is uncertain
- Kidney disease is progressing rapidly
- Stage 4 to 5 chronic kidney disease (CKD)
- Kidney biopsy is being considered

Referral Considerations

- Refer patients to nephrologist when considering management with steroids, immunosuppression, hemodialysis or transplant. (AIII)
- A diagnosis of membroproliferative glomerulonephritis is made in HIV/HCV co-infected patients (AII)

Case 5: 58 Year Old African American Female

Past Medical History:
- 12-year history of well-controlled type 2 diabetes mellitus.
- HIV/HCV Co-infection
- Metformin 850mg Twice Daily; ASA 81mg Once Daily

Laboratory Studies: (baseline)
- HIV RNA: 220,172 copies/mL
- CD4+ count: 290 cells/μL
- Serum Cr: 1.1 mg/dL
- eGFR: 52 mL/min/1.73m2
- Urinalysis: 1+ protein
- HCV Genotype 1a, HCV RNA: 7.0 x 10^7

Physical Examination
- unremarkable
Case 5: Continued (6 months)

- CD4+: 270 cells/μL
- HIV RNA: 275,000 copies/ml
- Serum Cr: 1.8 mg/dL
- eGFR: 49 mL/min/1.73m²
- Hemoglobin A1c: 7.8%
- Urinalysis: 2+ protein
- BP: is consistently 150/90 mm Hg or higher
- The patient is also motivated to treat her HCV

Stages of Chronic Kidney Disease

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<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73m²)</th>
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<tbody>
<tr>
<td>1</td>
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<tr>
<td>2</td>
<td>Kidney damage with mildly decreased GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderately decreased GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severely decreased GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney Failure</td>
<td>&lt; 15 (or dialysis)</td>
</tr>
</tbody>
</table>

Risk Factors for CKD

- HCV co-infection
- Family history
- Increased viral load (> 4,000 copies/ml)
- Lower CD4 count (< 350 cells/μL)
- Older age
- Tenofovir & Protease Inhibitor/ritonavir

CKD Among HIV Patients in Care in the US

Factors associated with CKD
- Older age
  - 40-59 years (HR: 2.8)
  - ≥60 years (HR: 7.8)
- Female gender (HR: 1.4)
- Longer duration of HIV (HR: 1.4)
- AIDS dx (HR: 2.1)
- CD4 <350 cells/μL (HR: 1.6)

Stage 3 or greater CKD: 7.6%

Which ART regimen would be best for this patient?

1. Tenofovir/Emtricitabine + Atazanavir/r
2. Abacavir/Lamivudine + Darunavir/r
3. Tenofovir/Emtricitabine + Efavirenz
4. Tenofovir/Emtricitabine + Raltegravir
### Use of HCV DAAs in HIV/HCV Co-Infection
**selected agents**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Telaprevir</th>
<th>Boceprevir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir</td>
<td>Monitor for Toxicity</td>
<td>Monitor of Toxicity</td>
</tr>
<tr>
<td>Atazanavir/r</td>
<td>No Dose Adjustment</td>
<td>Not Recommended</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Increase TVR 1125mg</td>
<td>Not Recommended</td>
</tr>
<tr>
<td>Darunavir/r</td>
<td>Not Recommended</td>
<td>Not Recommended</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>No Dose Adjustment</td>
<td>No Dose Adjustment</td>
</tr>
</tbody>
</table>

### Case 5: Continued

- The patient started a statin, an ACE inhibitor, and antiretroviral therapy regimen.

- Six months later, blood pressure is consistently below 130/80 mm Hg, low density lipoprotein (LDL) is 65 mg/dL, and her hemoglobin A1c is 5.8%. Her plasma HIV RNA level is undetectable and her CD4+ count has risen to 380 cells/μL.

- She began treatment with PegIFN + Ribavirin + Telaprevir for HCV.

### Management: Key Points
- Identify and treat factors associated with progression of CKD
  - Hypertension
  - Proteinuria
  - Glucose control

### Implications for Clinicians
- Assist diabetic patients to maintain glycemic control.
- Assist hypertensive patients to maintain normal blood pressure.
- Encourage & assist with tobacco cessation.
- Identify and minimize nephrototoxic agents. Monitor and dose adjust fixed-dose regimens.
- Nutritional counseling.