HIV ile İlişkili Böbrek Hastalıkları

Doç. Dr. Zeki SOYPAÇACI

İKÇÜ Atatürk Eğt. Arş. Hastanesi

Nefroloji B.D

GİRİŞ

- HIV enfeksiyonu, böbrek hastalığı için bilinen bir risk faktörüdür.
- Bir dizi farklı mekanizma yoluyla hem akut, hem de kronik böbrek hastalığına neden olabilir.
- Böbrek hastalığı, HIV ile enfekte hastalarda en önemli ölüm nedenlerinden biri.
- ABH ve KBH olanlarda ölüm oranı 6 kat artıyor.

Review > Curr Opin Nephrol Hypertens. 2018 May;27(3):144-152.
doi: 10.1097/MNH.0000000000000400.

Changing concepts of HIV infection and renal disease

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Affiliations + expand

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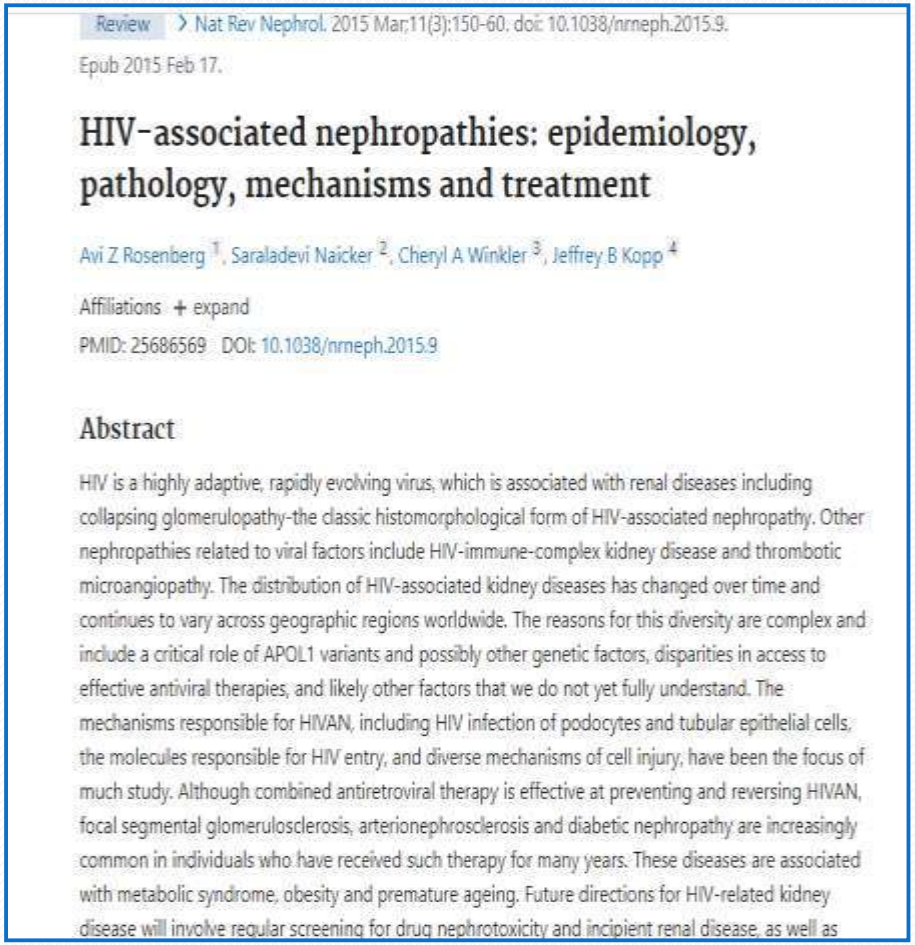
Abstract

Purpose of review: Human immunodeficiency virus (HIV)-associated nephropathy (HIVAN) was identified as the major renal manifestation of HIV infection early in the HIV epidemic. However, HIV infection now is associated with a different spectrum of renal lesions leading to chronic kidney disease. This review examines the changes in kidney injury occurring in the current HIV era and the factors involved in this transformation of disease expression.

Recent findings: The incidence of HIVAN and opportunistic infections in HIV-infected individuals has declined in concert with the use of effective combination antiretroviral agents. Chronic kidney disease has become more prevalent as patients infected with HIV are living longer and developing non-HIV-associated diseases such as hypertension and diabetes. Additionally, noncollapsing focal and segmental glomerulosclerosis, co-infection with hepatitis C, HIV-associated immune complex kidney disease, HIV-related accelerated aging, and antiretroviral therapies contribute to progressive loss of renal function.

Summary: HIV infection is now associated with a variety of renal lesions causing chronic kidney disease, not all of which are virally induced. It is important to determine the cause of renal function

- cART ile, klasik belirtileri olmadan, daha uzun yaşıyorlar.
- Diyabet veya HT gibi komorbiditelerde artış.
- Belirli HIV tedavilerinin nefrotoksisitesi ile ilişkili bozukluklar daha yaygın.



Review > Nat Rev Nephrol. 2015 Mar;11(3):150-60. doi: 10.1038/nrneph.2015.9. Epub 2015 Feb 17.

HIV-associated nephropathies: epidemiology, pathology, mechanisms and treatment

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Affiliations + expand

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Abstract

HIV is a highly adaptive, rapidly evolving virus, which is associated with renal diseases including collapsing glomerulopathy-the classic histomorphological form of HIV-associated nephropathy. Other nephropathies related to viral factors include HIV-immune-complex kidney disease and thrombotic microangiopathy. The distribution of HIV-associated kidney diseases has changed over time and continues to vary across geographic regions worldwide. The reasons for this diversity are complex and include a critical role of APOL1 variants and possibly other genetic factors, disparities in access to effective antiviral therapies, and likely other factors that we do not yet fully understand. The mechanisms responsible for HIVAN, including HIV infection of podocytes and tubular epithelial cells, the molecules responsible for HIV entry, and diverse mechanisms of cell injury, have been the focus of much study. Although combined antiretroviral therapy is effective at preventing and reversing HIVAN, focal segmental glomerulosclerosis, arterionephrosclerosis and diabetic nephropathy are increasingly common in individuals who have received such therapy for many years. These diseases are associated with metabolic syndrome, obesity and premature ageing. Future directions for HIV-related kidney disease will involve regular screening for drug nephrotoxicity and incipient renal disease, as well as

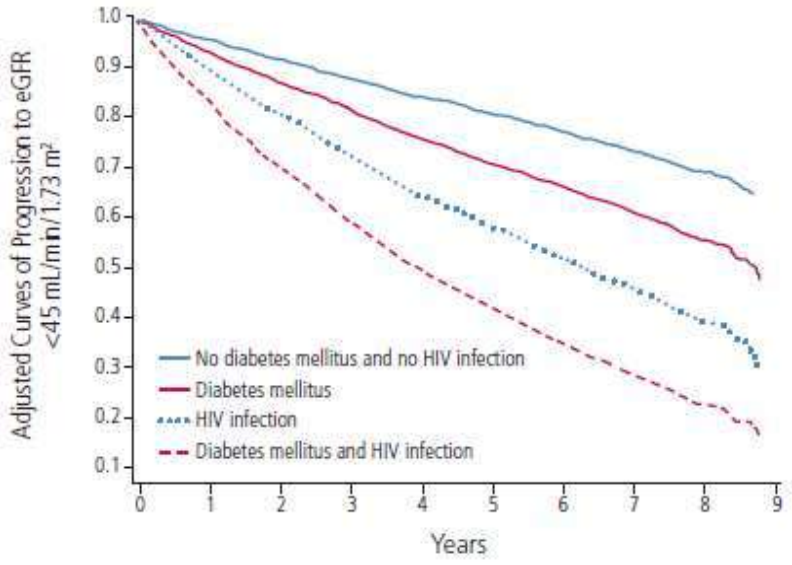

Figure 2. Additive effect of HIV infection and diabetes on progression of chronic kidney disease. Adapted from Medapalli et al.[9]

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Comorbid diabetes and the risk of progressive chronic kidney disease in HIV-infected adults: Data from the Veterans Aging Cohort Study

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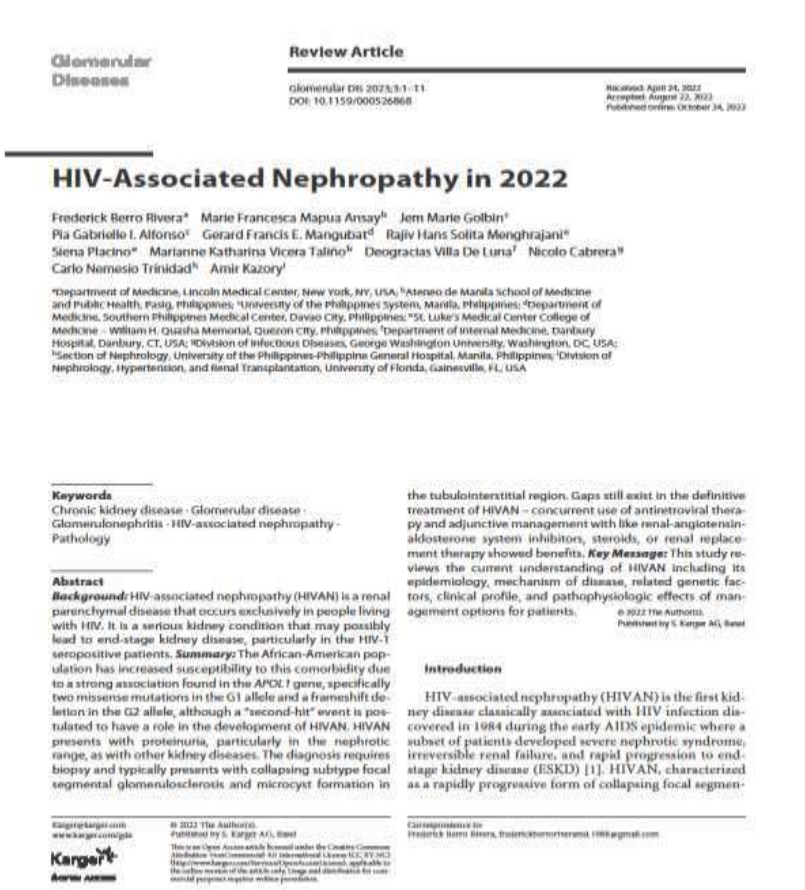
Abstract

Introduction—Approximately 15% of HIV-infected individuals have comorbid diabetes. Studies suggest that HIV and diabetes have an additive effect on chronic kidney (CKD) progression; however, this observation may be confounded by differences in traditional CKD risk factors.

Methods—We studied a national cohort of HIV-infected and matched HIV-uninfected individuals who received care through the Veterans Healthcare Administration. Subjects were divided into four groups based on baseline HIV and diabetes status, and the rate of progression to an estimated glomerular filtration rate (eGFR) < 45ml/min/1.73m^2 was compared using Cox-proportional hazards modeling to adjust for CKD risk factors.

- Hücrelere doğrudan zarar vermesi veya konakçı bağışıklık sisteminin sistemik ve lokal tepkilerinin bir sonucu.
- HIV böbrek epitel hücrelerini enfekte edip çoğalabilir,
- Klasik olarak kollapsing fokal segmental glomerülosklerozla giden ve doğrudan HIV ile ilişkili nefropati (HIVAN), HIV-immün kompleks böbrek hastalığı ve trombotik mikroanjiyopati olarak da ortaya çıkabilir.



Glomerular Diseases

Review Article

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HIV-Associated Nephropathy in 2022

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Keywords
Chronic kidney disease · Glomerular disease · Glomerulonephritis · HIV-associated nephropathy · Pathology

Abstract
Background: HIV-associated nephropathy (HIVAN) is a renal parenchymal disease that occurs exclusively in people living with HIV. It is a serious kidney condition that may possibly lead to end-stage kidney disease, particularly in the HIV-1 seropositive patients. ***Summary:*** The African-American population has increased susceptibility to this comorbidity due to a strong association found in the *APOL1* gene, specifically two missense mutations in the G1 allele and a frameshift deletion in the G2 allele, although a "second-hit" event is postulated to have a role in the development of HIVAN. HIVAN presents with proteinuria, particularly in the nephrotic range, as with other kidney diseases. The diagnosis requires biopsy and typically presents with collapsing subtype focal segmental glomerulosclerosis and microcyst formation in the tubulointerstitial region. Gaps still exist in the definitive treatment of HIVAN – concurrent use of antiretroviral therapy and adjunctive management with like renal-angiotensin-aldosterone system inhibitors, steroids, or renal replacement therapy showed benefits. ***Key Message:*** This study reviews the current understanding of HIVAN including its epidemiology, mechanism of disease, related genetic factors, clinical profile, and pathophysiologic effects of management options for patients.

Introduction

HIV-associated nephropathy (HIVAN) is the first kidney disease classically associated with HIV infection discovered in 1984 during the early AIDS epidemic where a subset of patients developed severe nephrotic syndrome, irreversible renal failure, and rapid progression to end-stage kidney disease (ESKD) [1]. HIVAN, characterized as a rapidly progressive form of collapsing focal segmen-

ŞEKİL 1 HIV DE BÖBREK HASARI MEKANİZMALARI

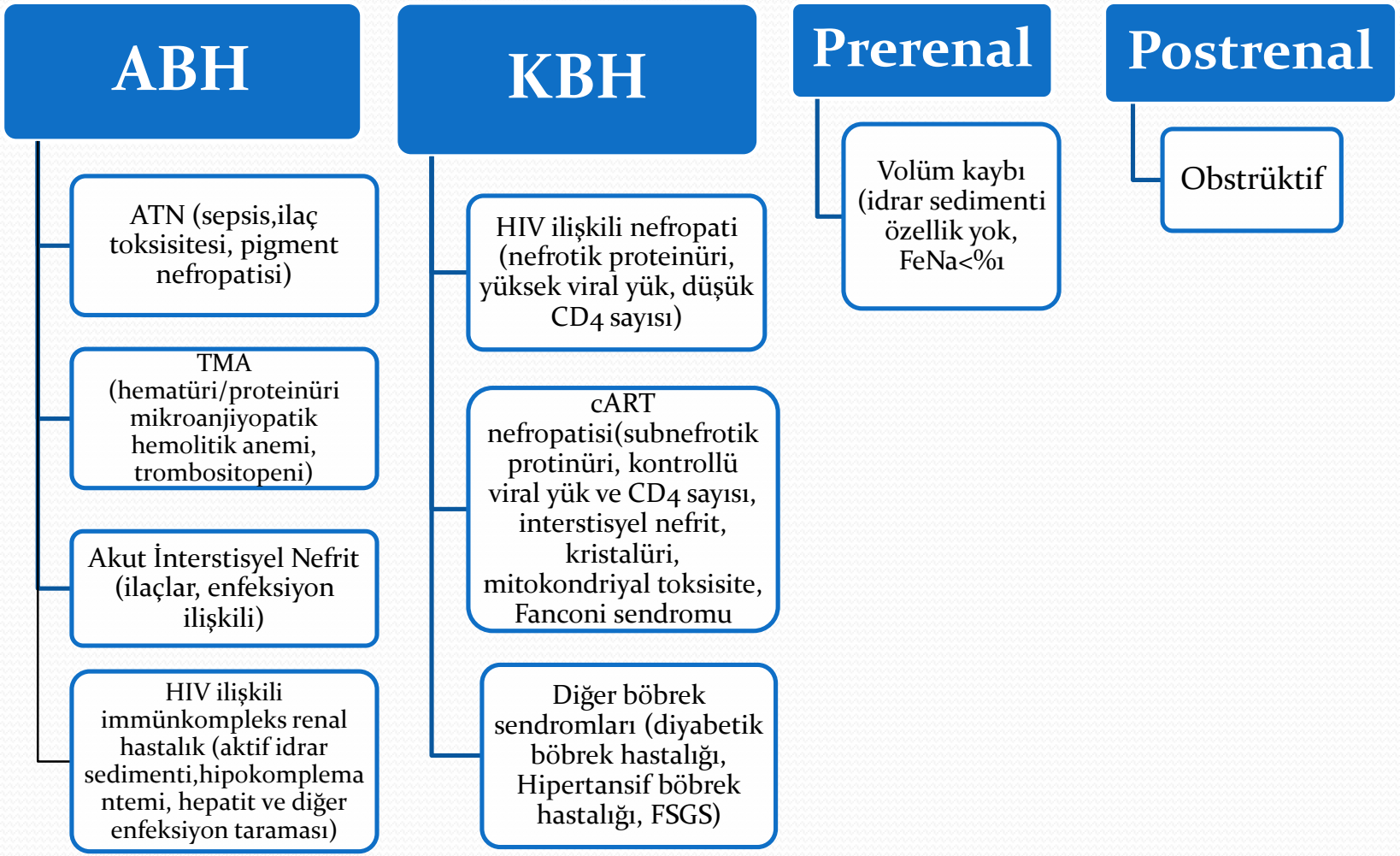


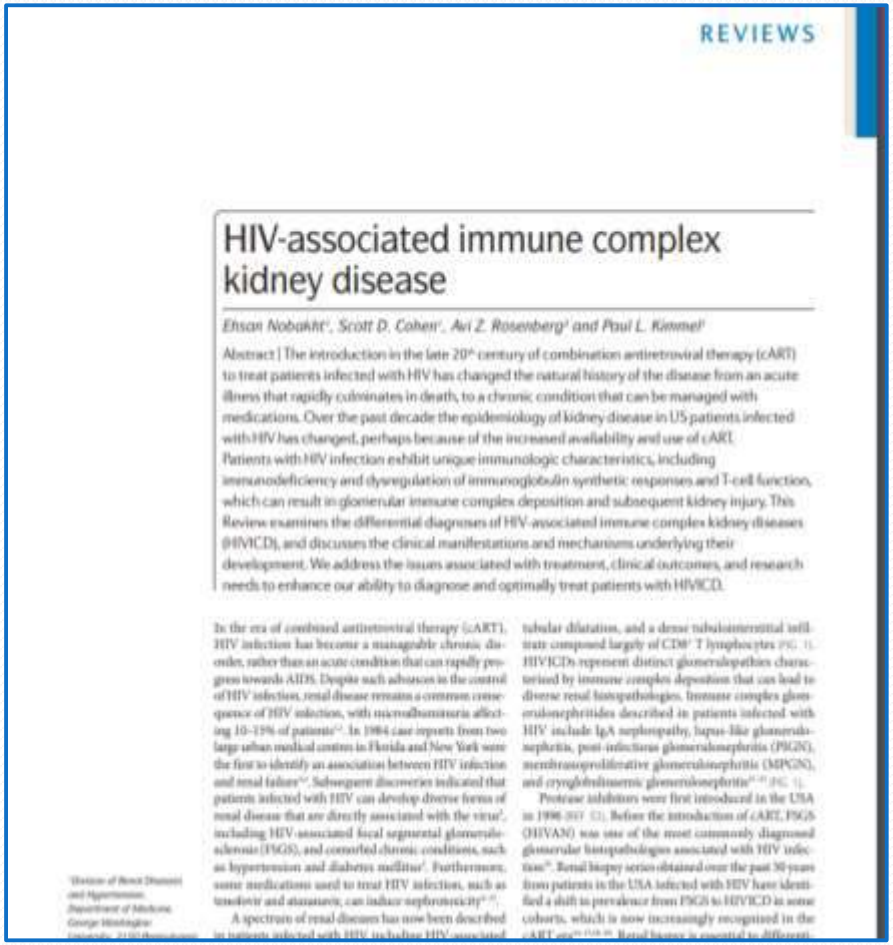
Table 1. Classification of HIV-related kidney disease and description of their treatment. Adapted from Swanepoel CR et al. "Kidney disease in the setting of HIV infection: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference" Kidney Int. 2018;93(3):545–559 (see reference [25]).

HIV-Related Kidney Disease	Directly Related to HIV Infection	First-Line Treatment *	Second-Line Treatment	Adjunctive Therapies
I. Glomerular-dominant				
a. Podocytopaties (e.g. HIVAN, FSGS)	X	ART	Steroid, Cys A	ACEi or ARB
b. Immune complex-mediated glomerular disease (e.g. MPGN, IgAN)		ART	Steroid	ACEi or ARB
II. Tubulointerstitial-dominant				
a. Tubulointerstitial injury in the setting of classic HIVAN	X	ART	Steroid	
b. Acute tubular injury or acute tubular necrosis (associated with ART)		Stop offending drug		
c. Drug-induced tubulointerstitial nephritis (other than ART)		Stop offending drug	Steroid	
d. Direct renal parenchymal infection by pathogens		Treat the underling infection		
e. Imuunologic dysfunction-related tubulointerstitial inflammation				
I. DILS II. IRIS		I. ART II. Treat the opportunistic infection/ART	I. Steroid II. Steroid	II. NSAID (risk of nephrotoxicity), thalidomide, hydroxychloroquine, anti-TNFalpha
f. Other tubulointerstitial inflammation in the setting of HIV		Treat underlining disease		
III. Vascular-dominant				
a. Thrombotic microangiopathy in the setting of HIV				
I. TTP II. aHUS	I. X II. X	I. ART, plasmapheresis II. ART, Eculizumab	I. Rituximab, bortezomib, Cys A	I. Sterodi/antiplatelet agents
b. Arteriosclerosis	X §	ART/reduce risk factors for atherosclerosis		
IV. Other, in the setting of HIV				
a. Diabetic nephrolopathy		Treat diabetes	ACEi or ARB	
b. Age-related nephrosclerosis		ART	ART/reduce risk factors for atherosclerosis	

Anti TNF-α, anti-tumor necrosis factor-α; ART, antiretroviral therapy; Cys A, Cyclosporine A; DILS, diffuse infiltrative lymphocytosis syndrome, FSGS, focal segmental glomerulosclerosis; HIVAN, HIV-associated nephropathy; IgAN, IgA nephropathy; IRIS, immune reconstitution inflammatory syndrome; MPGN, membranoproliferative glomerulonephritis; § Arteriosclerosis is due partly to cytopathic effect of HIV and to the traditional and non-traditional risk factors for vasculopathy; * According to current guidelines, ART is administered in all patients with the diagnosis of HIV infection regardless CD4 T-cell count. ART is indicated as the first-line approach when it is effective in the treatment of HIV-related kidney diseases.

HIV İlişkili Nefropati

- HAART'tan önce HIVAN, böbrek hastalığının en yaygın nedeniydi, %3,5-10 arası değişiyordu.
- Hızla son dönem böbrek hastalığına ilerleyecektir.
- Nefrotik düzeyde proteinüri, azalmış böbrek fonksiyonu.



REVIEWS

HIV-associated immune complex kidney disease

Ehsan Nobakht, Scott D. Cohen, Avi Z. Rosenberg and Paul L. Kimmel

Abstract | The introduction in the late 20th century of combination antiretroviral therapy (cART) to treat patients infected with HIV has changed the natural history of the disease from an acute illness that rapidly culminates in death, to a chronic condition that can be managed with medications. Over the past decade the epidemiology of kidney disease in US patients infected with HIV has changed, perhaps because of the increased availability and use of cART. Patients with HIV infection exhibit unique immunologic characteristics, including immunodeficiency and dysregulation of immunoglobulin synthetic responses and T-cell function, which can result in glomerular immune complex deposition and subsequent kidney injury. This Review examines the differential diagnoses of HIV-associated immune complex kidney diseases (HIVICD), and discusses the clinical manifestations and mechanisms underlying their development. We address the issues associated with treatment, clinical outcomes, and research needs to enhance our ability to diagnose and optimally treat patients with HIVICD.

Tablo 1. Böbrek Biyopsilerinde HIVAN Prevalansı

Study	Region	Year	No. of cases	Prevalence of HIVAN
D'agati et al. (63)	USA	1997	112	64.7%
Szczech et al. (28)	USA	2002	89	47.2%
Berliner et al. (64)	USA	2008	152	35%
Gerntholtz et al. (65)	S Africa	2006	104	27%
Han et al. (66)	S Africa	2006	30	83%
Nochy et al. (67)	France	1993	60	43%
Gutiérrez et al. (68)	Spain	2007	27	14.8%
Williams et al. (69)	London	1998	17	40%
Casanova et al. (66)	Italy	1995	26	None
Cavalcante et al. (29)	Brazil	2007	6	50%
Praditpornsilpa et al. (17)	Thailand	1999	26	None
Present Study	India		10	20%

HIVAN: Human immunodeficiency virus associated nephropathy

Original Article

Histological spectrum of renal disease in HIV/AIDS patients with significant proteinuria: An Indian perspective

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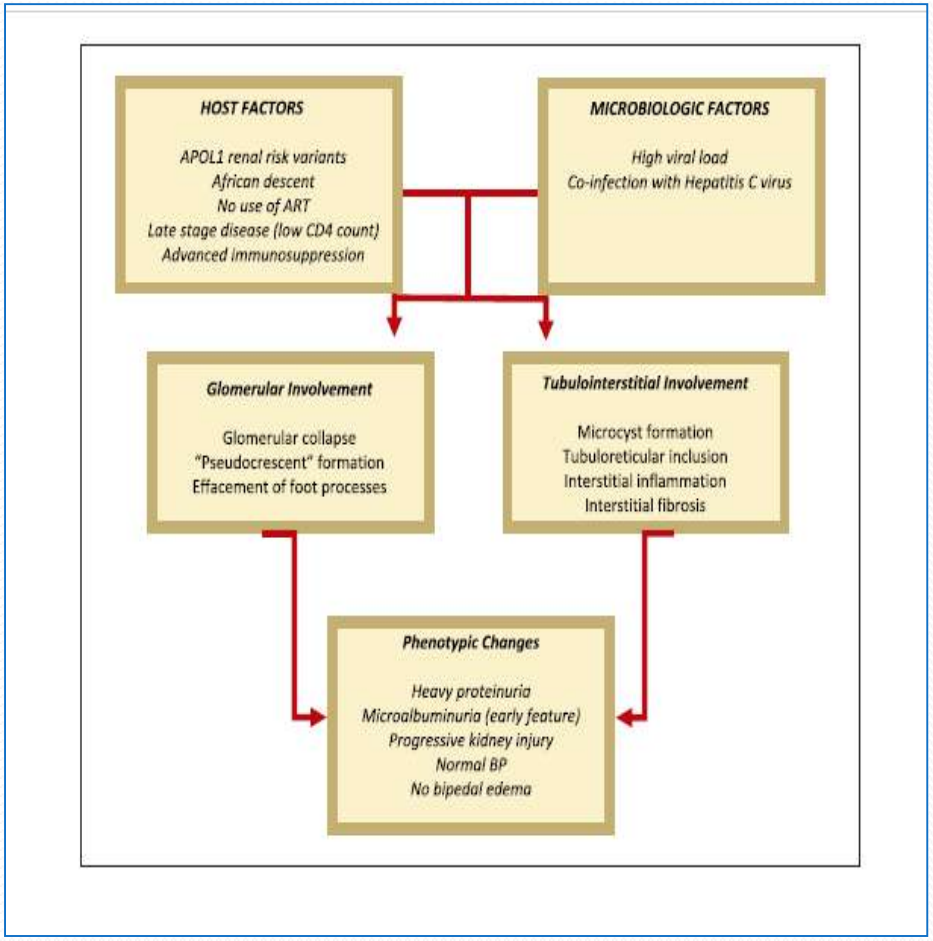
ABSTRACT

Background: Chronic kidney disease (CKD) has become epidemic in HIV/AIDS patients across Western and Eastern countries. HIV-associated nephropathy (HIVAN) has been consistently reported in studies from North America, Europe and African countries. However, studies from Asian countries are very sparse and differ strikingly in histological spectrum of renal disease, particularly in presence of HIVAN. **Objectives:** The study was carried out to in a teaching hospital from India to delineate the histological spectrum of renal disease and detect presence HIVAN in those with significant proteinuria (≥1gm/day). **Patients and Methods:** Urine analysis was done in 510 consecutive hospitalised HIV/AIDS patients after screening 640 such patients with age >18years. Patients with dipstick proteinuria ≥1+ were subjected to 24-hour urinary protein estimation. Renal biopsy was done in 10 patients with proteinuria ≥1gm/day. **Results:** Dipstick proteinuria ≥1+ was present in 29% patients. In patients undergoing kidney biopsy, the most frequent glomerular lesion was mesangial proliferative glomerulonephritis (30%) followed by HIVAN (20%). Tubulo-interstitial lesions were seen in 60% of biopsies. Pooled analysis of all the available kidney biopsy series from India revealed prevalence of HIVAN to be 16.5%. **Conclusion:** Contrary to the popular belief, HIVAN appears to be a common entity in this part of world too. High degree of clinical suspicion is required as diagnosis of HIVAN caries higher morbidity and mortality. Moreover, an early diagnosis and timely management can improve prognosis in such patients.

Keywords: Glomerular lesion, histopathology, HIVAN, kidney biopsy, renal biopsy

HIVAN Patofizyolojisi

- ABD'de öncelikle Afrika kökenli Amerikalılarda, özellikle CD4 sayısı belirgin azalmış ve viral yükü yüksek olanlarda ortaya çıkıyor.
- Konakçı faktörler (özellikle genetik), renal viral protein ekspresyonu, çevresel ve sosyoekonomik faktörler arasındaki karmaşık etkileşimlerle ortaya çıkmaktadır.



HIVAN Patoloji

- Tipik lezyon kollapsing FSGS.
- Glomerüler epitel hücrelerin dramatik hipertrofisi ve hiperplazisi ile birlikte, üriner boşluğu dolduran kollapsa uğramış glomerul.
- IgM, C3 ve C1q kollapsa uğramış segmentlerde ve mesanjiyal alanlarda tespit edilir.
- Tübüler mikrokistik dilatasyon,interstisyel inflamasyon, fibrozis ve tübüloretiküler inklüzyon cisimcikleri yer alır.

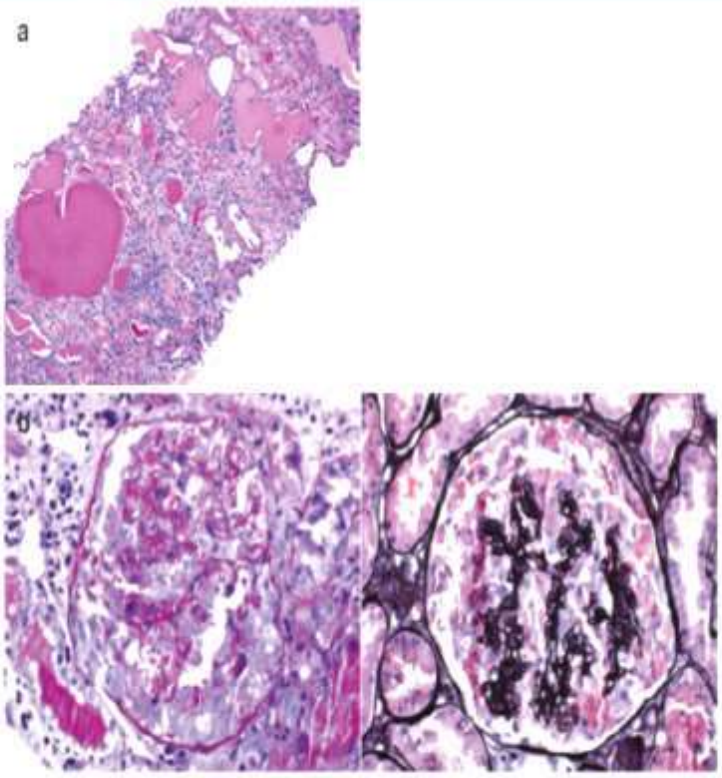


Fig. 8.2 Histology of HIVAN. (a) Light microscopy revealing microcystic tubular dilatation. (b) Light microscopy and silver stain showing collapsing lesion. (Courtesy of Alejandro Best MD, Arkana Laboratories)

HIVAN Kliniği

- Klasik HIVAN, APOL1 risk aleli, Güney Afrikalılar ve düşük CD4+ T hücre sayısı ile güçlü bir şekilde ilişkilidir.
- Akut HIV enfeksiyonu sırasında ortaya çıkar.
- Nefrotik proteinüri ve SDBY'ye hızlı ilerleme.
- Böbrekler US'de sıklıkla ekojenik ve büyümüş.

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Research Paper

The epidemiology of kidney disease in people of African ancestry with HIV in the UK

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ABSTRACT

Background: Chronic kidney disease (CKD) is a leading cause of morbidity and mortality globally. The risk of CKD is increased in people of African ancestry and with Human Immunodeficiency Virus (HIV) infection.
Methods: We conducted a cross-sectional study investigating the relationship between region of ancestry (East, Central, South or West Africa) and kidney disease in people of sub-Saharan African ancestry with HIV in the UK between May 2018 and February 2020. The primary outcome was renal impairment (estimated glomerular filtration rate [eGFR] of <60 mL/min/1.73 m^2). Secondary outcomes were stage 5 CKD (eGFR <15 ml/min/1.73 m^2, on dialysis for over 3 months or who had received a kidney transplant), proteinuria (urine protein/creatinine ratio >50 mg/mmol), and biopsy-confirmed HIV-associated nephropathy (HIVAN), focal segmental glomerulosclerosis (FSGS) or arteriolonephrosclerosis. Multivariable robust Poisson regression estimated the effect of region of African ancestry on kidney disease outcomes.
Findings: Of the 2468 participants (mean age 48.1 [SD 9.8] years, 62% female), 193 had renal impairment, 87 stage 5 CKD, 126 proteinuria, and 43 HIVAN/FSGS or arteriolonephrosclerosis. After adjusting for demographic characteristics, HIV and several CKD risk factors and with East African ancestry as referent, West African ancestry was associated with renal impairment (prevalence ratio [PR] 2.06 [95% CI 1.40–3.04]) and stage 5 CKD (PR 2.23 [1.23–4.04]), but not with proteinuria (PR 1.27 [0.78–2.05]). West African ancestry (as compared to East/South African ancestry) was also strongly associated with a diagnosis of HIVAN/FSGS or arteriolonephrosclerosis on kidney biopsy (PR 6.44 [2.42–17.14]).
Interpretation: Our results indicate that people of West African ancestry with HIV are at increased risk of kidney disease. Although we cannot rule out the possibility of residual confounding, geographical region of origin appears to be a strong independent risk factor for CKD as the association did not appear to be explained by several demographic, HIV or renal risk factors.

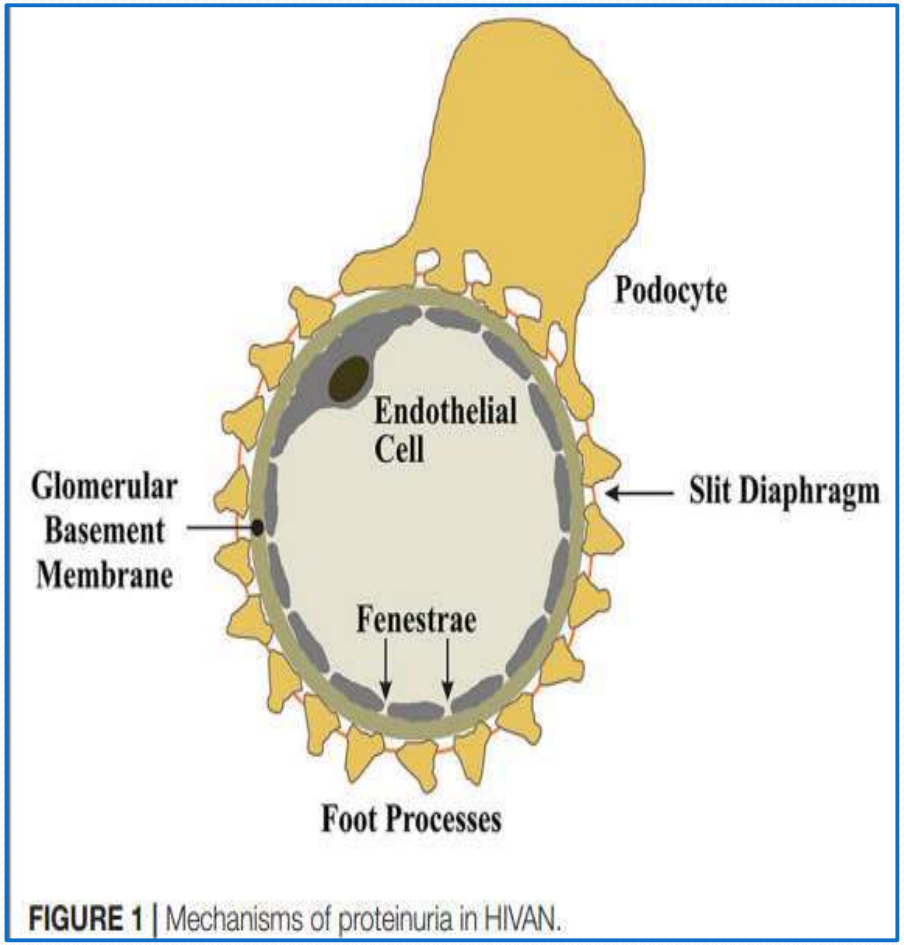

FIGURE 1 | Mechanisms of proteinuria in HIVAN.

frontiers in Medicine

MINI REVIEW

Mechanisms of Proteinuria in HIV

Gentzon Hall[1,2] and Christina M. Wyatt[1,3]*

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Proteinuria is common in the setting of HIV infection, and may reflect comorbid kidney disease, treatment-related nephrotoxicity, and HIV-related glomerular diseases. The mechanisms of podocyte and tubulointerstitial injury in HIV-associated nephropathy (HIVAN) have been the subject of intense investigation over the past four decades. The pathologic contributions of viral gene expression, dysregulated innate immune signaling, and ancestry-driven genetic risk modifiers have been explored in sophisticated cellular and whole animal models of disease. These studies provide evidence that injury-induced podocyte dedifferentiation, hyperplasia, cytoskeletal dysregulation, and apoptosis may cause the loss of glomerular filtration barrier integrity and slit diaphragm performance that facilitates proteinuria and tuft collapse in HIVAN. Although the incidence of HIVAN has declined with the introduction of antiretroviral therapy, the collapsing FSGS lesion has been observed in the context of other viral infections and chronic autoimmune disorders, and with the use of interferon-based therapies in genetically susceptible populations. This highlights the fact that the lesion is not specific to HIVAN and that the role of the immune system in aggravating podocyte injury warrants further exploration. This review will summarize our progress in characterizing the molecular mechanisms of podocyte dysfunction in HIVAN and other forms of HIV-associated kidney disease.

OPEN ACCESS

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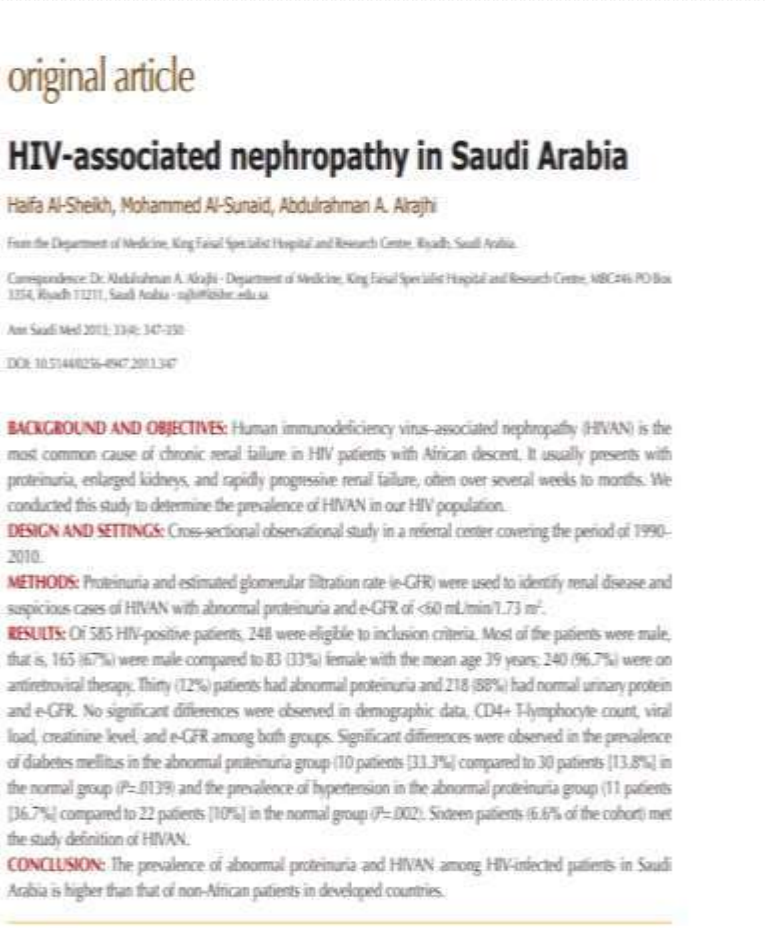
Keywords: podocyte, glomerular disease, HIVAN-associated nephropathy, APOL1, collapsing FSGS

- Tubulointerstisyel hastalık ve podosit düzleşmesinin derecesi, genellikle HIVAN'dan daha az belirgindir.
- HIVAN'dan farklı olarak Kafkasyalılarda, Afrika kökenli Amerikalılara göre daha sık görülür.
- Bu varyant genellikle ART ile tedavi edilen ve tespit edilemeyen viral yüke sahip hastalarda görülür.



original article

HIV-associated nephropathy in Saudi Arabia

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BACKGROUND AND OBJECTIVES: Human immunodeficiency virus-associated nephropathy (HIVAN) is the most common cause of chronic renal failure in HIV patients with African descent. It usually presents with proteinuria, enlarged kidneys, and rapidly progressive renal failure, often over several weeks to months. We conducted this study to determine the prevalence of HIVAN in our HIV population.

DESIGN AND SETTINGS: Cross-sectional observational study in a referral center covering the period of 1990-2010.

METHODS: Proteinuria and estimated glomerular filtration rate (e-GFR) were used to identify renal disease and suspicious cases of HIVAN with abnormal proteinuria and e-GFR of <60 mL/min/1.73 m^2.

RESULTS: Of 585 HIV-positive patients, 248 were eligible to inclusion criteria. Most of the patients were male, that is, 165 (67%) were male compared to 83 (33%) female with the mean age 39 years; 240 (96.7%) were on antiretroviral therapy. Thirty (12%) patients had abnormal proteinuria and 218 (88%) had normal urinary protein and e-GFR. No significant differences were observed in demographic data, CD4+ T-lymphocyte count, viral load, creatinine level, and e-GFR among both groups. Significant differences were observed in the prevalence of diabetes mellitus in the abnormal proteinuria group (10 patients [33.3%] compared to 30 patients [13.8%] in the normal group (P=.0139) and the prevalence of hypertension in the abnormal proteinuria group (11 patients [36.7%] compared to 22 patients [10%] in the normal group (P=.002). Sixteen patients (6.6% of the cohort) met the study definition of HIVAN.

CONCLUSION: The prevalence of abnormal proteinuria and HIVAN among HIV-infected patients in Saudi Arabia is higher than that of non-African patients in developed countries.

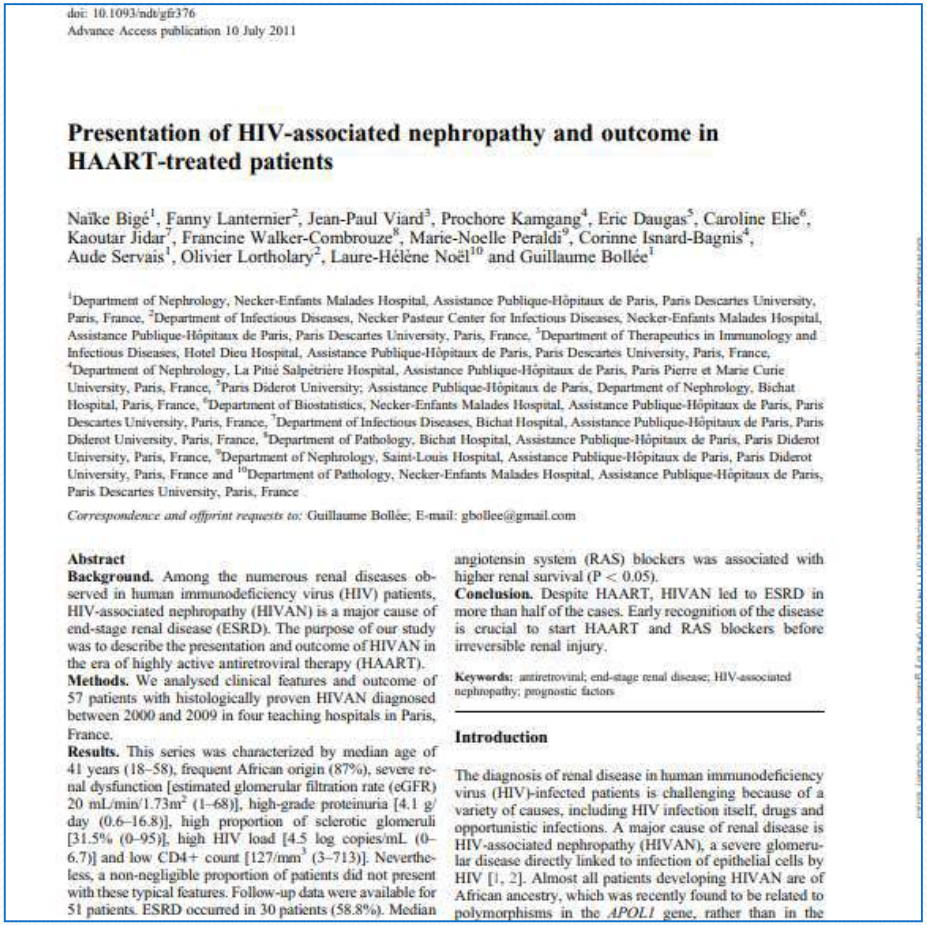
Tablo2. HIVAN Tedavisinde Anahtar Çalışmalar

Year	Author	Study type	Population	Findings
ART				
2008	Post et al. [26]	Retrospective cohort	Biopsy-proven or clinically diagnosed HIVAN	Renal survival not significantly improved by early initiation of ART
2012	Bige et al. [23]	Retrospective cohort	Biopsy-proven HIVAN	Median renal survival improved to 40 months compared to prior studies
2006	Atta et al. [56]	Retrospective cohort	Biopsy-proven HIVAN	Renal survival better in group treated with ART (HR = 0.3)
2004	Szczech et al. [57]	Retrospective cohort	Patients with HIV who underwent renal biopsy	ART slowed progression to ESRD in those with HIVAN (HR = 0.24)
2012	Wearne et al. [54]	Retrospective and prospective cohort	Biopsy-proven HIVAN	cART reduced mortality in patients with biopsy features of HIVAN (HR = 0.43)
RAAS inhibitors				
1997	Burns et al. [58]	Prospective cohort	Biopsy-proven and clinically diagnosed HIVAN	ACE inhibitors stabilized serum creatinine and 24-h protein excretion in patients with HIVAN
2003	Wei et al. [59]	Prospective cohort	Biopsy-proven HIVAN	ACE inhibitors reduced risk of ESRD (RR = 0.003) and had greater survival
2004	Szczech et al. [57]	Retrospective cohort	Patients with HIV who underwent renal biopsy	ACEi/ARB slowed progression to ESRD (HR = 0.41)
Steroids				
2000	Eustace et al. [60]	Retrospective cohort	Biopsy-proven HIVAN	Steroids slowed progression of azotemia on multivariate analysis (OR of improved renal outcome adjusted for serum creatinine = 39.1)
1998	Laradi et al. [61]	Retrospective cohort	Biopsy-proven HIVAN	Steroids slowed progression to ESRD (RR = 0.29)
Dialysis				
2003	Ahuja et al. [62]	Retrospective cohort	Patients with HIVAN on dialysis	No significant difference in survival between HD and PD (HR = 1.01)
2017	Ndlovu et al. [63]	Prospective cohort	Patients with HIV undergoing PD versus patients without HIV undergoing PD	Increased risk of peritonitis in patients with HIV undergoing PD (HR = 2.38)
Renal transplant				
2015	Waheed et al. [48]	Prospective cohort	Patients with biopsy-proven HIVAN undergoing renal transplant	Graft survival rates: 1 year = 100% 3 year = 81% Acute rejection rates 1 year = 18% 3 year = 27% Delayed graft function in 64%
2010	Stock et al. [64]	Prospective cohort	HIV-infected patients on ART undergoing renal transplant	Patient survival rates: 1 year = 94.6±2.0% 3 year = 88.2±3.8% Graft survival rates: 1 year = 90.4% 3 year = 73.7% Rejection rates: 1 year = 31% 3 year = 41%

HIVAN, HIV-associated nephropathy; RAAS, renal-angiotensin-aldosterone system; ART, antiretroviral therapy; cART, combination antiretroviral therapy; HD, hemodialysis; PD, peritoneal dialysis.

HIVAN Tedavisi

- cHAART,
- Yardımcı tedaviler RAAS blokajı ve prednizon.
- SDBY ilerleyenlerde diyaliz.
- Böbrek nakli kontrollü HIV hastalarında çok etkili.



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Presentation of HIV-associated nephropathy and outcome in HAART-treated patients

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Abstract

Background. Among the numerous renal diseases observed in human immunodeficiency virus (HIV) patients, HIV-associated nephropathy (HIVAN) is a major cause of end-stage renal disease (ESRD). The purpose of our study was to describe the presentation and outcome of HIVAN in the era of highly active antiretroviral therapy (HAART).

Methods. We analysed clinical features and outcome of 57 patients with histologically proven HIVAN diagnosed between 2000 and 2009 in four teaching hospitals in Paris, France.

Results. This series was characterized by median age of 41 years (18–58), frequent African origin (87%), severe renal dysfunction [estimated glomerular filtration rate (eGFR) 20 mL/min/1.73m^2 (1–68)], high-grade proteinuria [4.1 g/day (0.6–16.8)], high proportion of sclerotic glomeruli [31.5% (0–95)], high HIV load [4.5 log copies/mL (0–6.7)] and low CD4+ count [127/mm^3 (3–713)]. Nevertheless, a non-negligible proportion of patients did not present with these typical features. Follow-up data were available for 51 patients. ESRD occurred in 30 patients (58.8%). Median angiotensin system (RAS) blockers was associated with higher renal survival ($P < 0.05$).

Conclusion. Despite HAART, HIVAN led to ESRD in more than half of the cases. Early recognition of the disease is crucial to start HAART and RAS blockers before irreversible renal injury.

Keywords: antiretroviral; end-stage renal disease; HIV-associated nephropathy; prognostic factors

Introduction

The diagnosis of renal disease in human immunodeficiency virus (HIV)-infected patients is challenging because of a variety of causes, including HIV infection itself, drugs and opportunistic infections. A major cause of renal disease is HIV-associated nephropathy (HIVAN), a severe glomerular disease directly linked to infection of epithelial cells by HIV [1, 2]. Almost all patients developing HIVAN are of African ancestry, which was recently found to be related to polymorphisms in the *APOL1* gene, rather than in the

Tubulointerstisyel Baskın HIV ile İlgili Hastalıklar

- Tübülointerstisyel hastalık klasik HIVAN, ilaç toksisitesi veya enfeksiyonlardan kaynaklanmaktadır.
- **Bağışıklık** sisteminin HIV'e anormal tepkisiyle ilişkilidir: (i) diffüz infiltrasyonlu lenfositoz sendromu (DILS)
- (ii) yeniden immün yapılanma inflamatuar sendromu (IRIS).

Acute Renal Failure on Immune Reconstitution in an HIV-Positive Patient with Miliary Tuberculosis

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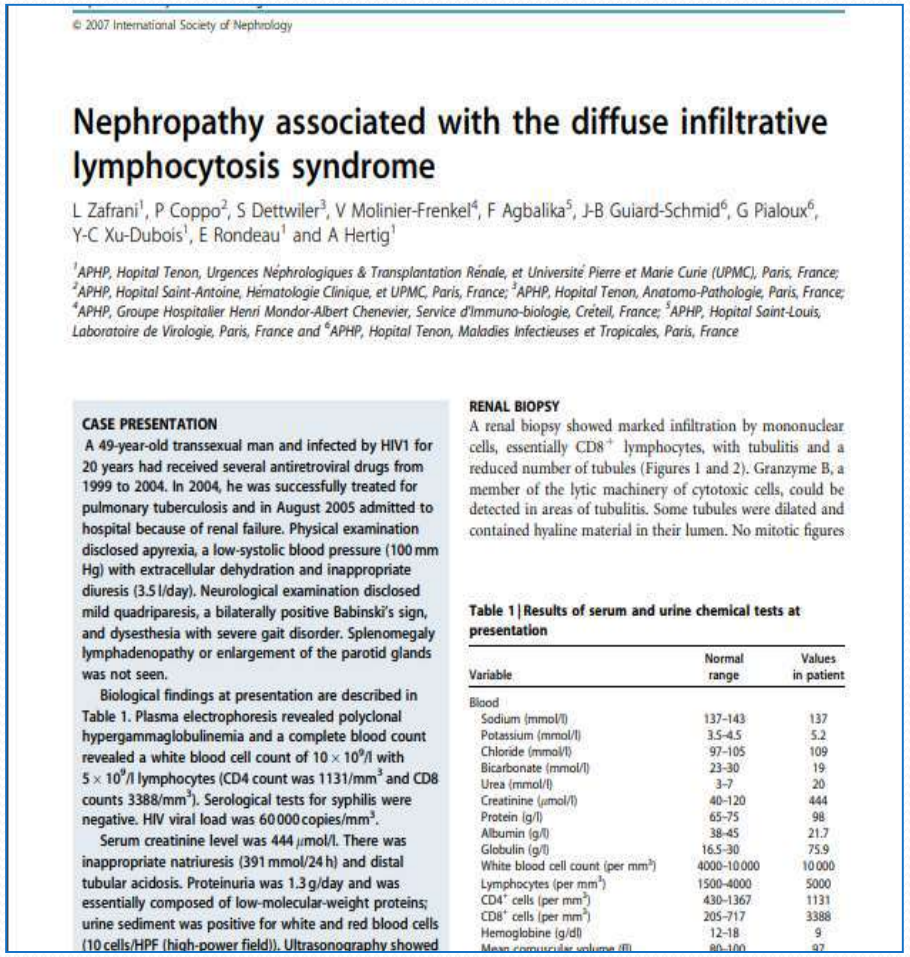
Immune reconstitution syndrome following HAART in human immunodeficiency virus (HIV)–infected patients is characterized by inflammatory worsening of organ functions despite improvement in HIV surrogate markers of HIV infection. We describe a patient with miliary tuberculosis and urinary shedding of acid fast bacilli who developed acute renal failure 8 weeks after initiation of antituberculosis therapy and 6 weeks after initiation of HAART. The diagnostic workup and further course of disease implicated immune reconstitution syndrome as the cause of acute renal failure.

Acute renal failure (ARF) is frequently encountered in patients with HIV infection [1,2]. In a recent retrospective study of 92 HIV-infected patients with ARF admitted to a nephrology unit [3], at least 10 different entities were diagnosed: hemolytic-uremic syndrome (in 35% of patients), acute tubular necrosis (in 26%), HIV-associated nephropathy (in 15%), acute interstitial nephritis (in 2%), obstructive renal failure due to lymphoma and drug- and paraprotein-mediated causes (in 17%), and various forms of glomerulonephritis (in 4%). In contrast to ARF due to prerenal and postrenal causes, renal forms of hospital admission. HIV infection (CD4 cell count, 69 cells/μL; virus load, 1,247,786 copies/mL) and miliary tuberculosis was diagnosed. Acid-fast bacteria were seen in bronchoalveolar lavage fluid and in urine specimens. *Mycobacterium tuberculosis* was identified by culture and specific PCR. The patient was initially treated with standard doses of 4 antituberculosis agents (isoniazid, rifampicin, pyrazinamid, and ethambutol). Primary prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) 3 times weekly was started. After 2 weeks, rifampicin was replaced with rifabutin at a reduced dosage of 150 mg q.o.d., at the time when HAART was initiated (zidovudine, lamivudine, and lopinavir/ritonavir) (figure 1). Drug-susceptibility testing of the *Mycobacterium tuberculosis* isolate revealed no resistance, and a 3-drug regimen consisting of isoniazid, pyrazinamid, and rifabutin was administered. The clinical condition improved, and the patient was referred to a rehabilitation clinic.

However, after 2 months, ARF developed with rising serum creatinine concentrations of 4.89 mg/dl. (433 μmol/L), and the patient was readmitted to the hospital. Overall, the clinical status had improved. There was no fever, coughing, or lymphadenopathy. Macrocytic hyperchromic anemia was found, with a hemoglobin concentration of 9 g/dL. The C-reactive protein level measured 95 mg/L (normal range, <5 mg/L), increasing to 142 mg/L. The HIV load had decreased by 4 $\log_{10}$ to 104 copies/mL, and the CD4 cell count had increased to 82 cells/μL. Urine analysis showed mild proteinuria with a tubulointerstitial pattern (urine protein to creatinine concentration of 53 mg/mmol, and ratios of α-1 microglobulin to creatinine and retinol-binding protein to creatinine increased by 31-fold and 46-fold, respectively) in addition to few granular casts and few leukocytes. Serial CT of the chest showed newly accentuated pulmonary infiltrates. Bronchoscopy and bronchoalveolar lavage were performed and revealed lymphocytosis, but yielded

Diffüz İnfiltrasyonlu Lenfositoz Sendromu (DILS)

- HIV antijenlerine karşı hiperimmün bir reaksiyon.
- Belirgin interstisyel CD8 T hücresi varlığıyla karakterize.
- Birinci basamak tedavisi ART.
- Ciddi organ fonksiyon bozukluklarını gidermek ve hızlı bir şekilde iyileşmesini sağlamak için altı ila sekiz haftalık steroid kullanılır .



Nephropathy associated with the diffuse infiltrative lymphocytosis syndrome

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CASE PRESENTATION

A 49-year-old transsexual man and infected by HIV1 for 20 years had received several antiretroviral drugs from 1999 to 2004. In 2004, he was successfully treated for pulmonary tuberculosis and in August 2005 admitted to hospital because of renal failure. Physical examination disclosed apyrexia, a low-systolic blood pressure (100 mm Hg) with extracellular dehydration and inappropriate diuresis (3.5 l/day). Neurological examination disclosed mild quadriparesis, a bilaterally positive Babinski's sign, and dysesthesia with severe gait disorder. Splenomegaly lymphadenopathy or enlargement of the parotid glands was not seen.

Biological findings at presentation are described in Table 1. Plasma electrophoresis revealed polyclonal hypergammaglobulinemia and a complete blood count revealed a white blood cell count of 10×10^9/l with 5×10^9/l lymphocytes (CD4 count was 1131/mm^3 and CD8 counts 3388/mm^3). Serological tests for syphilis were negative. HIV viral load was 60 000 copies/mm^3.

Serum creatinine level was 444 μmol/l. There was inappropriate natriuresis (391 mmol/24 h) and distal tubular acidosis. Proteinuria was 1.3 g/day and was essentially composed of low-molecular-weight proteins; urine sediment was positive for white and red blood cells (10 cells/HPF (high-power field)). Ultrasonography showed

RENAL BIOPSY

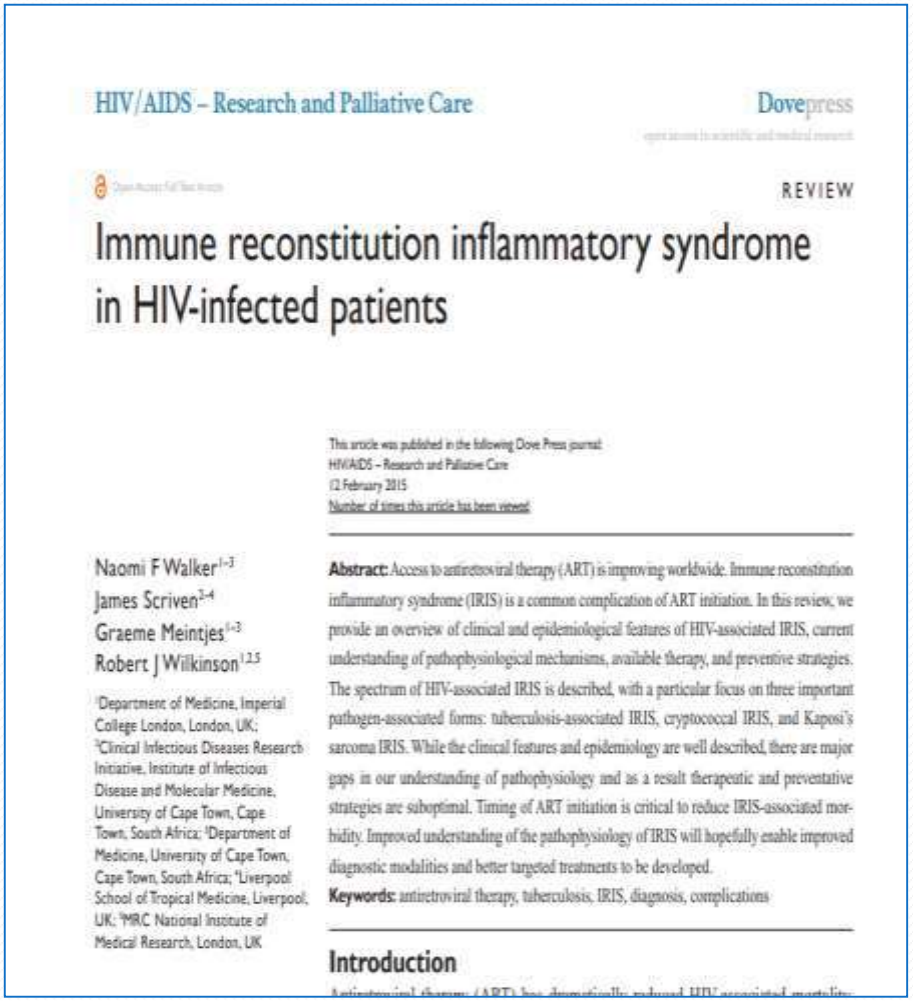
A renal biopsy showed marked infiltration by mononuclear cells, essentially $CD8^+$ lymphocytes, with tubulitis and a reduced number of tubules (Figures 1 and 2). Granzyme B, a member of the lytic machinery of cytotoxic cells, could be detected in areas of tubulitis. Some tubules were dilated and contained hyaline material in their lumen. No mitotic figures

Table 1 | Results of serum and urine chemical tests at presentation

Variable	Normal range	Values in patient
Blood		
Sodium (mmol/l)	137–143	137
Potassium (mmol/l)	3.5–4.5	5.2
Chloride (mmol/l)	97–105	109
Bicarbonate (mmol/l)	23–30	19
Urea (mmol/l)	3–7	20
Creatinine (μmol/l)	40–120	444
Protein (g/l)	65–75	98
Albumin (g/l)	38–45	21.7
Globulin (g/l)	16.5–30	75.9
White blood cell count (per mm^3)	4000–10 000	10 000
Lymphocytes (per mm^3)	1500–4000	5000
$CD4^+$ cells (per mm^3)	430–1367	1131
$CD8^+$ cells (per mm^3)	205–717	3388
Hemoglobine (g/dl)	12–18	9
Mean corpuscular volume (fl)	80–100	97

Yeniden İmmün Yapılanma İnflamatuar Sendromu (IRIS)

- Böbrek parankiminde yayılan enfeksiyöz antijenlere karşı yönlendirilen, ART'nin başlamasından sonra bağışıklık sisteminin iyileşmesiyle ortaya çıkan inflamatuar sendromdur.
- Yönetimi karmaşıktır, fizyopatolojisi bilinmemektedir.
- Çoğunda ART'ye devam ,
- Fırsatçı enfeksiyon tedavi edilir.
- Şiddetli böbrek hastalığı gelişen hastalarda steroidler.



HIV/AIDS – Research and Palliative Care

Dovepress

REVIEW

Immune reconstitution inflammatory syndrome in HIV-infected patients

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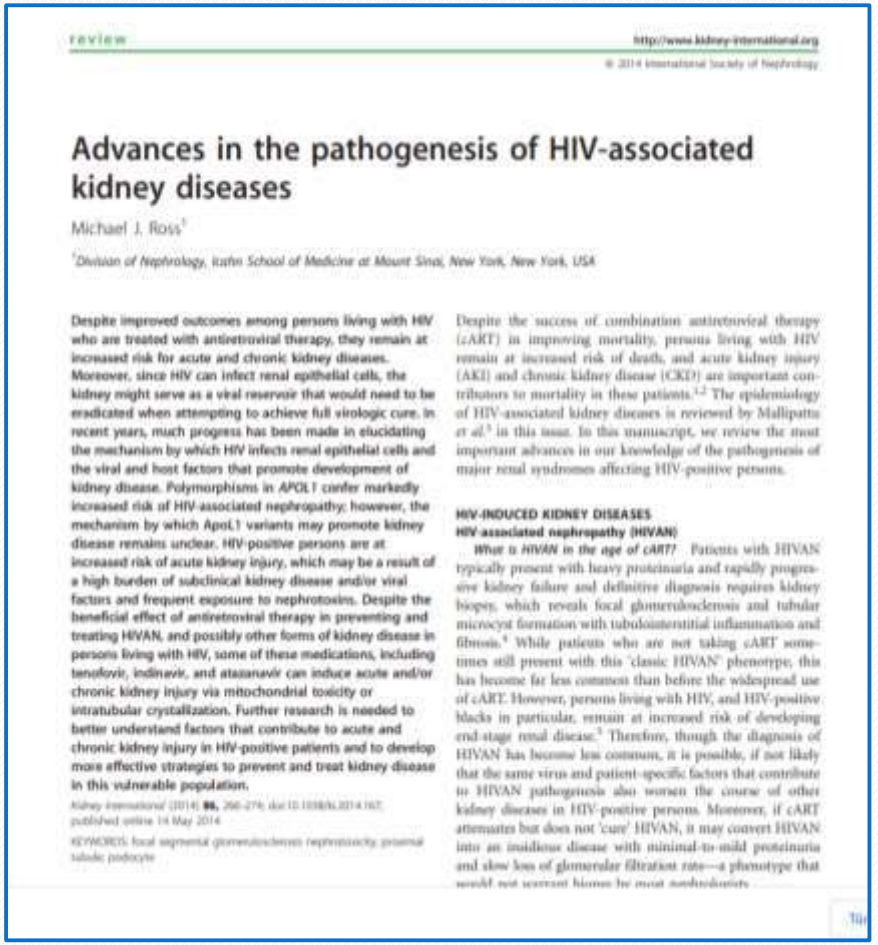
Abstract: Access to antiretroviral therapy (ART) is improving worldwide. Immune reconstitution inflammatory syndrome (IRIS) is a common complication of ART initiation. In this review, we provide an overview of clinical and epidemiological features of HIV-associated IRIS, current understanding of pathophysiological mechanisms, available therapy, and preventive strategies. The spectrum of HIV-associated IRIS is described, with a particular focus on three important pathogen-associated forms: tuberculosis-associated IRIS, cryptococcal IRIS, and Kaposi's sarcoma IRIS. While the clinical features and epidemiology are well described, there are major gaps in our understanding of pathophysiology and as a result therapeutic and preventative strategies are suboptimal. Timing of ART initiation is critical to reduce IRIS-associated morbidity. Improved understanding of the pathophysiology of IRIS will hopefully enable improved diagnostic modalities and better targeted treatments to be developed.

Keywords: antiretroviral therapy, tuberculosis, IRIS, diagnosis, complications

Introduction

HIV ile İlişkili İmmün Kompleks Böbrek Hastalığı (HIVICK)

- HIV enfeksiyonunda glomerüler immün kompleks birikimi.
- HIV + hastalarda böbrek biyopsisinde en sık tanıdır.
- ART takiben, bağışıklık sistem modülasyonu, bağışıklığın yeniden yapılanması ve bağışıklık kompleksi birikmesi,



review

http://www.kidney-international.org

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Advances in the pathogenesis of HIV-associated kidney diseases

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Despite improved outcomes among persons living with HIV who are treated with antiretroviral therapy, they remain at increased risk for acute and chronic kidney diseases. Moreover, since HIV can infect renal epithelial cells, the kidney might serve as a viral reservoir that would need to be eradicated when attempting to achieve full virologic cure. In recent years, much progress has been made in elucidating the mechanism by which HIV infects renal epithelial cells and the viral and host factors that promote development of kidney disease. Polymorphisms in *APOL1* confer markedly increased risk of HIV-associated nephropathy; however, the mechanism by which ApoL1 variants may promote kidney disease remains unclear. HIV-positive persons are at increased risk of acute kidney injury, which may be a result of a high burden of subclinical kidney disease and/or viral factors and frequent exposure to nephrotoxins. Despite the beneficial effect of antiretroviral therapy in preventing and treating HIVAN, and possibly other forms of kidney disease in persons living with HIV, some of these medications, including tenofovir, indinavir, and atazanavir can induce acute and/or chronic kidney injury via mitochondrial toxicity or intratubular crystallization. Further research is needed to better understand factors that contribute to acute and chronic kidney injury in HIV-positive patients and to develop more effective strategies to prevent and treat kidney disease in this vulnerable population.

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KEYWORDS: focal segmental glomerulosclerosis, nephrotoxicity, proximal tubule, podocyte

Despite the success of combination antiretroviral therapy (cART) in improving mortality, persons living with HIV remain at increased risk of death, and acute kidney injury (AKI) and chronic kidney disease (CKD) are important contributors to mortality in these patients.[1,2] The epidemiology of HIV-associated kidney diseases is reviewed by Mallipattu *et al.*[3] in this issue. In this manuscript, we review the most important advances in our knowledge of the pathogenesis of major renal syndromes affecting HIV-positive persons.

HIV-INDUCED KIDNEY DISEASES

HIV-associated nephropathy (HIVAN)

What is HIVAN in the age of cART? Patients with HIVAN typically present with heavy proteinuria and rapidly progressive kidney failure and definitive diagnosis requires kidney biopsy, which reveals focal glomerulosclerosis and tubular microcyst formation with tubulointerstitial inflammation and fibrosis.[4] While patients who are not taking cART sometimes still present with this 'classic HIVAN' phenotype, this has become far less common than before the widespread use of cART. However, persons living with HIV, and HIV-positive blacks in particular, remain at increased risk of developing end-stage renal disease.[5] Therefore, though the diagnosis of HIVAN has become less common, it is possible, if not likely that the same virus and patient-specific factors that contribute to HIVAN pathogenesis also worsen the course of other kidney diseases in HIV-positive persons. Moreover, if cART attenuates but does not 'cure' HIVAN, it may convert HIVAN into an insidious disease with minimal-to-mild proteinuria and slow loss of glomerular filtration rate—a phenotype that would not warrant biopsy by most nephrologists

- Hepatit B ve C ile birlikte enfeksiyon neden olmakta.
- cART öncesi çalışmalarda, glomerülonefrit ile sonuçlanabilen, bağışıklık kompleksleri oluşturabilen, anti-HIV antikorları gösterilmiş.
- Mekanizma ve ART sonrası önemi bilinmemektedir.

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HIV and renal disease: a contemporary review

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Affiliations + expand

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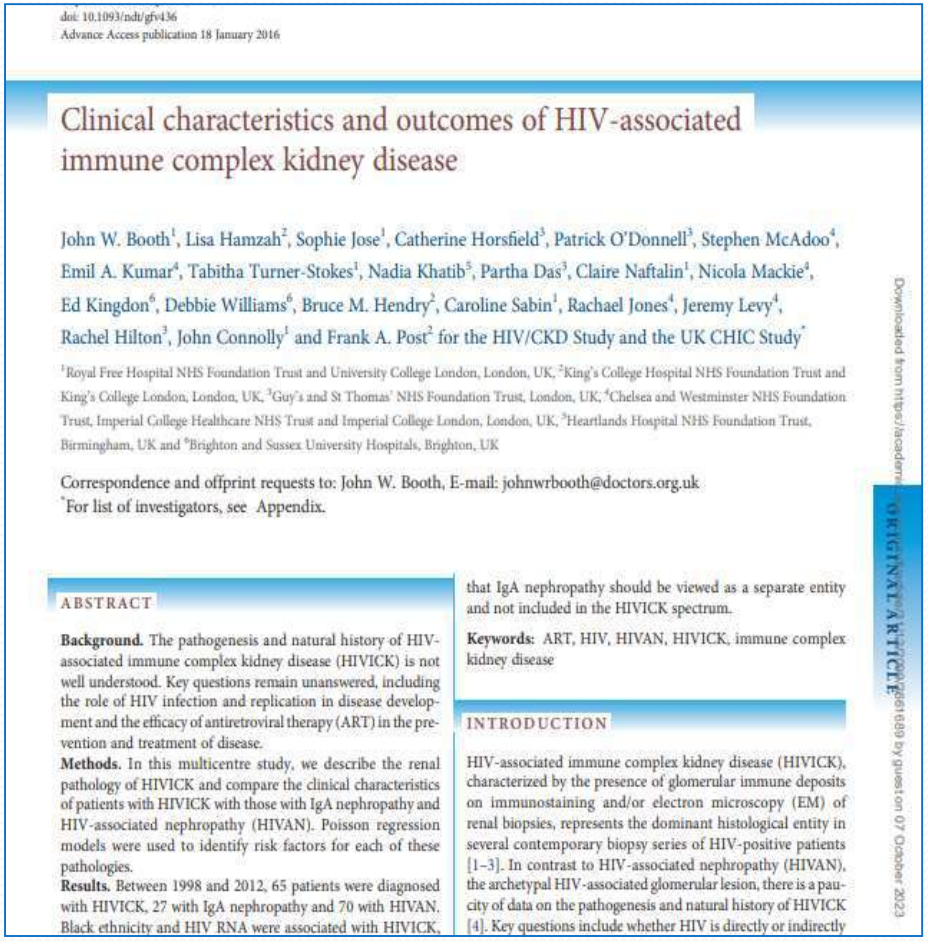
Abstract

The presence of human immunodeficiency virus (HIV)-related kidney disease is an important cause of mortality and morbidity. HIV infection induces renal injury by direct cytotoxicity or immune complex-mediated glomerulonephritis in patients with genetic susceptibility factors. In the last decades, with the development and diffusion of combination antiretroviral therapy, which has prolonged patient survival, there has been a shift in the spectrum of renal diseases in HIV-infected patients, with the decrease of glomerular diseases and increase in the role of nephrotoxicity and co-morbidities. This review provides a contemporary and critical review on the main renal syndromes occurring in HIV-infected patients.

Keywords: HIV; renal disease.

- HIVICK tanısı genellikle HIV testi pozitif çıktıktan birkaç yıl sonra konulur.
- İmmün kompleks böbrek hastalığı, IgA nefropatisi, lupus benzeri nefrit, membranöz Np ve MPGN.
- HIVICK tanısı, diğer ikincil nedenler dışlanarak konur.



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Clinical characteristics and outcomes of HIV-associated immune complex kidney disease

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ABSTRACT

Background. The pathogenesis and natural history of HIV-associated immune complex kidney disease (HIVICK) is not well understood. Key questions remain unanswered, including the role of HIV infection and replication in disease development and the efficacy of antiretroviral therapy (ART) in the prevention and treatment of disease.

Methods. In this multicentre study, we describe the renal pathology of HIVICK and compare the clinical characteristics of patients with HIVICK with those with IgA nephropathy and HIV-associated nephropathy (HIVAN). Poisson regression models were used to identify risk factors for each of these pathologies.

Results. Between 1998 and 2012, 65 patients were diagnosed with HIVICK, 27 with IgA nephropathy and 70 with HIVAN. Black ethnicity and HIV RNA were associated with HIVICK, that IgA nephropathy should be viewed as a separate entity and not included in the HIVICK spectrum.

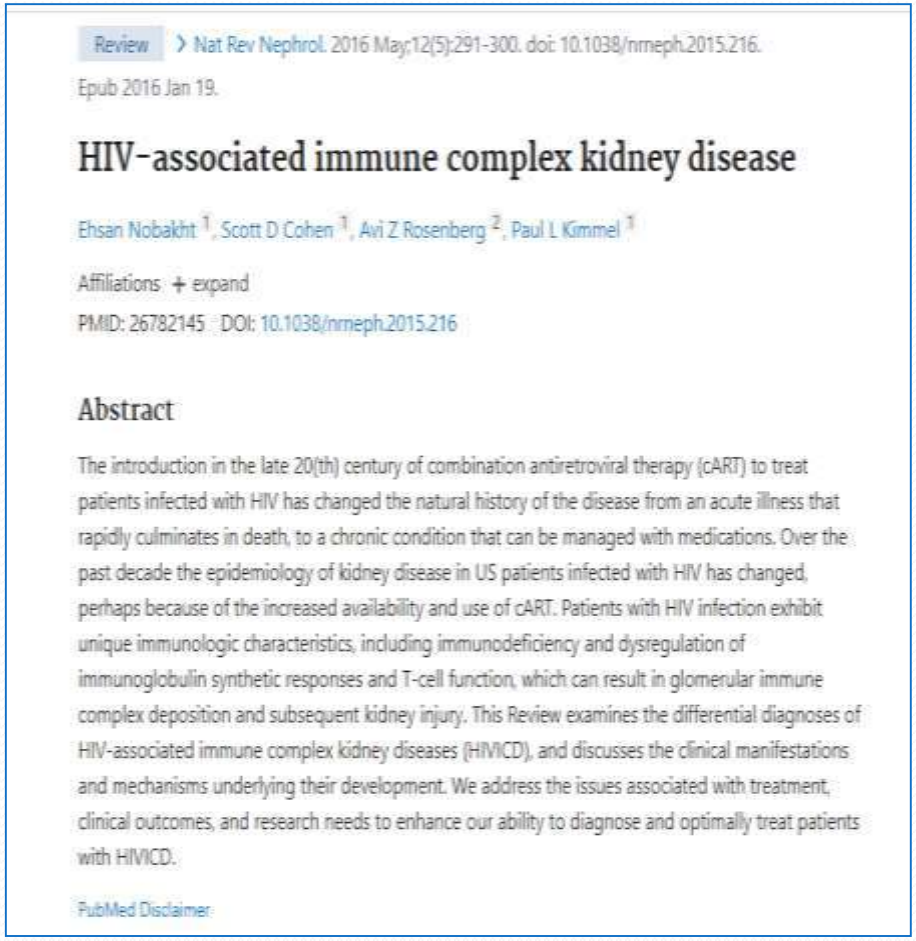
Keywords: ART, HIV, HIVAN, HIVICK, immune complex kidney disease

INTRODUCTION

HIV-associated immune complex kidney disease (HIVICK), characterized by the presence of glomerular immune deposits on immunostaining and/or electron microscopy (EM) of renal biopsies, represents the dominant histological entity in several contemporary biopsy series of HIV-positive patients [1–3]. In contrast to HIV-associated nephropathy (HIVAN), the archetypal HIV-associated glomerular lesion, there is a paucity of data on the pathogenesis and natural history of HIVICK [4]. Key questions include whether HIV is directly or indirectly

HIVICK Tedavisi

- HIVAN'a benzer şekilde, HIVICK'i tedavi etmenin dört ana yolu vardır:
- (1) Kombine HAART,
- (2) İmmünosupresanlar (steroidler)
- (3) RAAS blokajı,
- (4) Ko-morbiditelerin tedavisi.



Review > Nat Rev Nephrol. 2016 May;12(5):291-300. doi: 10.1038/nrneph.2015.216. Epub 2016 Jan 19.

HIV-associated immune complex kidney disease

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PMID: 26782145 DOI: 10.1038/nrneph.2015.216

Abstract

The introduction in the late 20(th) century of combination antiretroviral therapy (cART) to treat patients infected with HIV has changed the natural history of the disease from an acute illness that rapidly culminates in death, to a chronic condition that can be managed with medications. Over the past decade the epidemiology of kidney disease in US patients infected with HIV has changed, perhaps because of the increased availability and use of cART. Patients with HIV infection exhibit unique immunologic characteristics, including immunodeficiency and dysregulation of immunoglobulin synthetic responses and T-cell function, which can result in glomerular immune complex deposition and subsequent kidney injury. This Review examines the differential diagnoses of HIV-associated immune complex kidney diseases (HIVICD), and discusses the clinical manifestations and mechanisms underlying their development. We address the issues associated with treatment, clinical outcomes, and research needs to enhance our ability to diagnose and optimally treat patients with HIVICD.

HIV ile İlişkili Trombotik Mikroanjiyopati

- Geç evre HIV/AIDS'in iyi bilinen bir komplikasyonudur.
- cART sonrası görülme sıklığı önemli ölçüde azalmıştır.
- Patogenezi henüz aydınlatılmamış olsa da, endotel hasarının kaynağı, ilaçlar, proinflamatuar moleküller ve antifosfolipid antikorlar gibi diğer faktörlerle birlikte, dolaşımdaki viral proteinlere maruz kalma olduğu öne sürülmektedir.

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Inflammation in Atherosclerosis: From Pathophysiology to Practice

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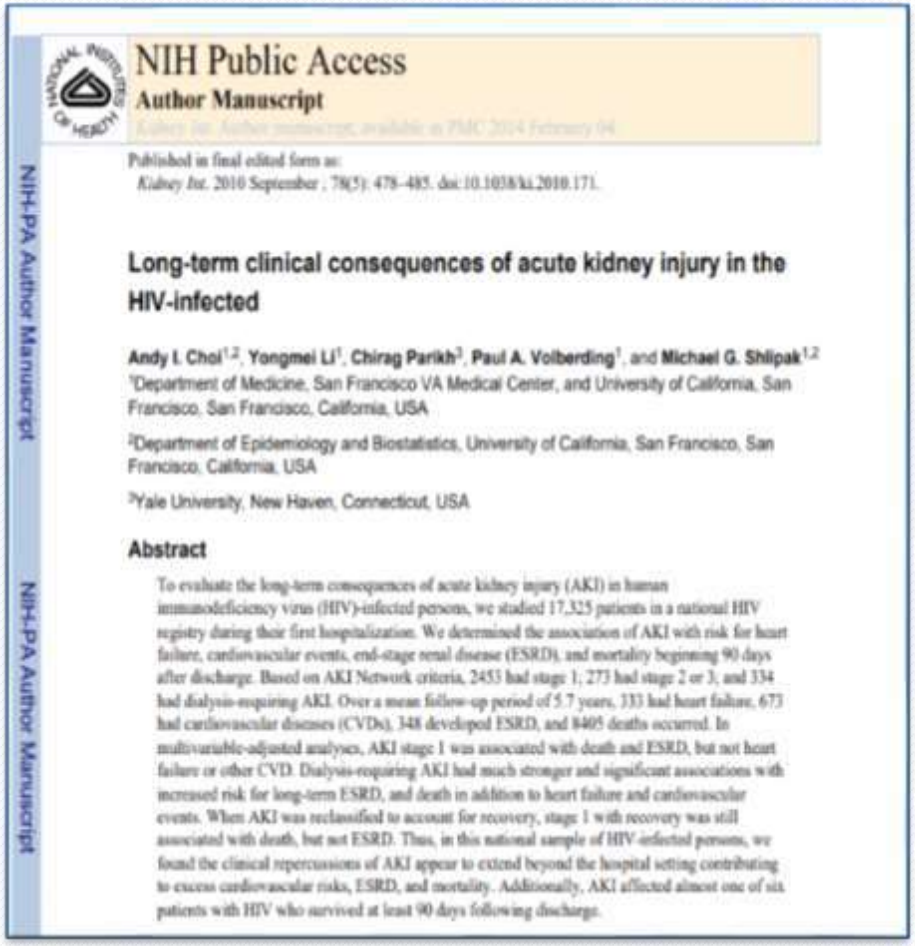
Abstract

Just three decades ago the prevailing viewpoint envisaged atherosclerosis as a bland proliferative process. (1) According to that concept, endothelial denuding injury led to platelet aggregation and release of platelet-derived growth factor which would trigger the proliferation of smooth muscle cells in the arterial intima, and form the nidus of the atherosclerotic plaque. This cellular model of atherosclerosis updated Virchow's concepts of atherosclerosis as a response to injury formulated in the mid-nineteenth century. The advent of the cell biological era of atherosclerosis supplanted the simplistic concept of the atheroma as a passive deposition of lipid debris on the artery wall. Beyond the vascular smooth muscle cells long recognized in atherosclerotic lesions, subsequent work identified immune cells and mediators at work in atheromata, implicating inflammatory mechanisms in disease development. (2) The advent of gene-targeting technology enabled the testing of the roles of specific molecules in the development of experimental atherosclerosis in mice. Such data demonstrated a critical role for hypercholesterolemia and also supported the participation of immune mechanisms in the pathogenesis of atherosclerosis. (3)

Akut Böbrek Hasarı

- HIV ile enfekte kişilerde genel topluma göre daha yaygındır.
- Kalp yetmezliği, KVH, SDBY ve mortalite yönünden risk artışı ile ilişkili.



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Long-term clinical consequences of acute kidney injury in the HIV-infected

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Abstract

To evaluate the long-term consequences of acute kidney injury (AKI) in human immunodeficiency virus (HIV)-infected persons, we studied 17,325 patients in a national HIV registry during their first hospitalization. We determined the association of AKI with risk for heart failure, cardiovascular events, end-stage renal disease (ESRD), and mortality beginning 90 days after discharge. Based on AKI Network criteria, 2453 had stage 1; 273 had stage 2 or 3; and 334 had dialysis-requiring AKI. Over a mean follow-up period of 5.7 years, 333 had heart failure, 673 had cardiovascular diseases (CVDs), 348 developed ESRD, and 8405 deaths occurred. In multivariable-adjusted analyses, AKI stage 1 was associated with death and ESRD, but not heart failure or other CVD. Dialysis-requiring AKI had much stronger and significant associations with increased risk for long-term ESRD, and death in addition to heart failure and cardiovascular events. When AKI was reclassified to account for recovery, stage 1 with recovery was still associated with death, but not ESRD. Thus, in this national sample of HIV-infected persons, we found the clinical repercussions of AKI appear to extend beyond the hospital setting contributing to excess cardiovascular risks, ESRD, and mortality. Additionally, AKI affected almost one of six patients with HIV who survived at least 90 days following discharge.

- Son yıllarda çok daha ciddi ABH görülme sıklığında önemli artış.
- Sepsis, ciddi ABH için yaygın bir faktör.

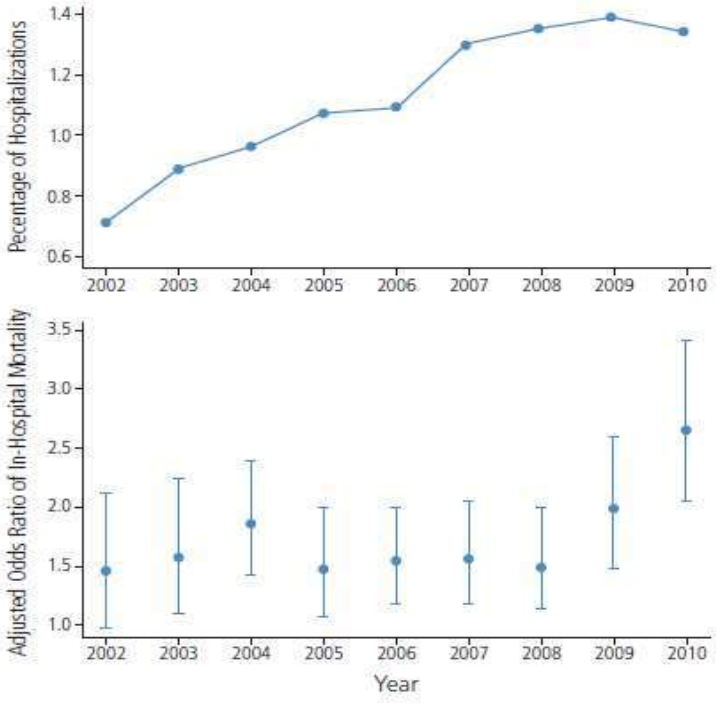
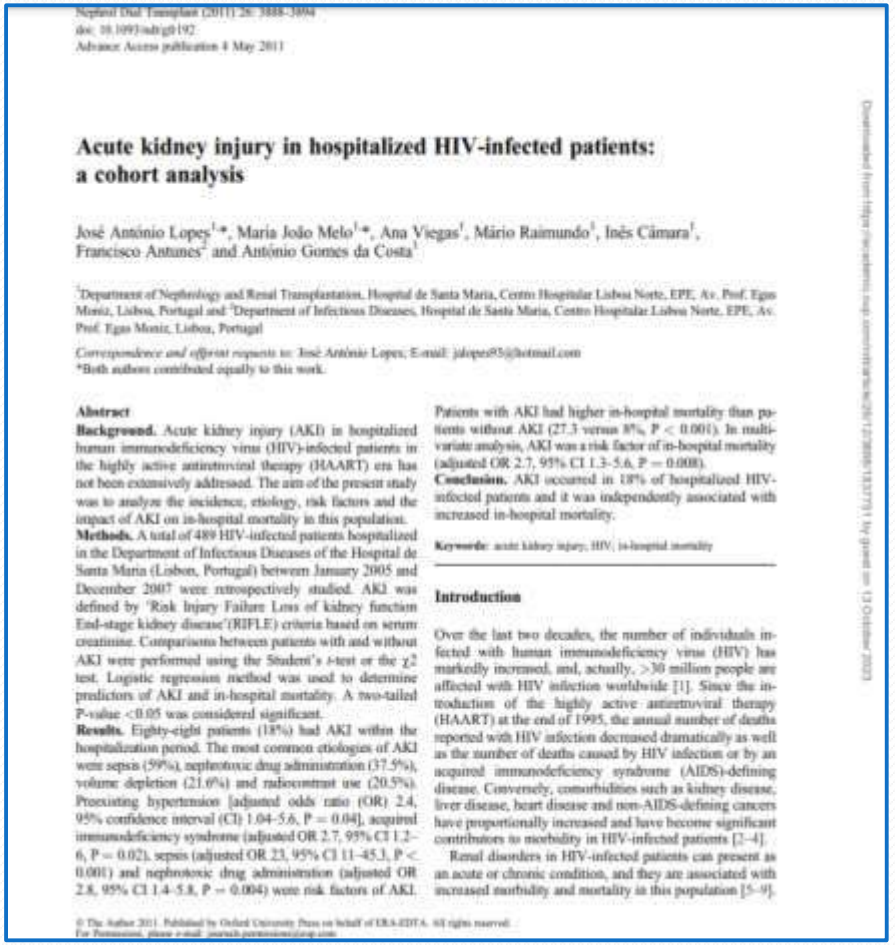


Figure 1. Proportion of hospitalizations among HIV-infected persons complicated by dialysis-dependent acute kidney injury (top), and adjusted odds ratio of in-hospital mortality associated with dialysis-dependent acute kidney injury (bottom). Adapted from Nadkarni et al.[6]

- Hastaneye yatırılmış HIV enfekte 489 hastayı içeren kohort çalışmada ABY insidansı %18.
- 750 hastanın izlendiği prospektif başka bir kohortta en az 1 ABY epizod gelişimi %10 dan fazla bulunmuş.



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Acute kidney injury in hospitalized HIV-infected patients: a cohort analysis

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*Both authors contributed equally to this work.

Abstract

Background. Acute kidney injury (AKI) in hospitalized human immunodeficiency virus (HIV)-infected patients in the highly active antiretroviral therapy (HAART) era has not been extensively addressed. The aim of the present study was to analyze the incidence, etiology, risk factors and the impact of AKI on in-hospital mortality in this population.

Methods. A total of 489 HIV-infected patients hospitalized in the Department of Infectious Diseases of the Hospital de Santa Maria (Lisbon, Portugal) between January 2005 and December 2007 were retrospectively studied. AKI was defined by 'Risk Injury Failure Loss of kidney function End-stage kidney disease'(RIFLE) criteria based on serum creatinine. Comparisons between patients with and without AKI were performed using the Student's *t*-test or the χ^2 test. Logistic regression method was used to determine predictors of AKI and in-hospital mortality. A two-tailed P-value <0.05 was considered significant.

Results. Eighty-eight patients (18%) had AKI within the hospitalization period. The most common etiologies of AKI were sepsis (59%), nephrotoxic drug administration (37.5%), volume depletion (21.6%) and radiocontrast use (20.5%). Preexisting hypertension [adjusted odds ratio (OR) 2.4, 95% confidence interval (CI) 1.04–5.6, P = 0.04], acquired immunodeficiency syndrome (adjusted OR 2.7, 95% CI 1.2–6, P = 0.02), sepsis (adjusted OR 23, 95% CI 11–45.3, P < 0.001) and nephrotoxic drug administration (adjusted OR 2.8, 95% CI 1.4–5.8, P = 0.004) were risk factors of AKI. Patients with AKI had higher in-hospital mortality than patients without AKI (27.3 versus 8%, P < 0.001). In multivariate analysis, AKI was a risk factor of in-hospital mortality (adjusted OR 2.7, 95% CI 1.3–5.6, P = 0.008).

Conclusion. AKI occurred in 18% of hospitalized HIV-infected patients and it was independently associated with increased in-hospital mortality.

Keywords: acute kidney injury; HIV; in-hospital mortality

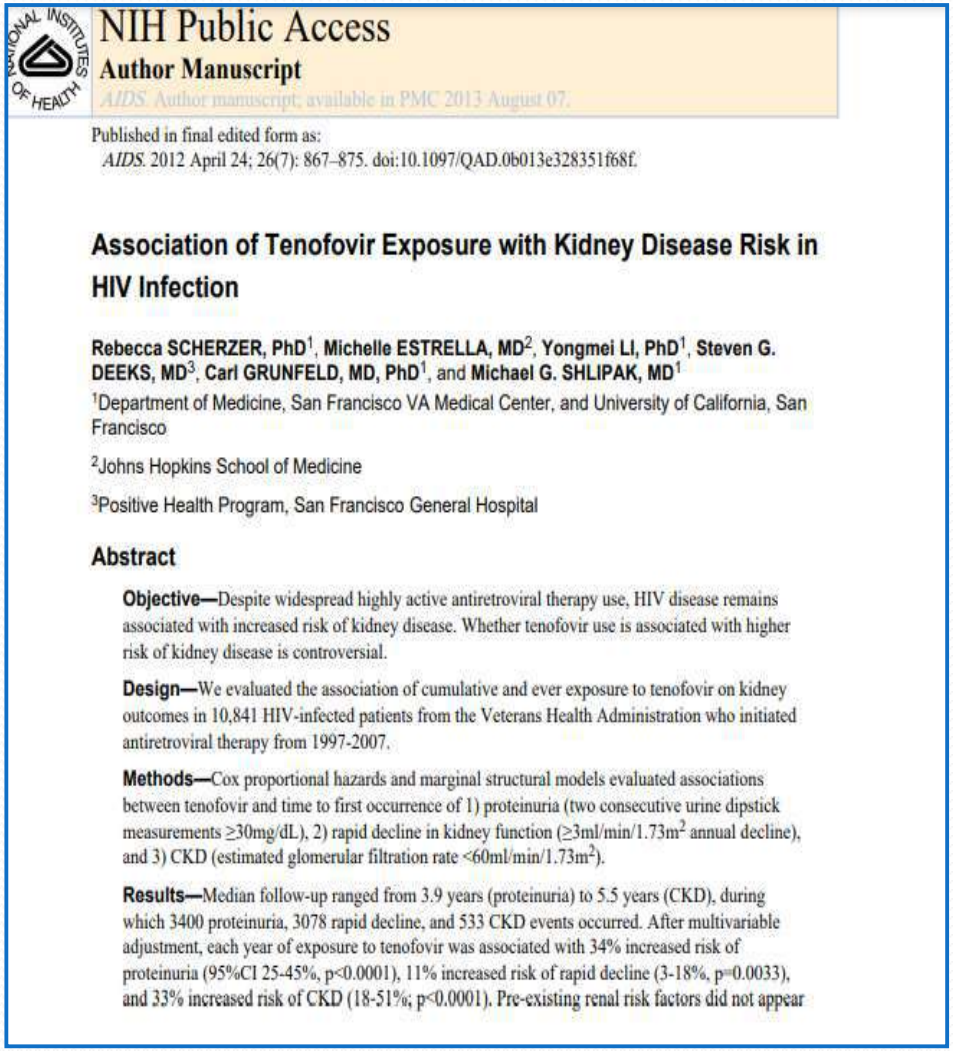
Introduction

Over the last two decades, the number of individuals infected with human immunodeficiency virus (HIV) has markedly increased, and, actually, >30 million people are affected with HIV infection worldwide [1]. Since the introduction of the highly active antiretroviral therapy (HAART) at the end of 1995, the annual number of deaths reported with HIV infection decreased dramatically as well as the number of deaths caused by HIV infection or by an acquired immunodeficiency syndrome (AIDS)-defining disease. Conversely, comorbidities such as kidney disease, liver disease, heart disease and non-AIDS-defining cancers have proportionally increased and have become significant contributors to morbidity in HIV-infected patients [2–4].

Renal disorders in HIV-infected patients can present as an acute or chronic condition, and they are associated with increased morbidity and mortality in this population [5–9].

Tedaviye Bağlı Böbrek Toksisitesi

- Böbrekte en güçlü hasara yol açan ART, proteaz inhibitörleridir (özellikle indinavir ve atazanavir) ve tenofovir disoproksil fumarat (TDF).
- Araştırmalar TDF'nin KBH riskinde %14 artışla ilişkili.
- Kronik interstisyel nefrit veya obstrüktif Np bağlı skarla ortaya çıkabilir.



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Association of Tenofovir Exposure with Kidney Disease Risk in HIV Infection

Rebecca SCHERZER, PhD[1], **Michelle ESTRELLA, MD**[2], **Yongmei LI, PhD**[1], **Steven G. DEEKS, MD**[3], **Carl GRUNFELD, MD, PhD**[1], and **Michael G. SHLIPAK, MD**[1]

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[3]Positive Health Program, San Francisco General Hospital

Abstract

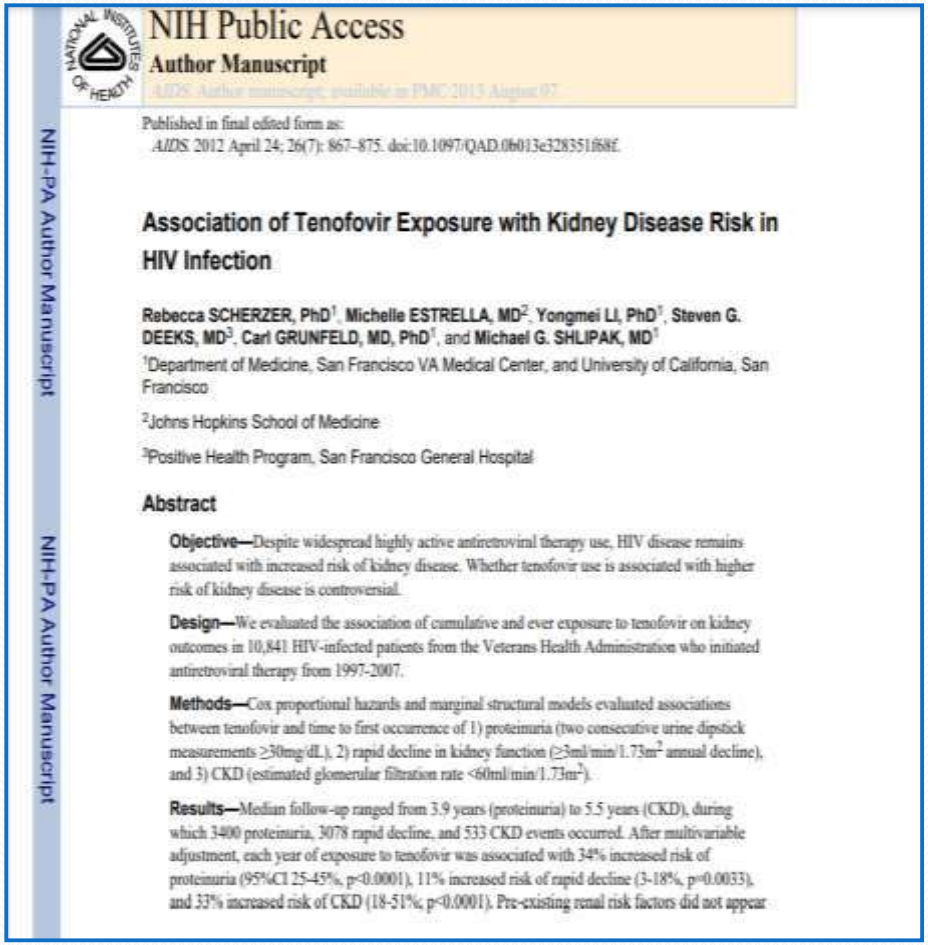
Objective—Despite widespread highly active antiretroviral therapy use, HIV disease remains associated with increased risk of kidney disease. Whether tenofovir use is associated with higher risk of kidney disease is controversial.

Design—We evaluated the association of cumulative and ever exposure to tenofovir on kidney outcomes in 10,841 HIV-infected patients from the Veterans Health Administration who initiated antiretroviral therapy from 1997-2007.

Methods—Cox proportional hazards and marginal structural models evaluated associations between tenofovir and time to first occurrence of 1) proteinuria (two consecutive urine dipstick measurements ≥30mg/dL), 2) rapid decline in kidney function (≥3ml/min/1.73m^2 annual decline), and 3) CKD (estimated glomerular filtration rate <60ml/min/1.73m^2).

Results—Median follow-up ranged from 3.9 years (proteinuria) to 5.5 years (CKD), during which 3400 proteinuria, 3078 rapid decline, and 533 CKD events occurred. After multivariable adjustment, each year of exposure to tenofovir was associated with 34% increased risk of proteinuria (95%CI 25-45%, p<0.0001), 11% increased risk of rapid decline (3-18%, p=0.0033), and 33% increased risk of CKD (18-51%; p<0.0001). Pre-existing renal risk factors did not appear

- İndinavir, interstisyel nefrit ve nefrolitiazis ile en güçlü şekilde ilişkili,
- Tüm Pİ, idrarda zayıf şekilde çözündüğü için renal inflamasyon veya taş oluşumuna yol açan kristalüri gelişir.
- Atazanavir ile daha yüksek olabilir ve bu ilaç gözlemsel çalışmalarda azalmış GFR ile birliktedir.



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- TDF'ye bağlı böbrek toksisitesi klinik bir tanıdır.
- Proksimal tübüler disfonksiyon yanı sıra GFR'de azalma,
- Hipofosfatemi, glikozüri, proteinüri ve yüksek serum kreatinin düzeyi ile birlikte tipik tübüler yaralanma ile başvuran bir kişi için biyopsi gerekmez.
- Bx, atipik durumlarda veya komorbiditeler veya ART seçenekleri sınırlı olduğunda,
- Alternatif tedavi mevcutsa, öneri TDF'nin kesilmesidir.

MAJOR ARTICLE

Systematic Review and Meta-analysis: Renal Safety of Tenofovir Disoproxil Fumarate in HIV-Infected Patients

Ryan D. Cooper,[1] Natasha Wiebe,[1] Nathaniel Smith,[2] Philip Keiser,[3] Saraladevi Naicker,[4] and Marcello Tonelli[1,2,3]

[1]Departments of Medicine and [2]Public Health Sciences and [3]Division of Critical Care Medicine, University of Alberta, Edmonton, Canada; [3]Center for Public Health Practice, Arkansas Department of Health, Little Rock, Arkansas; [3]University of Texas, Medical Branch, Galveston, Texas; and [4]Department of Internal Medicine, University of Witwatersrand, Johannesburg, South Africa

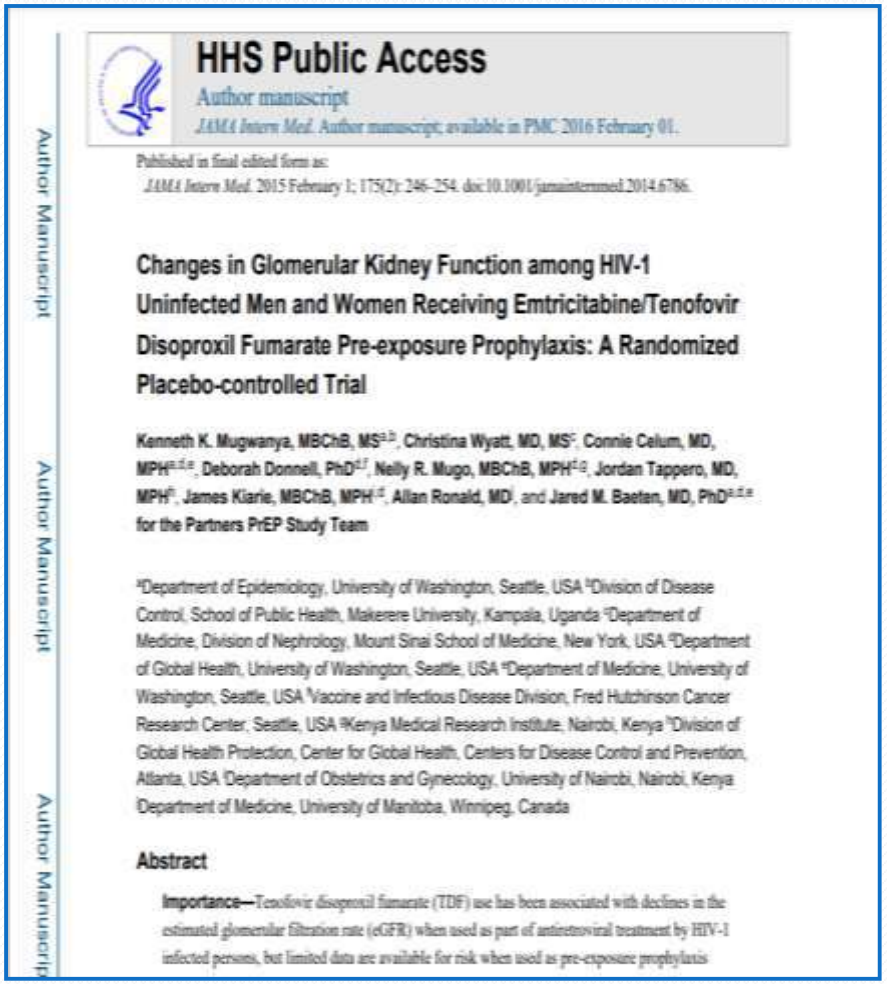
Background. The efficacy of tenofovir disoproxil fumarate (TDF) as part of combination antiretroviral treatment (ART) has been demonstrated in several randomized, controlled trials. However, an increasing number of case reports suggest that TDF use may be associated with significant nephrotoxicity. Our objective was to determine the renal safety of TDF-containing ART regimens for HIV-infected individuals.

Methods. MEDLINE, EMBASE, Global Health, Scopus, Biosis Previews, Cochrane Library, Web of Science, and existing systematic reviews were searched. Prospective studies comparing TDF-containing with non-TDF containing ART regimens were selected for inclusion. We extracted data on study characteristics, participant characteristics, therapeutic interventions, renal function, bone density, and fracture rates.

Results. A total of 17 studies (including 9 randomized, controlled trials) met the selection criteria. Median sample size was 517 participants. Constituent ART regimens were diverse. There was a significantly greater loss of kidney function among the TDF recipients, compared with control subjects (mean difference in calculated creatinine clearance, 3.92 mL/min; 95% confidence interval [CI], 2.13–5.70 mL/min), as well as a greater risk of acute renal failure (risk difference, 0.7%; 95% CI, 0.2–1.2). There was no evidence that TDF use led to increased risk of severe proteinuria, hypophosphatemia, or fractures.

Conclusions. Although TDF use was associated with a statistically significant loss of renal function, the clinical magnitude of this effect was modest. Our findings do not support the need to restrict TDF use in jurisdictions where regular monitoring of renal function and serum phosphate levels is impractical.

- TDF'ye ek olarak, Pİ indinavir, atazanavir ve ritonavir ile güçlendirilmiş lopinavir, kümülatif maruziyetle artan KBH riski ile ilişkilendirilmiştir.
- Bu artan risk, diğer güçlendirilmiş Pİ veya abakavir ile gözlenmemiş.
- İlaç-ilaç etkileşimleri de TDF ile ilişkili böbrek toksisitesi riskini artırabilir.
- Ritonavir ve kobisistat, tenofovirin plazma konsantrasyonlarını arttırır.



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Changes in Glomerular Kidney Function among HIV-1 Uninfected Men and Women Receiving Emtricitabine/Tenofovir Disoproxil Fumarate Pre-exposure Prophylaxis: A Randomized Placebo-controlled Trial

Kenneth K. Mugwanya, MBChB, MS[a,b], Christina Wyatt, MD, MS[c], Connie Celum, MD, MPH[a,d,e], Deborah Donnell, PhD[a,f], Nelly R. Mugo, MBChB, MPH[f,g], Jordan Tappero, MD, MPH[h], James Kiarie, MBChB, MPH[f], Allan Ronald, MD[i], and Jared M. Baeten, MD, PhD[a,d,e] for the Partners PrEP Study Team

[a]Department of Epidemiology, University of Washington, Seattle, USA [b]Division of Disease Control, School of Public Health, Makerere University, Kampala, Uganda [c]Department of Medicine, Division of Nephrology, Mount Sinai School of Medicine, New York, USA [d]Department of Global Health, University of Washington, Seattle, USA [e]Department of Medicine, University of Washington, Seattle, USA [f]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, USA [g]Kenya Medical Research Institute, Nairobi, Kenya [h]Division of Global Health Protection, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, USA [i]Department of Obstetrics and Gynecology, University of Nairobi, Nairobi, Kenya [i]Department of Medicine, University of Manitoba, Winnipeg, Canada

Abstract

Importance—Tenofovir disoproxil fumarate (TDF) use has been associated with declines in the estimated glomerular filtration rate (eGFR) when used as part of antiretroviral treatment by HIV-1 infected persons, but limited data are available for risk when used as pre-exposure prophylaxis

- Daha yeni ön ilaç tenofovir alafenamid (TAF), TDF ile karşılaştırıldığında böbrek toksisitesi riskini azaltabilir.
- TAF ile, tenofovirin plazma konsantrasyonları TDF'ye göre daha düşük olmasıyla böbrek ve kemik toksisitesi riski daha düşüktür.

Articles

Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials

Paul E. Sax, David Wohl, Michael T. Yin, Frank Post, Edwin DeJesus, Michael Saag, Anton Pozniak, Melanie Thompson, Daniel Podzamczer, Jean-Michel Molina, Shinichi Oka, Ellen Koenig, Bernd Trottier, Jaime Andrade-Villanueva, Gordon Custodio, Joseph M. Cavolello, Andrew Plummer, Lijie Zhong, Hagen Cao, Hal Martin, Christian Callebaut, Andrew R. Cheng, Marshall W. Fordyce, Scott McCallister, for the GS-US-292-0104/0111 Study Team*

Summary

Background Tenofovir disoproxil fumarate can cause renal and bone toxic effects related to high plasma tenofovir concentrations. Tenofovir alafenamide is a novel tenofovir prodrug with a 90% reduction in plasma tenofovir concentrations. Tenofovir alafenamide-containing regimens can have improved renal and bone safety compared with tenofovir disoproxil fumarate-containing regimens.

Methods In these two controlled, double-blind phase 3 studies, we recruited treatment-naive HIV-infected patients with an estimated creatinine clearance of 50 mL per min or higher from 178 outpatient centres in 16 countries. Patients were randomly assigned (1:1) to receive once-daily oral tablets containing 150 mg elvitegravir, 150 mg cobicistat, 200 mg emtricitabine, and 10 mg tenofovir alafenamide (E/C/F/tenofovir alafenamide) or 300 mg tenofovir disoproxil fumarate (E/C/F/tenofovir disoproxil fumarate) with matching placebo. Randomisation was done by a computer-generated allocation sequence (block size 4) and was stratified by HIV-1 RNA, CD4 count, and region (USA or ex-USA). Investigators, patients, study staff, and those assessing outcomes were masked to treatment group. All participants who received one dose of study drug were included in the primary intention-to-treat efficacy and safety analyses. The main outcomes were the proportion of patients with plasma HIV-1 RNA less than 50 copies per mL at week 48 as defined by the US Food and Drug Administration (FDA) snapshot algorithm (pre-specified non-inferiority margin of 12%) and pre-specified renal and bone endpoints at 48 weeks. These studies are registered with ClinicalTrials.gov, numbers NCT01780506 and NCT01797445.

Findings We recruited patients from Jan 22, 2013, to Nov 4, 2013 (2275 screened and 1744 randomly assigned), and gave treatment to 1733 patients (866 given E/C/F/tenofovir alafenamide and 867 given E/C/F/tenofovir disoproxil fumarate). E/C/F/tenofovir alafenamide was non-inferior to E/C/F/tenofovir disoproxil fumarate, with 800 (92%) of 866 patients in the tenofovir alafenamide group and 784 (90%) of 867 patients in the tenofovir disoproxil fumarate group having plasma HIV-1 RNA less than 50 copies per mL (adjusted difference 2·0%, 95% CI −0·7 to 4·7). Patients given E/C/F/tenofovir alafenamide had significantly smaller mean serum creatinine increases than those given E/C/F/tenofovir disoproxil fumarate (0·08 vs 0·12 mg/dL; p<0·0001), significantly less proteinuria (median % change −3 vs 28; p<0·0001), and a significantly smaller decrease in bone mineral density at spine (mean % change −1·30 vs −2·86; p<0·0001) and hip (−0·66 vs −2·55; p<0·0001) at 48 weeks.

Interpretation Through 48 weeks, more than 90% of patients given E/C/F/tenofovir alafenamide or E/C/F/tenofovir disoproxil fumarate had virological success. Renal and bone effects were significantly reduced in patients given E/C/F/tenofovir alafenamide. Although these studies do not have the power to assess clinical safety events such as renal failure and fractures, our data suggest that E/C/F/tenofovir alafenamide will have a favourable long-term renal and bone safety profile.

Funding Gilead Sciences.

- GFR'nin azaldığı bir ortamda TAF takiben tenofovir düzeyleri arttığından, devam eden çalışmalar bu popülasyonda uzun süreli kullanımının güvenliğini doğrulayana kadar, ilaca bağlı potansiyel böbrek toksisitesi açısından izlenmeli.
- Geçmişinde TDF'ye bağlı böbrek toksisitesi öyküsü olan bireylerde TAF'ın güvenliği araştırılmamıştır.

Articles

Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials

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Interpretation Through 48 weeks, more than 90% of patients given E/C/F/tenofovir alafenamide or E/C/F/tenofovir disoproxil fumarate had virological success. Renal and bone effects were significantly reduced in patients given E/C/F/tenofovir alafenamide. Although these studies do not have the power to assess clinical safety events such as renal failure and fractures, our data suggest that E/C/F/tenofovir alafenamide will have a favourable long-term renal and bone safety profile.

Funding Gilead Sciences.

HIV ile Enfekte Kişilerde SDBY Yönetimi

- SDBY olanlar hem hemodiyaliz hem de periton diyalizi için adaydır.
- Böbrek Tx için değerlendirilmeli.
- HIV ile enfekte böbrek nakli alıcıları önemli ilaç-ilaç etkileşimleri.
- HIV ile enfekte donörlerden HIV ile enfekte alıcılara böbrek naklinin güvenliği değerlendirilmiş.

N Engl J Med. 2015 February 12; 372(7): 613–620. doi:10.1056/NEJMoa1408896.

HIV-Positive–to–HIV-Positive Kidney Transplantation — Results at 3 to 5 Years

Elmi Muller, M.B., Ch.B., M.Med., Zunaid Barday, M.B., Ch.B., Marc Mendelson, M.D., Ph.D., and **Delawir Kahn, M.B., Ch.B., Ch.M.**
Transplant Unit, Department of Surgery (E.M.), Division of Nephrology, Department of Medicine (Z.B.), Division of Infectious Diseases and HIV Medicine, Department of Medicine (M.M.), and the Department of Surgery (D.K.), University of Cape Town, Groote Schuur Hospital, Cape Town, South Africa

Abstract

BACKGROUND—The outcome of kidney transplantation in human immunodeficiency virus (HIV)–positive patients who receive organs from HIV-negative donors has been reported to be similar to the outcome in HIV-negative recipients. We report the outcomes at 3 to 5 years in HIV-positive patients who received kidneys from HIV-positive deceased donors.

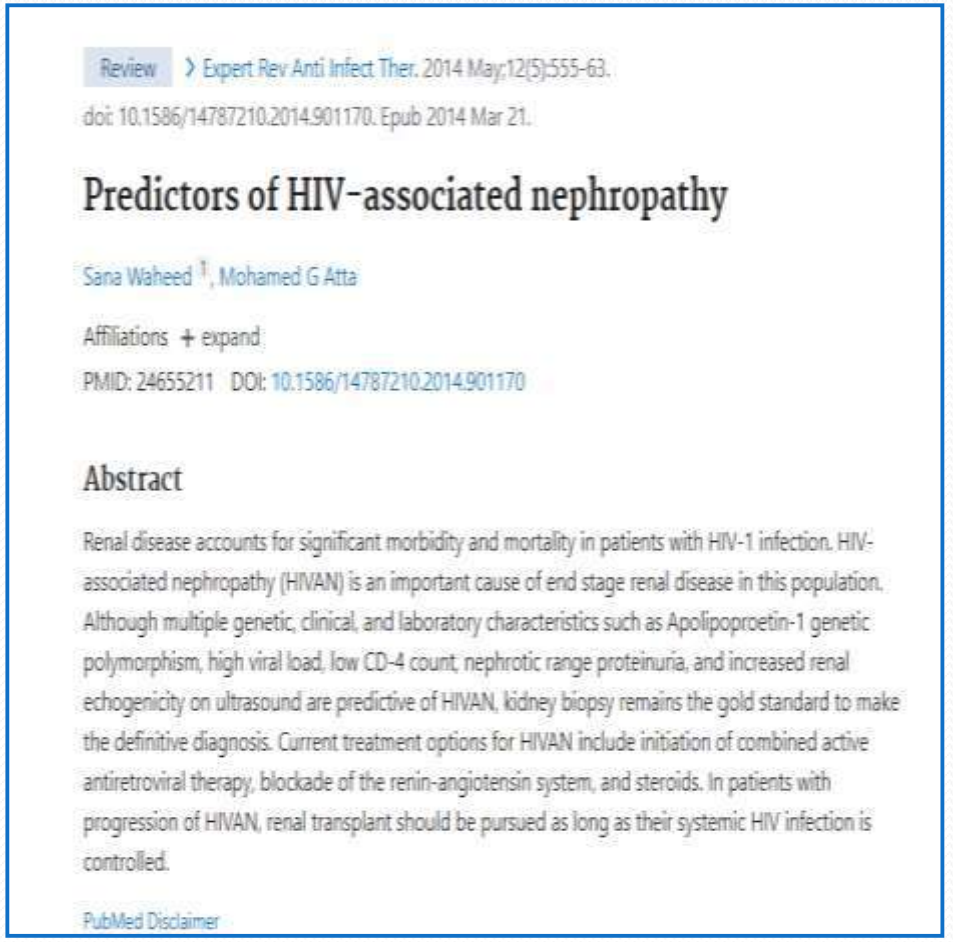
METHODS—We conducted a prospective, nonrandomized study of kidney transplantation in HIV-infected patients who had a CD4 T-cell count of 200 per cubic millimeter or higher and an undetectable plasma HIV RNA level. All the patients were receiving antiretroviral therapy (ART). The patients received kidneys from deceased donors who tested positive for HIV with the use of fourth-generation enzyme-linked immunosorbent assay at the time of referral. All the donors either had received no ART previously or had received only first-line ART.

RESULTS—From September 2008 through February 2014, a total of 27 HIV-positive patients underwent kidney transplantation. Survivors were followed for a median of 2.4 years. The rate of survival among the patients was 84% at 1 year, 84% at 3 years, and 74% at 5 years. The corresponding rates of graft survival were 93%, 84%, and 84%. (If a patient died with a functioning graft, the calculation was performed as if the graft had survived.) Rejection rates were 8% at 1 year and 22% at 3 years. HIV infection remained well controlled, with undetectable virus in blood after the transplantation.

CONCLUSIONS—Kidney transplantation from an HIV-positive donor appears to be an additional treatment option for HIV-infected patients requiring renal-replacement therapy.

Hikaye ve Fizik Muayene

- HIVAN, klasik olarak GFR'de hızlı bir düşüş ve nefrotik aralıkta proteinüri ile kendini gösterir.
- Alt ekstremitelerde ödem ve hipertansiyon gibi nefropatinin diğer belirtileri nadirdir.
- Bu popülasyonda eşlik eden durumlar ve enfeksiyonlar muhtemel olduğundan, diğer etiyolojilerin dışlanması önemlidir.



Review › Expert Rev Anti Infect Ther. 2014 May;12(5):555-63.

doi: 10.1586/14787210.2014.901170. Epub 2014 Mar 21.

Predictors of HIV-associated nephropathy

Sana Waheed [1], Mohamed G Atta

Affiliations + expand

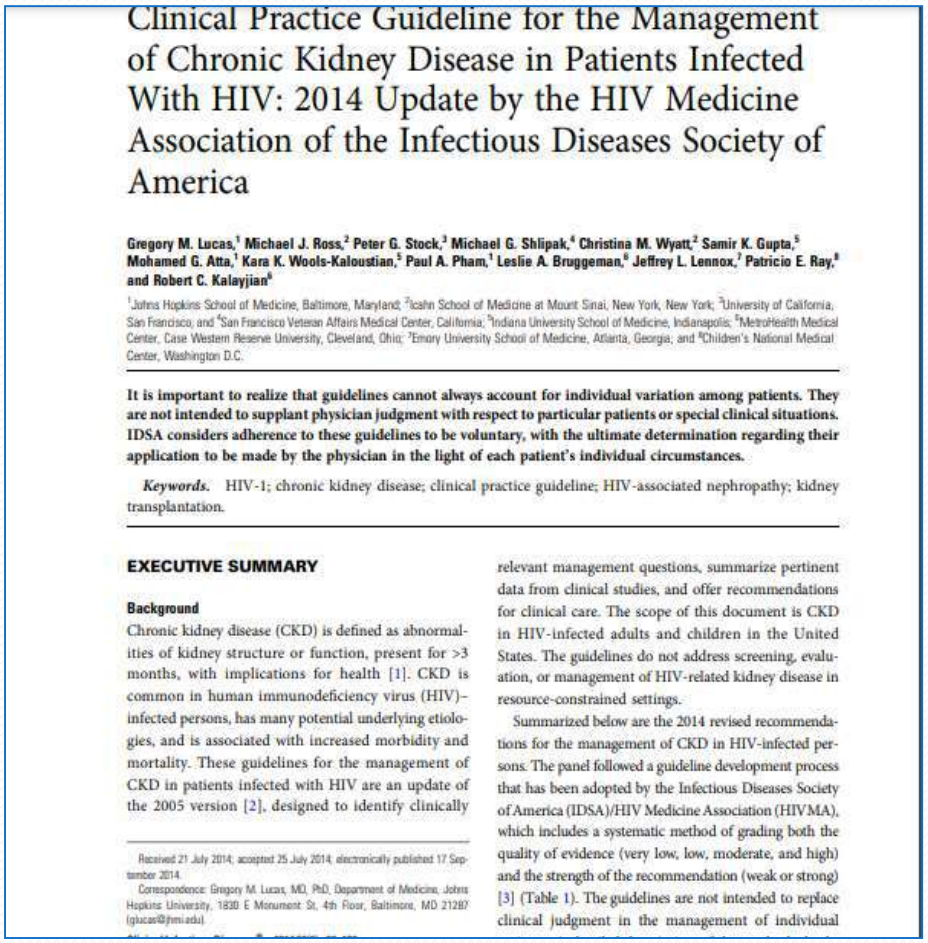
PMID: 24655211 DOI: 10.1586/14787210.2014.901170

Abstract

Renal disease accounts for significant morbidity and mortality in patients with HIV-1 infection. HIV-associated nephropathy (HIVAN) is an important cause of end stage renal disease in this population. Although multiple genetic, clinical, and laboratory characteristics such as Apolipoproetin-1 genetic polymorphism, high viral load, low CD-4 count, nephrotic range proteinuria, and increased renal echogenicity on ultrasound are predictive of HIVAN, kidney biopsy remains the gold standard to make the definitive diagnosis. Current treatment options for HIVAN include initiation of combined active antiretroviral therapy, blockade of the renin-angiotensin system, and steroids. In patients with progression of HIVAN, renal transplant should be pursued as long as their systemic HIV infection is controlled.

Nefrolojik Değerlendirme

- Amerika Enfeksiyon Hastalıkları Derneği HIV Tıp Derneği'nin kılavuzları,
- HIV + hastalarda HIV nefropati taramasının serum kreatinin ve eGFR yanı sıra,
- İdrar tahlili veya kantitatif proteinüri ölçümü,
- ART başlangıcında veya değiştirildiğinde ve HIV ile enfekte stabil hastalarda yılda en az iki kez ölçülmesi gerektiğini belirtmektedir.



Clinical Practice Guideline for the Management of Chronic Kidney Disease in Patients Infected With HIV: 2014 Update by the HIV Medicine Association of the Infectious Diseases Society of America

Gregory M. Lucas,[1] Michael J. Ross,[2] Peter G. Stock,[3] Michael G. Shlipak,[4] Christina M. Wyatt,[2] Samir K. Gupta,[5] Mohamed G. Atta,[1] Kara K. Wools-Kaloustian,[5] Paul A. Pham,[1] Leslie A. Bruggeman,[6] Jeffrey L. Lennox,[7] Patricio E. Ray,[8] and Robert C. Kalayjian[6]

[1]Johns Hopkins School of Medicine, Baltimore, Maryland; [2]Icahn School of Medicine at Mount Sinai, New York, New York; [3]University of California, San Francisco, and [4]San Francisco Veteran Affairs Medical Center, California; [5]Indiana University School of Medicine, Indianapolis; [6]MetroHealth Medical Center, Case Western Reserve University, Cleveland, Ohio; [7]Emory University School of Medicine, Atlanta, Georgia; and [8]Children's National Medical Center, Washington D.C.

It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. IDSA considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

Keywords. HIV-1; chronic kidney disease; clinical practice guideline; HIV-associated nephropathy; kidney transplantation.

EXECUTIVE SUMMARY

Background

Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health [1]. CKD is common in human immunodeficiency virus (HIV)–infected persons, has many potential underlying etiologies, and is associated with increased morbidity and mortality. These guidelines for the management of CKD in patients infected with HIV are an update of the 2005 version [2], designed to identify clinically relevant management questions, summarize pertinent data from clinical studies, and offer recommendations for clinical care. The scope of this document is CKD in HIV-infected adults and children in the United States. The guidelines do not address screening, evaluation, or management of HIV-related kidney disease in resource-constrained settings.

Summarized below are the 2014 revised recommendations for the management of CKD in HIV-infected persons. The panel followed a guideline development process that has been adopted by the Infectious Diseases Society of America (IDSA)/HIV Medicine Association (HIVMA), which includes a systematic method of grading both the quality of evidence (very low, low, moderate, and high) and the strength of the recommendation (weak or strong) [3] (Table 1). The guidelines are not intended to replace clinical judgment in the management of individual

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- Böbrek USg, HIVAN tanısı için olası bir invazif olmayan test olarak değerlendirilmiş.
- Böbrek ekojenitesinin yüksek puanlarının HIVAN için güçlü belirleyici, düşük puanların ise etkili bir şekilde dışlayabildiği gösterilmiş.
- Hastaların çoğunun ekojenite skorları bu iki değer arasında yer almakta.

Review > Nat Rev Nephrol. 2015 Mar;11(3):150-60. doi: 10.1038/nrneph.2015.9. Epub 2015 Feb 17.

HIV-associated nephropathies: epidemiology, pathology, mechanisms and treatment

Avi Z Rosenberg [1], Saraladevi Naicker [2], Cheryl A Winkler [3], Jeffrey B Kopp [4]

Affiliations + expand

PMID: 25686569 DOI: 10.1038/nrneph.2015.9

Abstract

HIV is a highly adaptive, rapidly evolving virus, which is associated with renal diseases including collapsing glomerulopathy-the classic histomorphological form of HIV-associated nephropathy. Other nephropathies related to viral factors include HIV-immune-complex kidney disease and thrombotic microangiopathy. The distribution of HIV-associated kidney diseases has changed over time and continues to vary across geographic regions worldwide. The reasons for this diversity are complex and include a critical role of APOL1 variants and possibly other genetic factors, disparities in access to effective antiviral therapies, and likely other factors that we do not yet fully understand. The mechanisms responsible for HIVAN, including HIV infection of podocytes and tubular epithelial cells, the molecules responsible for HIV entry, and diverse mechanisms of cell injury, have been the focus of much study. Although combined antiretroviral therapy is effective at preventing and reversing HIVAN, focal segmental glomerulosclerosis, arterionephrosclerosis and diabetic nephropathy are increasingly common in individuals who have received such therapy for many years. These diseases are associated with metabolic syndrome, obesity and premature ageing. Future directions for HIV-related kidney disease will involve regular screening for drug nephrotoxicity and incipient renal disease, as well as

- Böbrek biyopsisi genellikle kesin tanıya ulaşmanın tek yoludur.
- Biyopsi endikasyonları genel popülasyonla aynıdır.
- Böbrek biyopsisi yapma kararı, klinik tabloyu, alternatif tanı olasılığını, tedavi seçeneklerini ve işlemle ilişkili riskleri dikkate almalıdır.
- Tedavi farklı olduğundan, HIVAN hastalarını cART'ın neden olduğu nefropatiye karşı ayırmak önemli.

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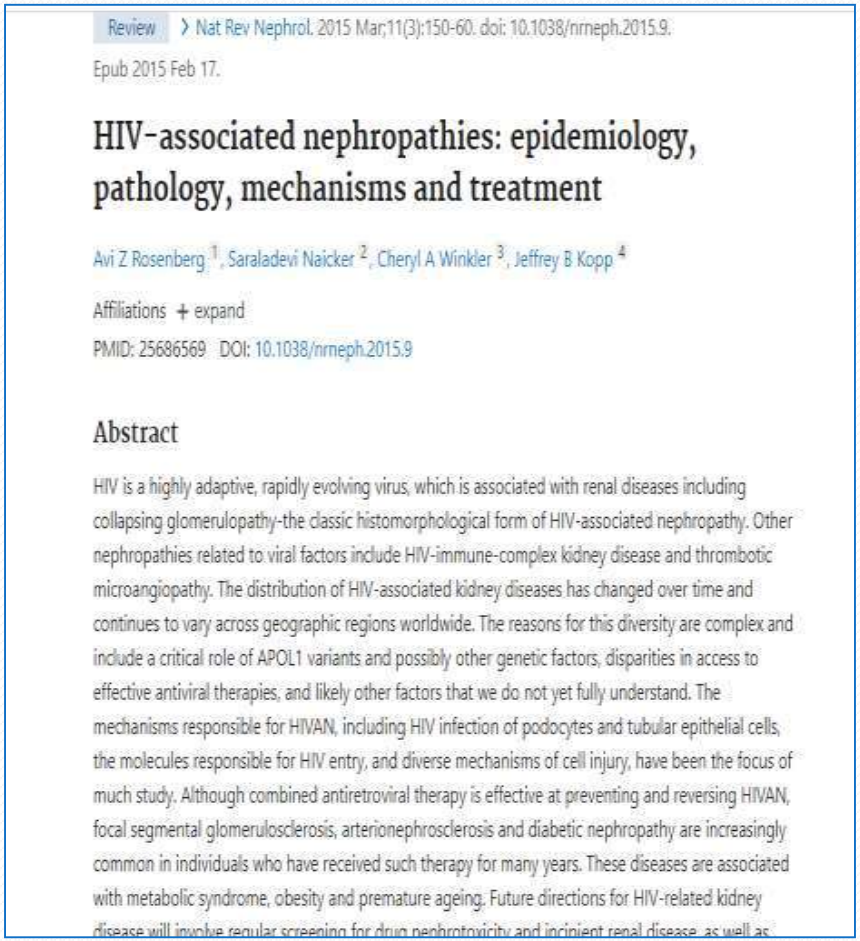
HIVAN ve Tedaviye Bağlı Böbrek Hastalık Ayırıcı Tanısı

- HIVAN'lı hastalar öykü ve fizik muayene bulgularının yanı sıra,
- CD4 sayısı <200 hücre/mm3,
- Viral yük >400 kopya/mL,
- Böbrek fonks. hızlı düşüş,
- Proteinüri >300 mg/24 saat,
- İdrar tahlilinde silendirler,
- Yoğun kortikal ekojeniteye sahip büyük boyutlu böbrekler.



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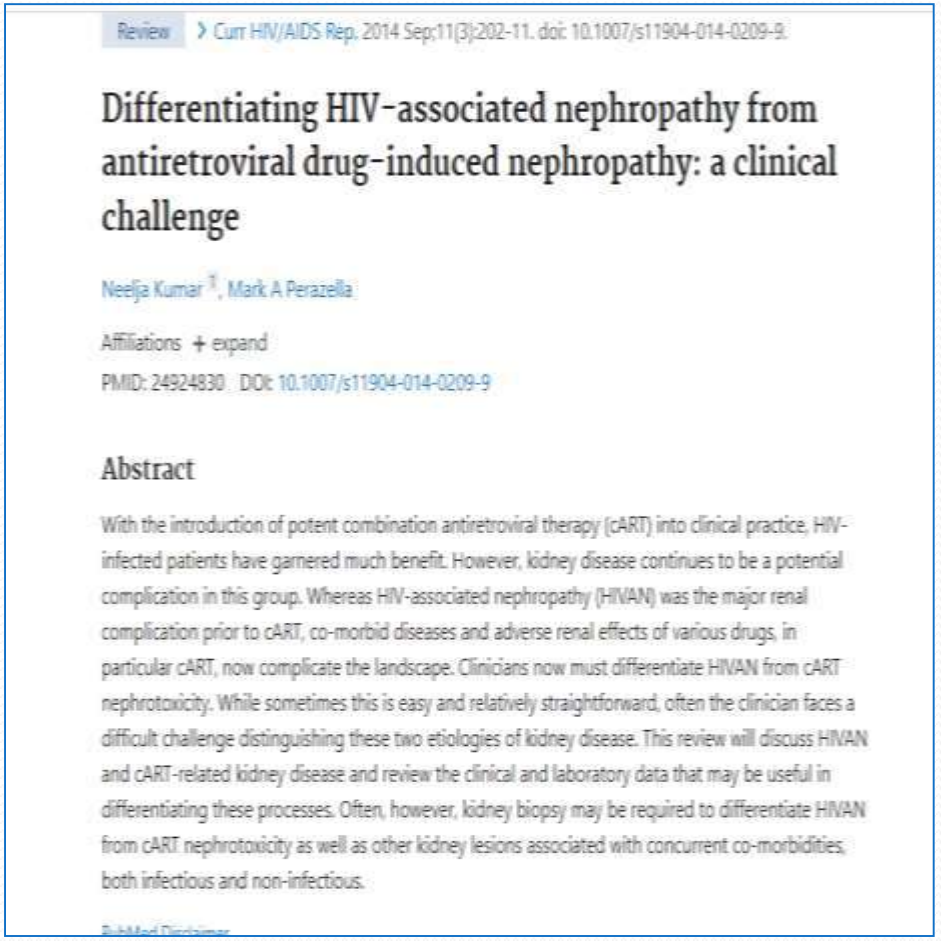
cART Bağlı Nefropati

- CD4 sayısı >200 hücre/mm3,
- Viral yük <400 kopya/mL,
- Proteinüri <30 mg/24 saat,
- Böbrek fonks. hafif bir azalma,
- Hematüri veya lökositüri,
- İdrarda iğne veya çubuk benzeri kristaller,
- Dikkat çekmeyen Usg bulguları.



Review > Curr HIV/AIDS Rep. 2014 Sep;11(3):202-11. doi: 10.1007/s11904-014-0209-9.

Differentiating HIV-associated nephropathy from antiretroviral drug-induced nephropathy: a clinical challenge

Neelja Kumar [1], Mark A Perazella

Affiliations + expand

PMID: 24924830 DOI: 10.1007/s11904-014-0209-9

Abstract

With the introduction of potent combination antiretroviral therapy (cART) into clinical practice, HIV-infected patients have garnered much benefit. However, kidney disease continues to be a potential complication in this group. Whereas HIV-associated nephropathy (HIVAN) was the major renal complication prior to cART, co-morbid diseases and adverse renal effects of various drugs, in particular cART, now complicate the landscape. Clinicians now must differentiate HIVAN from cART nephrotoxicity. While sometimes this is easy and relatively straightforward, often the clinician faces a difficult challenge distinguishing these two etiologies of kidney disease. This review will discuss HIVAN and cART-related kidney disease and review the clinical and laboratory data that may be useful in differentiating these processes. Often, however, kidney biopsy may be required to differentiate HIVAN from cART nephrotoxicity as well as other kidney lesions associated with concurrent co-morbidities, both infectious and non-infectious.

HIVAN Ayırıcı Tanı

- HIVICK,
- MPGN (eş zamanlı hepatit C)
- Amiloidoz,
- Minimal değişiklik hastalığı,
- Enfeksiyon sonrası GN,
- Trombotik mikroanjiyopati,
- Diyabetik nefropati,
- İgA nefropatisi,
- Membranöz glomerülopati,

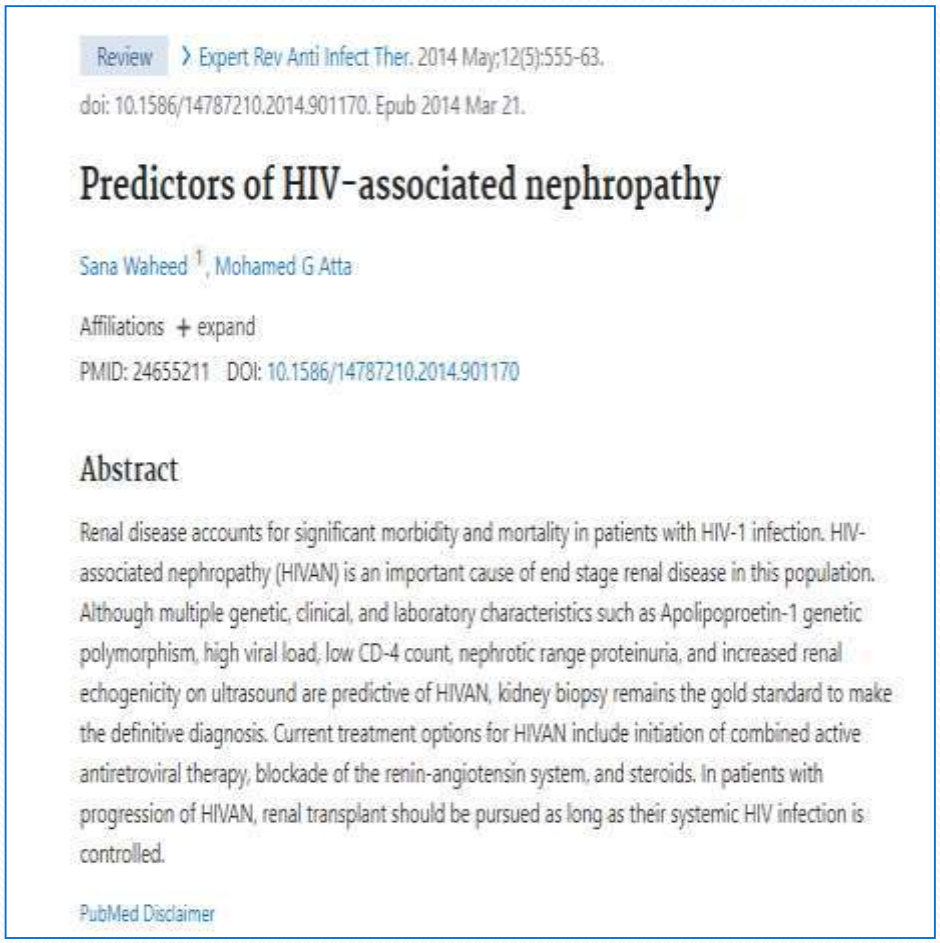
Table 1. Differential diagnosis: possible histologic patterns in patients suspected of having HIVAN

	Clinical features	Histopathologic findings
HIVAN	Nephrotic range proteinuria, renal insufficiency; edema and hypertension are less prominent findings even in the setting of renal failure [49]	Collapsing type of FSGS with segmental or global retraction of the glomerular capillary walls and luminal occlusion, cystic tubular dilatation, interstitial inflammation, the presence of TRI bodies
Classic FSGS	Nephrotic syndrome (proteinuria, edema, hypercholesterolemia, hypoalbuminemia)	Idiopathic or secondary to segmental necrosis or nephron loss. Segment of tuft replaced by fibrosis
Membranous proliferative glomerulonephritis	Nephrotic syndrome or mixed nephrotic-nephritic syndrome (hematuria, hypertension, oliguria, edema)	Hypercellular, hyperlobular glomeruli with double-contour GBM
Renal amyloidosis	Proteinuria often severe enough to produce nephrotic syndrome	Deposition of insoluble fibrillar protein in glomerulus and vessel walls, stains with Congo and Sirius red
Diabetic nephropathy	Proteinuria, sometimes with nephrotic syndrome but may progress to features of chronic renal failure	Diffuse and nodular glomerulosclerosis, hyalinized arterioles, capsular drops, fibrin caps, thickened GBM
ICGN	Variable depending on etiology. Usually within a spectrum of nephrotic and nephritic symptoms	The site of immune complex deposition is dependent on the size of the complexes which is dependent on the antigen and the type of immunoglobulin produced by the host
Minimal-change nephropathy	Nephrotic syndrome without hematuria and usually without impairment of renal function	Normal light microscopy and immunofluorescence, "fused" podocyte foot processes on electron microscopy
Thrombotic microangiopathy	Symptoms of acute kidney injury with variable extrarenal manifestations such as thrombocytopenia, microangiopathic hemolytic anemia, and fever [50]	Thrombi in glomerular capillaries, arteries, and arterioles which distend the vascular lumen and entrap red and white blood cells [51]. Bloodless appearance with glomerular endothelial cell swelling. [51]
HIVICK	Lupus-like lesions in some PLHIV without serologic evidence of lupus. [47] Commonly presents with proteinuria, hematuria, reduced GFR, and low levels of complements [47]	Variable mesangial and endocapillary hypercellularity [47]. Tubuloreticular aggregates in endothelial cells [47]. "Full-house" staining with mesangial and variable capillary wall granular deposits [47]. Immune complex deposits on electron microscopy [47]

HIVAN, HIV-associated nephropathy; FSGS, focal segmental glomerulosclerosis; PLHIV, people living with HIV; TRI, tubuloreticular inclusion; ICGN, immune complex glomerulonephritis; HIVICK, HIV-immune complex disease. Adapted from Wheater's Functional Histology E-Book: a Text and Colour Atlas,

HIVAN Prognoz

- cART öncesi HIVAN, 2-4 ay içinde SDBH hızla ilerleyen agresif bir hastalıktı.
- Şu anda prognoz daha iyi.
- HIVAN'lı hastaların durumu, böbrek hastalığının diğer nedenleri olan hastalardan sürekli daha kötüdür.



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HIVAN Komplikasyonları

- HIVAN'ın temel komplikasyonu KBH'ye ilerleme ve SDBY'dir.
- Diğer komplikasyonlar arasında çok daha az yaygın hipertansiyon ve alt ekstremite ödemi.

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Hasta Eğitimi

- Hastalar antiretroviral ilaçlara uymaları,
- Birinci basamak hekimleri ve nefrologları ile düzenli takipleri konusunda teşvik edilmelidir.

Sonuçların İyileştirilmesine Yönelik Öneriler

- HIVAN'ın agresif doğası nedeniyle, hızlı tanı ve tedavi yapılmalıdır.
- Ekip yaklaşımı hasta sonuçlarını iyileştirecektir.
- Ekipte birinci basamak sağlık hizmeti sağlayıcısı, nefrolog ve enfeksiyon hastalıkları uzmanı bulunmalıdır.
- HIV'li her hastada, HIV ilişkilendirme kılavuzlarına göre sık sık böbrek fonksiyon testleri takip edilmelidir.

- Alternatif tanılar ve işlemle ilişkili riskler dikkate alındıktan sonra biyopsi düşünülmelidir.
- Girişimsel radyolog ve patologun ekibin bir parçası olması gerekecektir.
- HIVAN'lı hastalarda cART'ın başlatılmasında CD4 sayısı ve viral yük, dikkate alınması gereken önlemler olmalıdır.

TEŞEKKÜR EDERİM