HIV Associated Nephropathy (HIVAN)

HIV-associated nephropathy (HIVAN) is a **major renal complication in patients with HIV**, particularly those who are **not on antiretroviral therapy (ART)**. It is characterized by a **rapidly progressive kidney disease** and is more common among individuals with **advanced HIV** or those **noncompliant with ART**.

Epidemiology

- HIVAN occurs **almost exclusively in individuals of African descent**, accounting for **~90% of HIVAN-related end-stage renal disease (ESRD)** cases.
- Risk is significantly **reduced with early and sustained ART**.
- A strong association exists between HIVAN and **APOL1 gene polymorphisms**, particularly among individuals of West African ancestry.

Pathogenesis

- **Direct infection** of renal epithelial cells (podocytes and tubular cells) by HIV plays a critical role.
- **Systemic immune dysregulation** and **genetic susceptibility** (especially APOL1 variants) contribute to disease progression.
- HIVAN is histologically identified as a **collapsing form of focal segmental glomerulosclerosis (FSGS)** with prominent **tubulointerstitial inflammation and microcystic dilation**.

Clinical Presentation

Patients with HIVAN often present with features of **nephrotic syndrome** and rapidly declining renal function.

Key Features:

Clinical Feature	Description
Proteinuria	Nephrotic-range (>3.5 g/day)
Renal Function	Elevated serum creatinine (azotemia)
Serum Albumin	Hypoalbuminemia
Lipids	Hyperlipidemia
Urinalysis	Microhematuria, leukocytes, hyaline casts, oval fat bodies
Blood Pressure	Typically **normal or low**, not hypertensive
Kidney Ultrasound	Normal to enlarged kidneys, **high echogenicity**
CD4 Count	Often <200 cells/?L
Electrolytes	Hyponatremia, hyperkalemia (due to nephrotic state or SIADH)
Complement Levels	Usually normal

Differential Diagnosis

The spectrum of HIV-related kidney disease includes:

1. Glomerular-Dominant Nephropathies

- **HIVAN** (collapsing FSGS)
- **HIV Immune Complex Kidney Disease (HIVICK)**

2. Tubulointerstitial-Dominant Nephropathies

- ART-induced acute tubular injury
- Drug-induced interstitial nephritis (non-ART)
- Opportunistic infections (bacterial, viral, fungal)
- Tubulointerstitial injury related to HIVAN

3. Vascular-Dominant Nephropathies

- **Thrombotic microangiopathy**
- **HIV-associated atherosclerosis**

4. Other Nephropathies in HIV

- Diabetic nephropathy
- Age-related nephrosclerosis

Diagnosis

- **Renal biopsy** is the gold standard: shows collapsing glomerulopathy, microcystic tubular dilation, and interstitial inflammation.
- **HIV viral load** , **CD4 count** , and **APOL1 genotyping** may support diagnosis and risk stratification.
- **Imaging** (renal ultrasound): typically reveals **large, echogenic kidneys** .

Management

1. Antiretroviral Therapy (ART)

- **Cornerstone of treatment** : slows progression, may reverse HIVAN in early stages.
- Early initiation of ART improves renal and overall survival outcomes.

2. Adjunctive Therapies

Therapy	Role
ACE inhibitors/ARBs	Reduce proteinuria and slow CKD progression (e.g., captopril, losartan)

Therapy	Role
Corticosteroids	Considered in progressive disease unresponsive to ART; used cautiously due to side effects
Blood pressure control	Target <130/80 mmHg if proteinuric

?? Note: Long-term ART is associated with other nephrotoxic risks such as **arterionephrosclerosis** , **diabetic nephropathy** , and **non-collapsing FSGS** .

Prognosis

- Without treatment, HIVAN progresses rapidly to **end-stage renal disease (ESRD)** .
- **With ART** , kidney function can be stabilized or even improved, especially if treatment begins early.
- ESRD secondary to HIVAN is a leading cause of dialysis in HIV-positive patients in some regions.

Key Takeaways for Exams and Clinical Practice

- HIVAN is **more common in African descent** due to APOL1 gene variants.
- Presents with **nephrotic-range proteinuria** , **normal blood pressure** , and **echogenic enlarged kidneys** .
- **Initiate ART immediately** upon diagnosis.
- Add **ACE inhibitors or ARBs** to reduce proteinuria.
- Consider **renal biopsy** for definitive diagnosis if clinical suspicion is high.
- **Monitor renal function and proteinuria** closely in HIV-positive patients, especially if ART adherence is poor.