Kronik Böbrek Hastalığının Karakterindeki Değişiklik

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Kronik Böbrek Hastalığı Tanım

- Glomerül filtrasyon hızı (GFH)'nın 3 aydan uzun bir sürede 60 ml/ dk/1,73m^2'den düşük olması veya GFH'ında azalma olsun olmasın böbrekte 3 aydan uzun süren yapısal ve işlevsel bozukluk olarak tanımlanmaktadır .

- KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney DiseaseKidney International Supplements (2013) 3, 91–111

Azalmış GFH

- 3 aydan uzun süredir GFH <60 ml/min/1.73 m2 (GFH katagori G3a–G5)

Böbrek Hasarı (3 aydan uzun süredir)

- Albuminüri
- İdrar anormallikleri
- Tübüler bozukluklara bağlı elektrolit ve diğer bozukluklar
- Histolojide saptanan anormallikler
- Görüntüleme ile saptanan anormallikler
- Böbrek transplantasyon hikayesinin olması

Table 2. Definitions of AKI, CKD, and AKD

	Functional criteria	Structural criteria
AKI	Increase in SCr by 50% within 7 days, *OR* Increase in SCr by 0.3 mg/dl (26.5 µmol/l) within 2 days, *OR* Oliguria	No criteria
CKD	GFR <60 ml/min per 1.73 m^2 for >3 months	Kidney damage for >3 months
AKD	AKI, *OR* GFR <60 ml/min per 1.73 m^2 for <3 months, *OR* Decrease in GFR by ≥35% or increase in SCr by >50% for <3 months	Kidney damage for <3 months
NKD	GFR ≥60 ml/min per 1.73 m^2 Stable SCr	No damage

GFR assessed from measured or estimated GFR. Estimated GFR does not reflect measured GFR in AKI as accurately as in CKD. Kidney damage assessed by pathology, urine or blood markers, imaging, and—for CKD—presence of a kidney transplant. NKD indicates no functional or structural criteria according to the definitions for AKI, AKD, or CKD. Clinical judgment is required for individual patient decision-making regarding the extent of evaluation that is necessary to assess kidney function and structure.

AKD, acute kidney diseases and disorders; AKI, acute kidney injury; CKD, chronic kidney disease; GFR, glomerular filtration rate; NKD, no known kidney disease; SCr, serum creatinine.

GFR categories (ml/min/ 1.73 m^2) Description and range		
G1	Normal or high	≥90
G2	Mildly decreased	60-89
G3a	Mildly to moderately decreased	45-59
G3b	Moderately to severely decreased	30-44
G4	Severely decreased	15-29
G5	Kidney failure	<15

Albüminüri Evreleri	AER (mg/gün)	Tanımlar
A1	<30	Normal/yüksek normal
A2	30-300	Yüksek
A3	>300	Çok yüksek

Epidemiyoloji

- Dünyada KBH hastalığının prevelansı %8-13 arasındadır.
- Genç populasyonda düşük GFH <60mL/min/1.73 m^2 prevelansı %1,8 ile nispeten düşük saptanmıştır.

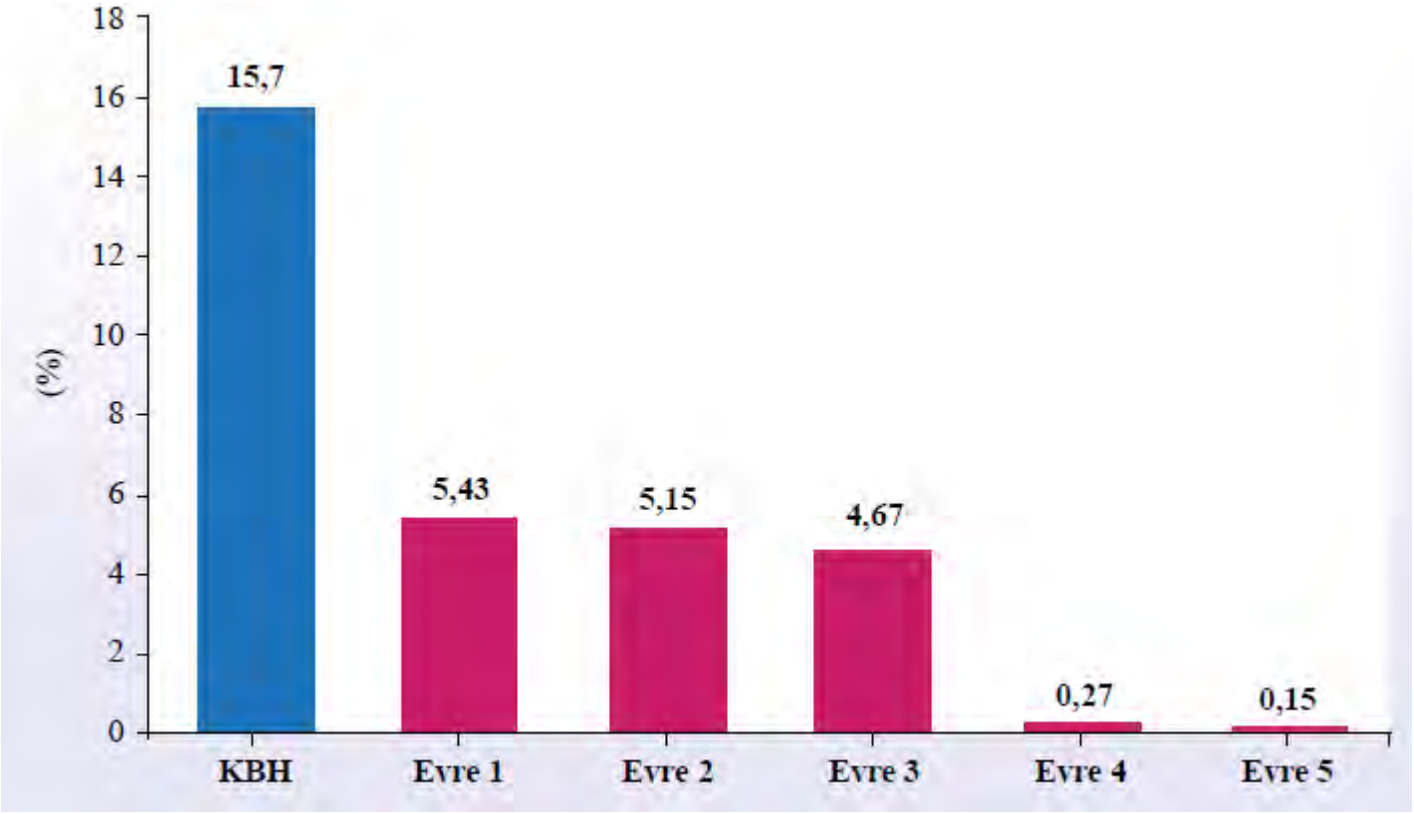
- Delanaye P et al Epidemiology of chronic kidney disease:think (at least) twice Clinical Kidney Journal, 2017, vol. 10, no. 3, 370–374

Toplum temelli epidemiyolojik çalışmalarda mikroalbüminüri ve kronik böbrek hastalığı prevalansları.

Çalışma	Ülke	Tasarım	Olgu Sayısı	MA (%)	KBH (%)
NHANES III	ABD	KÇ/L	15.626	12	11
PREVEND	Hollanda	KÇ/L	40.000	7	-
NEOERICA	İngiltere	KÇ/Hizmet bazlı	130.226	-	11 (K), 6(E)
HUNT II	Norveç	KÇ	65.181	6	10
EPIC-Nor folk	İngiltere	KÇ	23.964	12	-
MONICA	Almanya	KÇ	2.136	8	-
AusDiab	Avustralya	KÇ	11.247	6	10
TAIWAN	Tayvan	KÇ/L	462.293	-	12
Beijing	Çin	KÇ	13.925	-	13
Takahata	Japonya	KÇ	2.321	14	-
CREDIT	Türkiye	KÇ/L	10.748	10,2	15,7

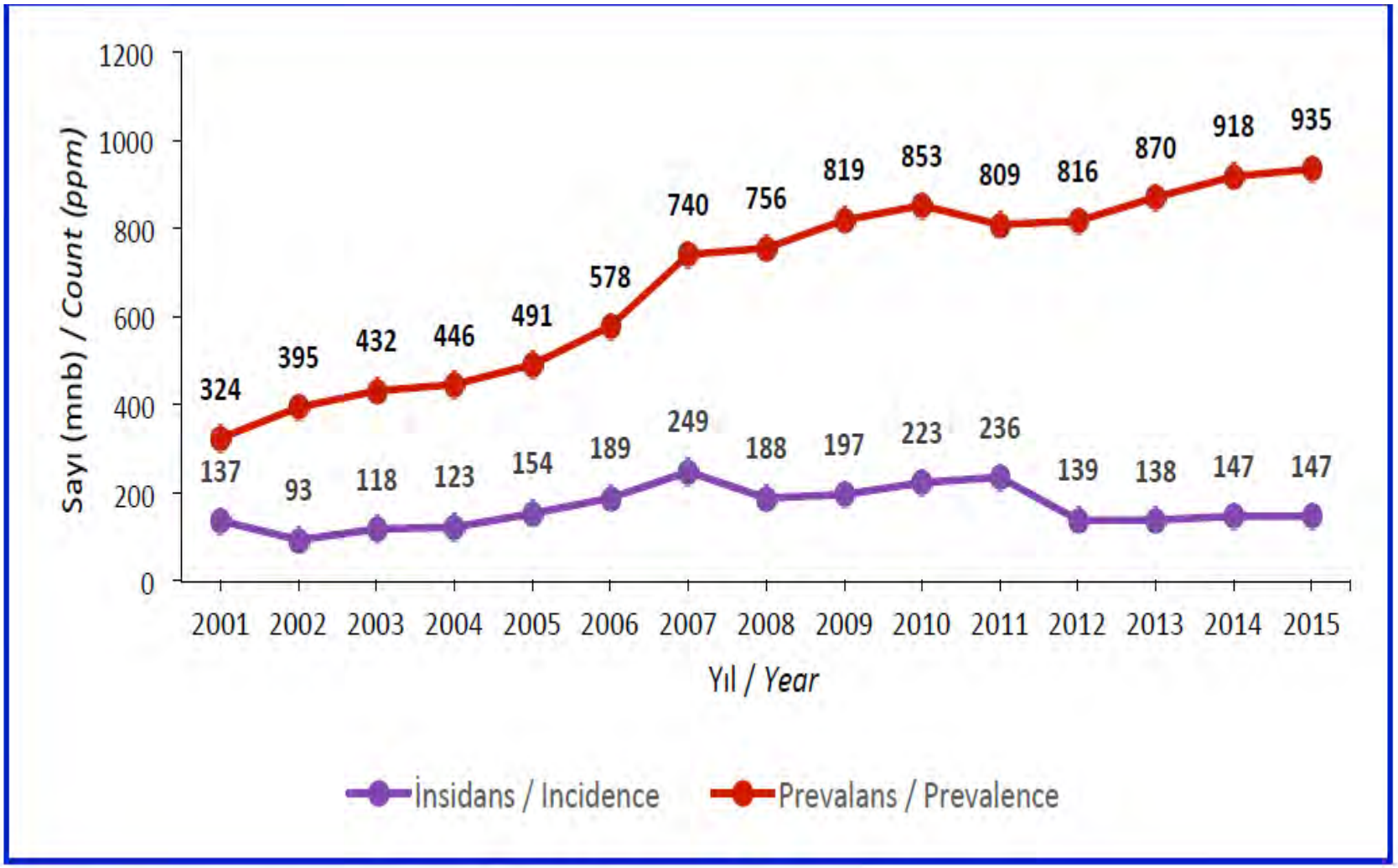
KÇ: Kesitsel çalışma; L: Longitudinal çalışma; MA: Mikroalbüminüri; KBH: Kronik böbrek hastalığı; K: Kadın; E: Erkek

Türkiye'de erişkin popülasyonda kronik böbrek hastalığı prevalansı ve evrelere göre dağılımı (CREDIT çalışması).



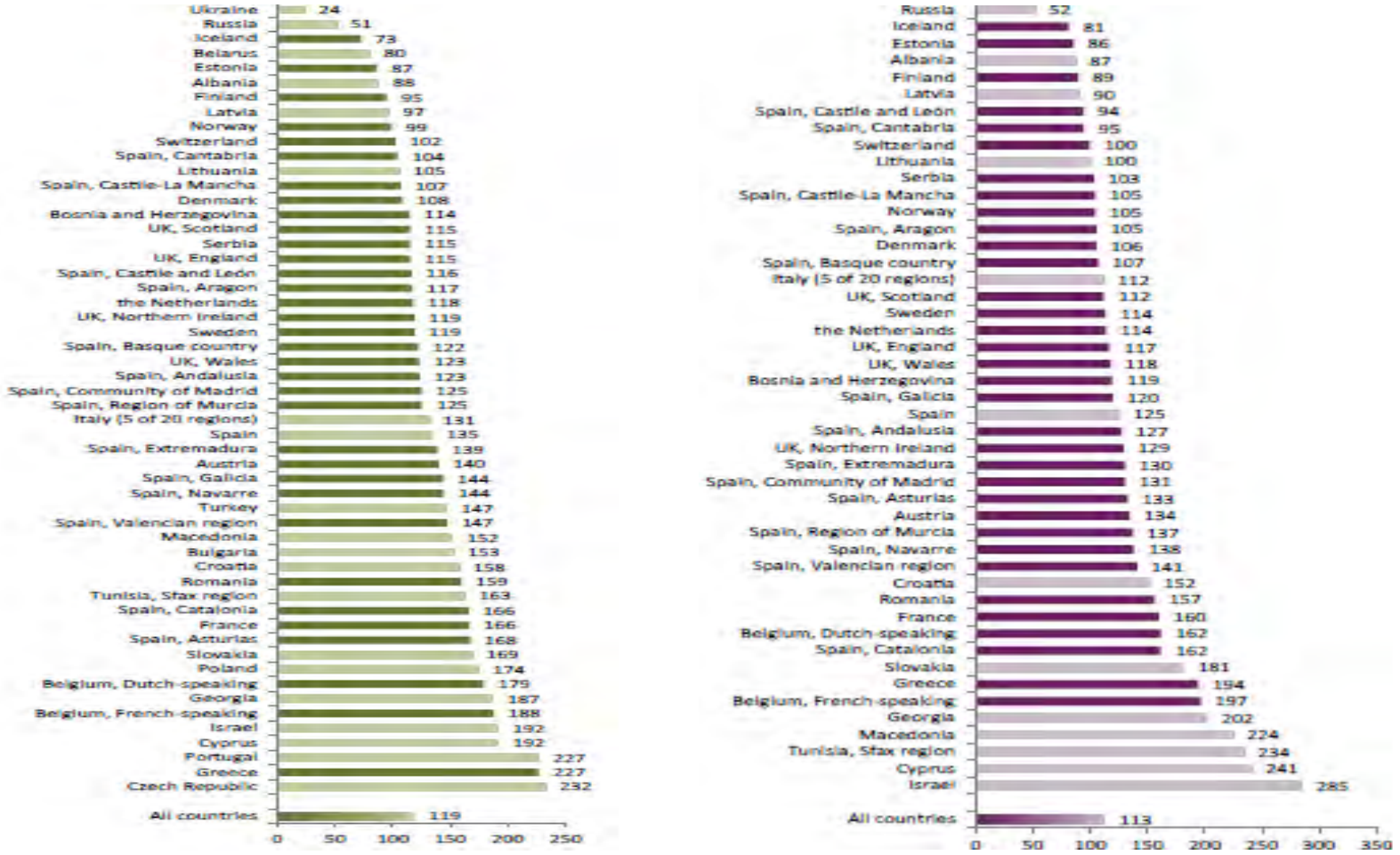
- KBH prevelnsı %6,1 (CKD EPI)
- KBH prevelansı %10 (MDRD)
- Düşük eGFH<60ml/dk %1,8 (CKD EPI) ve %6,0 (MDRD)
- Subsahran Afrikada KBH prevelansı %13,9 saptanmıştır.

- Adeniyi AB et al. Prevalence of chronic kidney disease and association witk cardiovascular risk factors among teachers in cape Town, South Africa. Chronic kidney journal 2017
- Stanifer J et al. The epidemiology of chronic kidney disease in sub saharan Africa: a systemic review and metaanalysis . Lancet Glob health 2014.



ŞEKİL 1. Türkiye'de RRT gerektiren SDBY insidansı ve prevalansı.

ERA-EDTA 2015 **yılı yıllık raporuna göre çeşitli ülkelerde son dönem böbrek yetmezliğinin insidansı**



Milyon nüfus başına

	n	%
Diabetes mellitus / *Diabetes mellitus*	1804	34.61
Tip 1 DM / *Type 1 DM*	362	6.94
Tip 2 DM / *Type 2 DM*	1442	27.67
Hipertansiyon / *Hypertension* *	1405	26.96
Glomerülonefrit / *Glomerulonephritis*	309	5.93
Polikistik böbrek hastalıkları / *Polycystic kidney diseases*	238	4.57
Amiloidoz / *Amyloidosis*	98	1.88
Tübülointerstisyel nefrit / *Tubulointerstitial nephritis*	94	1.80
Obstrüktif nefropati / *Obstructive nephropathy*	87	1.67
Renal vasküler hastalık / *Renal vascular disease*	52	1.00
Diğer / *Other*	426	8.17
Etyolojisi bilinmeyen / *Unknown etiology*	699	13.41
Toplam / *Total*	5212	100.00

Türkiye 2015 Yılı Ulusal Nefroloji, Diyaliz ve Transplantasyon Kayıt Sistemi Raporu (60 merkezin verileri)

Primer glomerulonefritler

- Minimal Değişiklik hastalığı
- Fokal segmental glomerulosklorosis
- C1q nefropati
- Membranöz Glomerulonefrit
- Membranoproliferatif glomerulonefrit
- Akut poststreptokokkal glomerulonefrit
- Immunglobulin A nefropati
- Fibriller glomerulonefrit
- Immunotaktoid glomerulonefrit
- Antiglomeruler basal memban glomerulonefrit
- Pauci immun glomerulonefrit (Granülomatoz

Mikro ve makro vasküler böbrek hastalıkları

- Trombotik mikroanjiopati (**HUS, aHUS**, TTP)
- Ateroembolik renal hastalıklar (**kolesterol kristal embolisi,)**
- Radyasyon nefropati
- Skleroderma
- Ork hücreli anemi
- Antifosfolipid sendromu
- Akut renal arter oklüzyonu
- Renal arter anevrizma
- Renal ven trombozu

HT nedenleri

- Renal parankimal hastalıklar
- Renovasküler hastalıklar
- Adrenokortikal hastalıklar
- Feokromasitoma
- Hipo-hipertiroidizm
- Hiperparatiroidizm
- Akromegali
- Nörolojenik hastalıklar
- İatrojenik ve diğer nedenler (oral kontraseptif, mineralokortikoid ve glukokortikoid kullanımı, antidepresan, alkol maruziyeti)

Kanser ve renal hastalıklar

*Prerenal
sepsis,
volüm deplesyonu (kusma, ishal, mukozit)
Hepatorenal sendrom
Kapiller leak sendromu
Hiperkalsemi
*İntrensek
Akut tubuler nekroz
İskemik (sepsis/şok), Nefrotoksik kullanımı
*Tubulointerstisyel nefritler (TLS, fosfat nefropatisi, allerjik reaksiyon, pivelonefrit

Kistik böbrek hastalıkları

- ODPBH
- ORPBH
- Otozomal dominant veya x ilişkili ODPBH
- Tuburosklerosis
- Von Hippel Lindavu sendromu
- Familyal renal hamartomaz ilişkili hiperparatiroidizm ve jaw tumor sendromu
- Hepatosit nükleer faktor 1 ilişkili nefropati
- Orofacial digital sendrom
- Otozomal dominant meduller kistik böbrek hastalığı

Genetik Böbrek hastalıkları

- FSGS
- SLE ve IgA nefropati
- Apolipoprotein L1
- Non APOL1 ilişkili hipertansif nefropati afrikan amerikalılarda
- Genetik komponentli diabetik nefropati

Glomerullerin genetik hastalıkları

- **Alport sendromu**
- İnce bazal membran nefropati
- HANACH sendromu (herediter anjiopati, nefropati, anevrizma, kas krampları)
- Pierson’s sendromu
- Konjenital nefrotik sendrom
- Steroid dirençli nefrotik sendrom
- Alfa aktinin 4 hastalığı , TRPC6, CD2AP (FSGS)
- MYH9 hastalığı
- PLCE1 hastalığı (familiyal diffüz mesangial sklerozis)

Renal tubuler genetik hastalıklrı

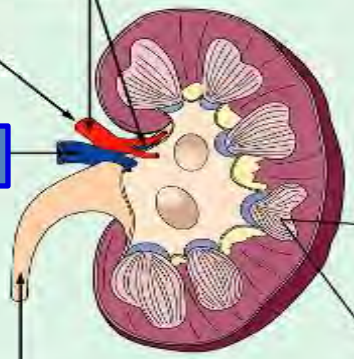
- Fankoni sendromu
- Dent’s hastalığı
- Oculocerebrorenal distrofi (Lowe sendromu)
- Sistinozis
- Glikojenozis
- Trizinomi
- Galaktozomi
- Wilson hastalığı
- Herediter fruktoz intoleransı
- Renal amino acid transport bozuklukları
- Renal fosfat transport bozuklukları

Nefrotoksik Ajanların Yol Açtığı Akut Böbrek Yetmezliği

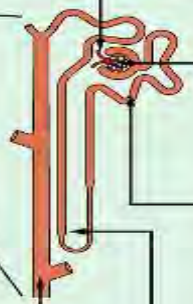
2. Renal arter

1.Prerenal Azotemi
Antihipertnsif ilaçlar , Diüretikler

9. Renal ven



3.Küçük Damar Hastalıkları:
Hemodinamik
NSAİD, ACEi, ARB, Radyokontrast maddeler, Siklosporin, Takrolimus, Norepinefrin, Kokain
Trombotik mikroanjiopati
Siklosporin, Takrolimus, Mitomisin C, Klopidogrel, Kinin, Oral kontraseptifler



4. Glomerüler Hastalıklar:
Hızlı Seyirli Glomerülonefrit :
D-penisilamin, Hidralazin, Propiltiyourasil, Organik solventler, Amfetamin, Silika bileşikleri

8.Postrenal tıkanma:
Papiller nekroz (*NSAİD,bileşik analjezikler*), üriner retansiyon (*antikolinerjikler,trisiklik antidepresanlar)*

5. Akut Tubüler Nekroz:
Amfoteresin, Aminoglikozitler, Sisplatin, İfosfamid, Asetaminofen, Ağır metaller, Herbal tedavisi, Radyokontrast maddeler, Pentamidin, Organik solventler, Parakuat, İV immunglobulinler

7.İntratübüler tıkanma:
Kristal oluşumu: Asiklovir, Etilen glikol, Sulfonamidler, Metotraksat, İndovir, Triamteren.

6. Akut İnterstisyel Nefrit:
Antibiyotikler (Penisilinler,Sefalosporinler,Rifampisin, Sulfametaksazol, Siprofloksasin)), NSAİD, lup ve tiyazid diüretikler, Allopurinol, Simetidin, Mesalazin, Analjezikler.

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İlaç İle ilşkili Böbrek Hastalığı

Primary etiology	Drug	Clinical or laboratory findings	Treatment
Decreased kidney perfusion	Diuretics, NSAIDs, ACE-I, cyclosporin, tacrolimus, radiocontrast media, interleukin-2, vasodilators (hydralazine, calcium-channel blockers, minoxidil, diazoxide)	Benign urine sediment, FE_{Na} <1%, UOsm >500	Suspend or discontinue medication, volume replacement as clinically indicated
Thrombotic microangiopathy	Cyclosporin, tacrolimus, mitomycin C, conjugated estrogens, quinine,5-fluorouracil, ticlopidine, clopidogrel, interferon, valaciclovir, gemcitabine, bleomycin	Fever, microangiopathic, hemolytic anemia, thrombocytopenia	Discontinue medication, provide supportive care, plasmapheresis if indicated
Cholesterol emboli	Heparin, warfarin, streptokinase	Fever, microangiopathic, hemolytic anemia, thrombocytopenia	Discontinue medication, provide supportive care, plasmapheresis if indicated

Tubular toxicity	Aminoglycosides, radiocontrast media, cisplatin, nedaplatin, methoxyflurane, outdated tetracycline, amphotericin B, cephaloridine, streptozocin, tacrolimus, carbamazepine, mithramycin, quinolones, foscarnet, pentamidine, i.v. gammaglobulin, fosfamide, zoledronate, cidofovir, adefovir, tenofovir, mannitol, dextran, hydroxyethylstarch	FE_{Na} >2%, UOsm <350, urinary sediment with granular casts, tubular epithelial cells	Discontinue medication, provide supportive care
Rhabdomyolysis	Lovastatin, ethanol, codeine, barbiturates, diazepam	Elevated CPK, ATN urine sediment	Discontinue medication, provide supportive care
Severe hemolysis	Quinine, quinidine, sulfonamides, hydralazine, triamterene, nitrofurantoin, mephenytoin	High LDH, decreased hemoglobin	Discontinue medication, provide supportive care
Immune-mediated interstitial inflammation	Penicillin, methicillin ampicillin, rifampin, sulfonamides, thiazides, cimetidine, phenytoin, allopurinol, cephalosporins, cytosine arabinoside, furosemide, interferon, NSAIDs, ciprofloxacin, clarithromycin, telithromycin, rofecoxib, pantoprazole, omeprazole, atazanavir	Fever, rash, eosinophilia, urine sediment showing pyuria, white-cell casts, eosinophiluria	Discontinue medication, provide supportive care

Primary etiology	Drug	Clinical or laboratory findings	Treatment
Glomerulopathy	Gold, penicillamine, captopril, NSAIDs, lithium, mefenamate, fenoprofen, mercury, interferon-α, pamidronate, fenclofenac, tolmetin, foscarnet	Edema, moderate to severe proteinuria, RBCs, RBC casts possible	Discontinue medication, provide supportive care
Intratubular obstruction (crystalluria and/or renal lithiasis)	Aciclovir, methotrexate, sulfanilamide, triamterene, indinavir, foscarnet, ganciclovir	Sediment can be benign with severe obstruction, ATN might be observed	Discontinue medication, provide supportive care
Ureteral obstruction (secondary to retroperitoneal fibrosis)	Methysergide, ergotamine, dihydroergotamine, methyldopa, pindolol, hydralazine, atenolol	Benign urine sediment, hydronephrosis on ultrasound	Discontinue medication, decompress ureteral obstruction by intrarenal stenting or percutaneous nephrostomy

- Nephron. 2017 Jun 9. doi: 10.1159/000474960. [Epub ahead of print]
- **Fibrotic Changes Mediating Acute Kidney Injury to Chronic Kidney Disease Transition.**
- Ó hAinmhire E[1], Humphreys BD.
- **Author information**
- **Abstract**
- End-stage renal disease (ESRD) is common, costly, and it results from progressive chronic kidney disease (CKD). ESRD claims many lives every year. It is increasingly recognized that

AKI tamamen iyileşme olsada uzun dönem sonra KBH ve SDBY ile sonuçlanabilir.

- Nephron. 2017 Jun 9. doi: 10.1159/000476078. [Epub ahead of print]
- **Epigenetic Changes in the Acute Kidney Injury-to-Chronic Kidney Disease Transition.**
- Nangaku M[1], Hirakawa Y, Mimura I, Inagi R, Tanaka T.
- **Author information**
- **Abstract**
- Previously acute kidney injury (AKI) had been believed to be a transient event, and recovery from AKI had been thought to lead to no

Fabri Hastalığı

- X ilişkili glikosfingolipid metabolizma hastalığıdır.
- İnsidansı 1/3100 ve 1/117000 arasındadır.

- X kromozomu üzerindeki GLA geninde Alfa galaktozidaz A eksikliği sonucu gelişmektedir.

Fabry

- Kardiyovasküler, renal, gastrointestinal ve nörolojik tutulumlar olmaktadır.
- Kadınlarda bulgular nadir olur ve organ tutulumu olmayabilir.

Organ tutulumu	Semptomlar
Sinir sistemi	Akroparestezi Sinirsel sağırlık İşitme kaybı, tinnitus Sıcağa tahammülsüzlük
Gastrointestinal sistem	Bulantı, kusma, diyare, postprandiyal şişkinlik ve ağrı, erken doyma hissi, kilo alamama
Deri	Anjiokeratomlar, hipohidrozis
Göz	Korneal ve lentiküler opasiteler, vaskülopati (retina ve konjunktiva)
Böbrek	Proteinüri, hematüri, tübüler konsantrasyon yeteneği bozulması, hiperfiltrasyon,
Kalp	Aritmiler, sol ventriküler hipertrofi, PR aralığının azalması, kapak yetersizlikleri

Tanı ve Tedavi

- İdrarda Gb3 atılımı artar
- GLA geninde mutasyon saptanması
- Renal biyopsi glikosfingolipid birikimi (Glycotriaosylceramide)
- Semptomatik tedavi ve enzim replasman tedavisi yapılmaktadır
- Agalsidaze alfa ve agalsidaze beta enzim replasmanı

Hemolitik Üremik Sendrom

- Hemolitik uremik sendrom, non-immün mikroanjiopatik hemolitik anemi, trombositopeni ve akut böbrek yetersizliği ile tanımlanan klinik sendromdur.
- Tipik formu shiga-toxin üreten enterohemorajik E coli (EHEC) ve atipik formu kontrolsüz alternatif kompleman yolu aktivasyonu ve sekonder nedenler (aHUS).
- İncomplet HUS, akut renal yetersizlik ve trombositopeni veya mikroanjiopatik hemolitik anemi olması ile tanımlanır

Etyoloji

- Çocuklarda bazı aHUS olgularda metil malonik asidüri ile ilişkilidir, daha sıklıkla (çocuklarda HUS olgularının % 5'şi) norominidaz enzimi üreten invaziv stretokok pnömoni, H1N1 viral enfeksiyonu sonucu gelişebilir.

- Erişkinlerde trombotik mikroanjiopati; HIV enfeksiyonu, kanser, ilaçlar [kemoterapötik ilaçlar, kalsinörin ilaçlar

- Complement factor H, C3, factor B, factor I, anti-factor H autoantibodies, thrombomodulin (CD141), MCP (CD46), CFHR1/3 deficiency with anti-factor H autoantibodies, **Diacylglycerol kinase epsilon (DGKE)**

- Jokiranta TS. HU and atypical HUS. From www.bloodjournal.org by guest on April 18, 2017.

Atypical hemolytic uremic syndrome: genetic contributions, clinical presentations and risk of discontinuation of eculizumab.

Genes	Chr. locus	Proteins	Proportion to atypical HUS	Clinical presentations	Risk of discontinuation of eculizumab[14]
C3	19p13.3	Complement C3	2-8%[15]	Typically present in childhood, 60% develop ESRD. 57% response to plasma exchange6	High[16]
CD46	1q32.2	Membrane cofactor protein	5-9%15,[17]	Typically present in childhood, milder acute episode. 80% complete remission, 60-70% of individuals remain dialysis free even after several recurrences[6]	Low
CFB	6p21.33	Complement factor B	Rare[15,18]	Presenting both in childhood and adulthood. Higher variability. 70% eventually ESRD19	
CFH	1q31.3	Complement factor H	21-22%[15]	High risk of relapse, 60-80% ESRD or death. Liver-kidney transplantation20	High[21]
CFHR1-5	1q31.3	Complement factor H-related protein 1	*CFHR3/CFHR1* deletion: 28%[22] *CFH/CFHR1* hybrid: 3-5% *CFRH1/CFHR4* deletion: rare	Poor clinical prognosis and high risk of post-transplant recurrence[23-25]	Low for homozygous CFHR3/CFHR1 deletion
CFI	4q25	Complement factor I, C3b inactivator	4-8%[15]	Variable. 58% ESRD[6]	Low
DGKE	17q22	Diacylglycerol kinase epsilon	~27% of those present at age <1 year	Onset before 1-year old in homozygote patient.[26] Early chronic kidney disease	
THBD	20p11.21	Thrombomodulin	~5%	90% present in childhood. 50% ESRD. Plasma treatment induced disease remission in about 80% of acute episodes[6]	
CFH auto-antibody				Highly relapsing disease course. Significant gastrointestinal symptoms and/or diarrhea, thus, resembling eHUS. May have infection trigger.[27] Plasma exchange and immunosuppression therapy[28]	

Tedavi

- Plazma değişimi veya plazmaferezis
- Eculizumab
- CCX168 (faz 2 çalışmasında c5a reseptor antagonisti)
- İmmunsupresif ve steroid tedavisi

Otozomal dominant tubulointerstitial böbrek hastalıkları (ADTKD)

- UMOD
- MCU1
- REN
- **HDR syndrome** (hypoparathyroidism, deafness, and renal anomalies)
- ADTKD -HEPATOCYTE NUCLEAR
- FACTOR-1 BETA MUTATIONS

ADTKD-UMOD

- Nadir görülmektedir
- En yaygın formu hipourikozürik, hiperürisemi ve KBH
- İlerki yaşlarda hastalarda gut hastalığı gelişmektedir.
- Uromodulin kodlayan (Tom horsfal gliproteini) UMOD geninde mutsyon sonucu gelişmektedir.
- Böbrek taşları gelişebilir.
- Ortalama 47 (19 ve >75) yaşında SDBY gelişir.
- Gut engellemek için allopurinol

ADTKD-MUC1

Nadir görülmektedir.
Bu hastalığa ait semptom olmayabilir.
Ortalama 43 (17 ve >75) yaşında SDBY gelişir.
Tedavisi bilinmiyor.

ADTKD-REN

- Hipoproliferatif anemi
- Eritropoetin seviyesi azalmıştır
- Hiporeninemi
- Hipotansiyon, hiperkalemi, hipourikozürik ve hiperürisemi gut gelişir.
- Çocuklukta ABH
- Ortalama 50 (30 ve >60) yaşında SDBY gelişir.
- Tedavide düşük sodyumlu diyetten kaçınılmalıdır
- Fludrikortizon

Characteristics of 3 Major Causes of Autosomal Dominant Tubulointerstitial Kidney Disease

Characteristic	ADTKD-*UMOD*	ADTKD-*MUC1*	ADTKD-*REN*
Abbreviated name	Uromodulin Kidney Disease (ADTKD-UMOD)	Mucin-1 Kidney Disease (ADTKD-MUC1)	ADTKD-REN
Inheritance	Autosomal dominant	Autosomal dominant	Autosomal dominant
Urinary sediment	Bland	Bland	Bland
Gout	May occur in childhood; frequent	Occurs in advanced CKD, similar to other kidney diseases	May occur in childhood; frequent
Other symptoms	None	None	Anemia, mild hyperkalemia, mild hypotension, prone to acute kidney injury
Age of ESRD	47 (19 to >75)	43 (17 to >75)	50 (30 to >60)
Knockout mouse	No disease	No disease	Lethal mutation
Pathophysiology	Intracellular deposition of mutated uromodulin leading to CKD	Intracellular deposition of mutated mucin-1 leading to CKD	Intracellular deposition of mutated renin
Diagnosis	Genetic testing at commercial laboratory	Contact ableyer@wakehealth.edu	Genetic testing at research laboratory
Treatment	Allopurinol to prevent gout; may slow progression of CKD	No known treatment	High sodium diet or fludrocortisone

Alport Sendromu

- X bağlı dominant %80 (**COL4A5** geninde)
- Otozomal dominant %15(heterozigot mutasyonlar)
- Otozomal resesif %5 (COL4A3 ve COL4A4 geninde) geçmektedir.
- Tip IV α345 kollojen geninde mutasyon
- X bağlı olan daha çok erkekleri etkiler.

- Zhang Y, et al Renal, auricular, and ocular outcomes of Alport syndrome and their current management. Pediatr Nephrol
- Kashtan C. Alport syndrome: facts and opinions [version 1; referees: 2 approved] F1000Research 2017, 6(F1000 Faculty Rev):50 Last updated: 17 JAN 2017

Klinik

- Kulak, göz ve renal (bazal membran) tutulum olmaktadır.
- Mikroskopik hematüri (%100), %62-66 gross hematüri
- Proteinüri, nefrotik düzeyde proteinüri vardır.
- Sensörinöral işitme kaybı
- Oküler bozukluklar (anterior lentikonus, fleck retinopati, korneal distrofi)
- Leiomiyozis
- SDBY erkeklerde kaçınılmaz bir durumdur.
- Erkeklerin %90 40 yaşında SDBY gelişir

Tedavi

- ACEİ veya ARB
- Siklosporin proteinüriyi azaltmaktadır.
- Siklosporin tedavisi halen tartışmalıdır.
- Potansiyel tedaviler
- Stem cell therapy
- Bone marrow stem cells
- Amniotic fluid stem cells
- Mesenchymal stem cells
- Gene therapy
- Anti-inflammatory therapy
- DDR1 inhibitors
- EGFR inhibitors
- Integrin inhibitors
- Endothelin receptor antagonists

AJKD

Kidney Biopsy Teaching Case

Bile Cast Nephropathy Caused by Obstructive Cholestasis

Julien Aniort, MD,[1,a] Anaïs Poyet, MD,[1,a] Jean-Louis Kemeny, MD, PhD,[2] Carole Philipponnet, MD,[1] and Anne-Elisabeth Heng, MD, PhD[1]

Acute kidney injury (AKI) is a major complication in patients with liver disease. Although hepatorenal syndrome is frequently involved, bile cast nephropathy, characterized by tubular bile cast formation, has been scarcely described in the setting of severe liver failure. Few renal histology studies are available in these patients. We describe a case of bile cast nephropathy in a patient with obstructive cholestasis caused by stones in the common bile duct. The kidney biopsy confirmed this diagnosis, with several green casts in tubular

Bile cast nefropati, hiperbilirubinemiye bağlı olarak renal disfonksiyon gelişmesidir.
Proksimal tubullerde ve parankimde safra ve safra tuzları birikimi renal yetersizliği neden olur.
Etyoloji hepatik ve ekstrahepatik hiperbilrubinemi yapan nedenler.
Hiperbilirubinemi >12-15mg/dl
Renal biyopside bile cast gösterilmesidir.

Bile cast nefropati

- Hidrasyon
- steroid
- Ursodeoxycholic acid,
- cholestyramine ve N-acetylcysteine
- Plazmaferezis

Kolesterol Kristal emboli

- Ateş, miyalji, baş ağrısı, kilo kaybı olur.
- Livedo retikülaris, ayak parmağında gangren
- Böbrek, deri,göz, kas-iskelet sistemi ve sinir sistemi abdominal organ etkilenebilir.
- Etyolojik olarak; iatrojeniktir, aort cerrahisi, aort ve büyük damarlara invaziv girişimler (anjiografi, left kalp katetirazyonu, koroner anjioplasti)
- İnsidansı %1,1-4,5 arasındadır.
- Hiyalin ve granüler cast gözlenir. Hematüri, proteinüri, piyüri, eozinofilüri

Kolesterol embolisi

Kidney	**Acute or subacute kidney injury** **Renal infarction** **Chronic kidney disease** **Renal allograft failure** **Severe hard-to-control hypertension** **Extra-renal organs**
Skin	Livedo reticularis, Blue toe syndrome, Ulceration and gangrene, Purpura, Small nail bed infarcts, Leg, foot, or toe pain
Gastrointestinal system	Abdominal, flank, or back pain, Gastrointestinal bleeding, Diarrhea, Bowel ischemia, infarction, and obstruction, Pancreatitis, cholecystitis, and abnormal liver tests, Splenic infarcts
Eyes	Amaurosis fugax, Sudden blindness, Retinal plaques (Hollenhorst plaques)
Central Nervous System	Headache Amaurosis fugax, Stroke, Transient ischaemic attacks, Altered mental status, Paraparesis Mononeuropathy, Cerebral infarction, Spinal cord infarction
Muscle	Muscle pain, Arthralgias, Rhabdomyolysis Systemic signs, Fever, Anorexia,Fatigue Weight loss, Malaise,Myalgia

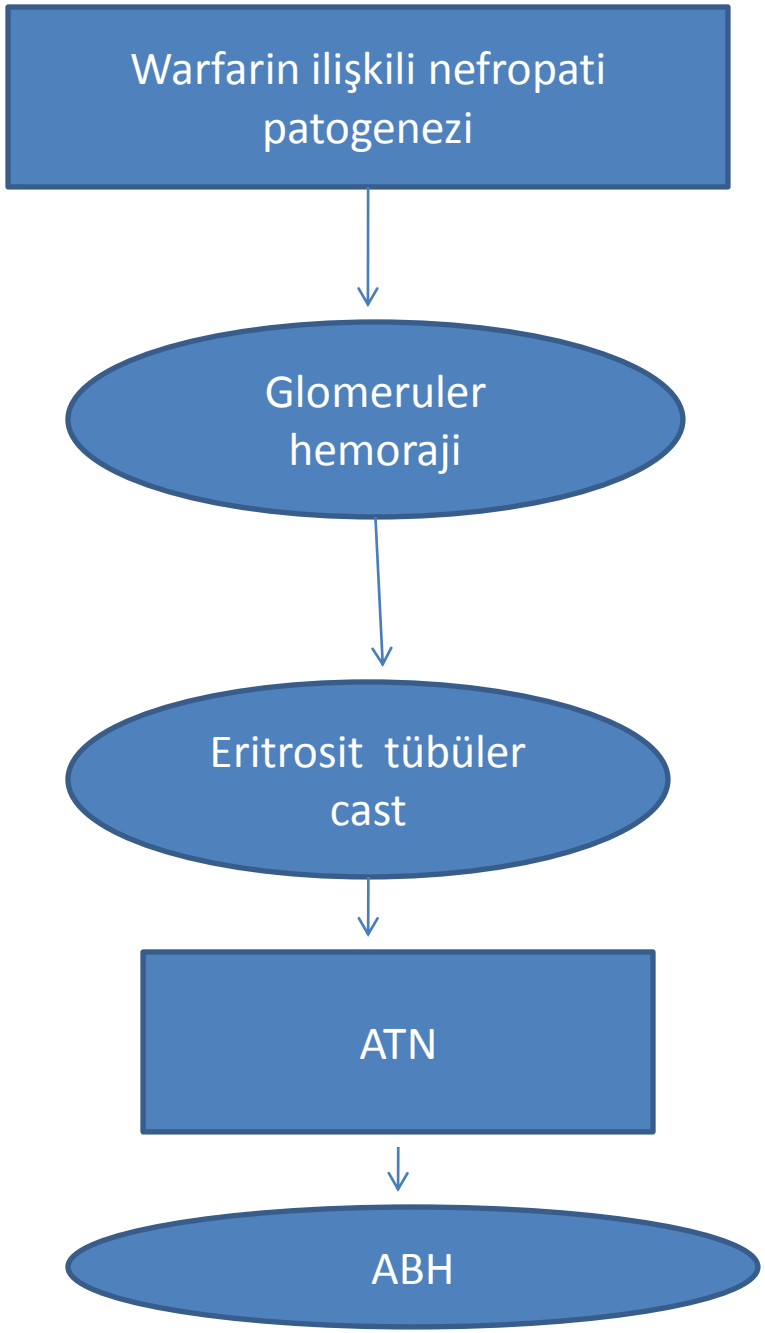
Tedavi

- Kortikosteroid 1mg/kg/gün
- Lipid düşürücü tedavi
- Antikoagulan ilaçlardan kaçınılması
- Diyaliz ve destek tedavileri

- Li X et al. **Cholesterol Crystal Embolism and Chronic Kidney Disease.** Int. J. Mol. Sci. **2017, 18, 1120**

Anticoagulant-Related Nephropathy
Is an AKI Elephant Hiding in Plain View?*
Brodsky SV etal. JOU RNAL OF THE AME R I CAN COL L EG E OF CARD I OLOGY

- Antikoagülan ilişkili nefropati sıklığı 6.8% ve 26%/yıl.
- KBH hastalarında %37 genel populasyonda %20
- Şiddetli glomeruler hemoraji, kırmızı kan hücre cast renal tubullerde tıkanmaya neden olur.
- Warfarin, heparin, dabigatran, apixaban gözlenmiştir.
- INR > 3
- Mortalite < %25 özellikle KBH hastalarında


Warfarin ilişkili nefropati patogenezi
Glomeruler hemoraji
Eritrosit tübüler cast
ATN
ABH

Tubulointerstitial Nephritis and Uveitis (TINU) Syndrome

- Tübülointerstisyel nefrit ve Üveit birlikteliğidir.
- Nadiren ilaçlar (antibiytik ve NSAİİ), infeksiyon, toksinler ve otoimmun hastalıklar.
- Tanı Renal biyopsi
- Tedavi steroid

Primer hiperparatiroid bağlı KBH

- Dehidratasyon
- Böbrek taşları
- Böbrek kist
- PTH artışı endotel hasarı, fibrozis ile ilişkilidir
- İnsülin direncine yol açar.
- Hipertansiyon
- Obezite
- Artmış yaş

Kristal nefropatisi

- Kristal birikimine bağlı, ABH, KBH, renal kolik, nefrokalsinozis yol açabilir.
- Kristal birikimi renal vaskülerde tip 1, nefronlarda tip 2 ve üriner sistemde tip 3 olarak tanımlanmaktadır.

Disease	Disease subtype	Crystal (source of the crystal-forming factor)	Renal damage	Treatment and management
Vascular crystallopathies (type 1)				
Cholesterol embolism	NA	Cholesterol	AKI	Control of cardiovascular risk factors, avoid catheter interventions and anticoagulants
Atherosclerotic renal artery stenosis	NA	Cholesterol, apatite, calcium–phosphate	CKD	Control of cardiovascular risk factors, especially hypertension
Tubular crystallopathies (type 2)				
Diet-induced crystal nephropathy	NA	Calcium oxalate monohydrate (whewellite), calcium oxalate dihydrate (weddelite), calcium–phosphate (oxalate and vitamin C-rich foods and drinks)	AKI	Stop exposure, increase fluid intake
Drug-induced crystal nephropathies	Tumour lysis syndrome	Uric acid	AKI	Rasburicase, increase fluid intake
	Drug-induced crystalluria	Drug crystals	AKI	Stop exposure, increase fluid intake
	Acute phosphate nephropathy	Calcium–phosphate		
Enteric crystal nephropathy	NA	Calcium oxalate monohydrate (whewellite) (bariatric surgery, IBD, coeliac disease)	AKI	Avoid dietary oxalate intake, increase fluid intake, treat enteric disease
Short bowel syndrome	NA	Calcium oxalate dihydrate (weddelite)		
Myogen crystal nephropathy	NA	Myoglobin (rhabdomyolysis)	AKI	Increase fluid intake
Cholemic crystal nephropathy (bile cast nephropathy)	NA	Bile pigment	AKI	Increase fluid intake, treat liver disorder or transplant
Paraprotein-induced crystal nephropathy (light chain cast nephropathy)	NA	Monoclonal light chains	AKI	Treat plasma cell dyscrasia, increase fluid intake

Genetic disorders	Genetic forms of RTA	Brushite, calcium carbonate, calcium oxalate, calcium–phosphate, hydroxapatite, struvite	CKD	Increase fluid intake, specific interventions to reduce mineral or metabolite excretion
	Genetic forms of hyperuricosuria	Uric acid		
	Primary hyperoxaluria	Calcium oxalate monohydrate (whewellite), calcium oxalate dihydrate (weddelite)		
	APRT deficiency	Adenine		
	Cystinosis	Cystine	CKD	Cysteamine
Genetic diseases that cause nephrocalcinosis	Dent disease, Lowe syndrome, idiopathic infantile hypercalcaemia and hypercalciuria	Calcium–phosphate, Calcium–pyrophosphate	CKD	Increase fluid intake, specific interventions to reduce mineral or metabolite excretion
Diet and drug-induced crystal nephropathy	NA	Uric acid (diets rich in sodium, fructose, sucrose)	CKD	Stop exposure, diet modifications, increase fluid intake, xanthine oxidase inhibition
Tophaceous gout	NA	Uric acid (diets low in potassium, calcium, phytate, fluid administration as part of Mesoamerican nephropathy treatment)	CKD	Xanthine oxidase inhibition, uricosuric drugs
Immunoglobulin-induced crystal nephropathies	Light chain cast nephropathy, proximal tubulopathy with or without Fanconi syndrome, crystalglobulinaemia, crystal-storing histiocytosis	Monoclonal light chains	CKD	Treat plasma cell dyscrasia, increase fluid intake
Chronic glomerular crystal nephropathies	Cryoglobulinaemia	Monoclonal and polyclonal IgG	CKD	Treat plasma cell dyscrasia, increase fluid intake
	Crystalglobulinaemia	Monoclonal light chains		
	Cystinosis	Cystine	CKD	Cysteamine

Urolithiasis (type 3)				
Genetic disorders	Genetic forms of RTA	Brushite, calcium carbonate, calcium oxalate, calcium–phosphate, Hydroxapatite, struvite	Colic	Increase fluid intake, specific interventions to reduce mineral or metabolite excretion
	Primary hyperoxaluria	Calcium oxalate monohydrate (whewellite), calcium oxalate dihydrate (weddelite)		
	Cystinosis	Cystine		
	APRT deficiency	Adenine		
	Genetic forms of hyperuricosuria and hypercalciuria (as listed above)	Uric acid, calcium oxalate, calcium–phosphate		
Diet or drug-induced crystal nephropathy	NA	Calcium oxalate, calcium–phosphate (diets rich in oxalate, sodium, fructose, vitamin C, sucrose, diets low in potassium, calcium, phytate)	Colic	Increase fluid intake, specific interventions to reduce mineral or metabolite excretion
Hyperuricosuric syndromes	NA	Uric acid	Colic	Increase fluid intake, specific interventions to reduce mineral or metabolite excretion
Drug crystalluria	NA	Drug crystals	Colic	Increase fluid intake, specific interventions to reduce mineral or metabolite excretion
Enteric oxalosis	NA	Calcium oxalate monohydrate (whewellite)	Colic	Avoid dietary oxalate intake
Short bowel syndrome	NA	Calcium oxalate dihydrate (weddelite) (bariatric surgery, IBD, coeliac disease)	Colic	Increase fluid intake, treat enteric disease

Primer Hiperoksalüri

- Peroksizomal hepatik enzim alanin-glioksilat aminotransferazın aktivitesindeki bir eksiklikten kaynaklanan bozukluktur.
- Otozomal resesif geçer.
- Oksalatın aşırı üretimi ile karakterizedir
- Tip 1 olguların %80 oluşturur.
- Erken nefrokalsinozis, ürolitiyazis ve nadiren SDBY ile ilişkilidir.

Primer Hiperoksalüri

- Alanin-glioksilat aminotransferaz karaciğer hücrelerinde gliyoksilatın glisine transaminasyonunu katalize eder.
- Gliyoksilatın aminasyon yetersizliği sonucunda peroksizomda gliyoksilat oksidaz veya sitozolde laktat dehidrogenaz enzimi ile aşırı oksalat oluşur.
- Artmış renal oksalat atılımı ile idrarda kalsiyum oksalat kristalleri meydana gelir, bunların çözünürlüğü düşüktür.
- Tekrarlayan üriner sistem taşları

AJKD
Case Report

C4 Glomerulopathy: A Disease Entity Associated With C4d Deposition

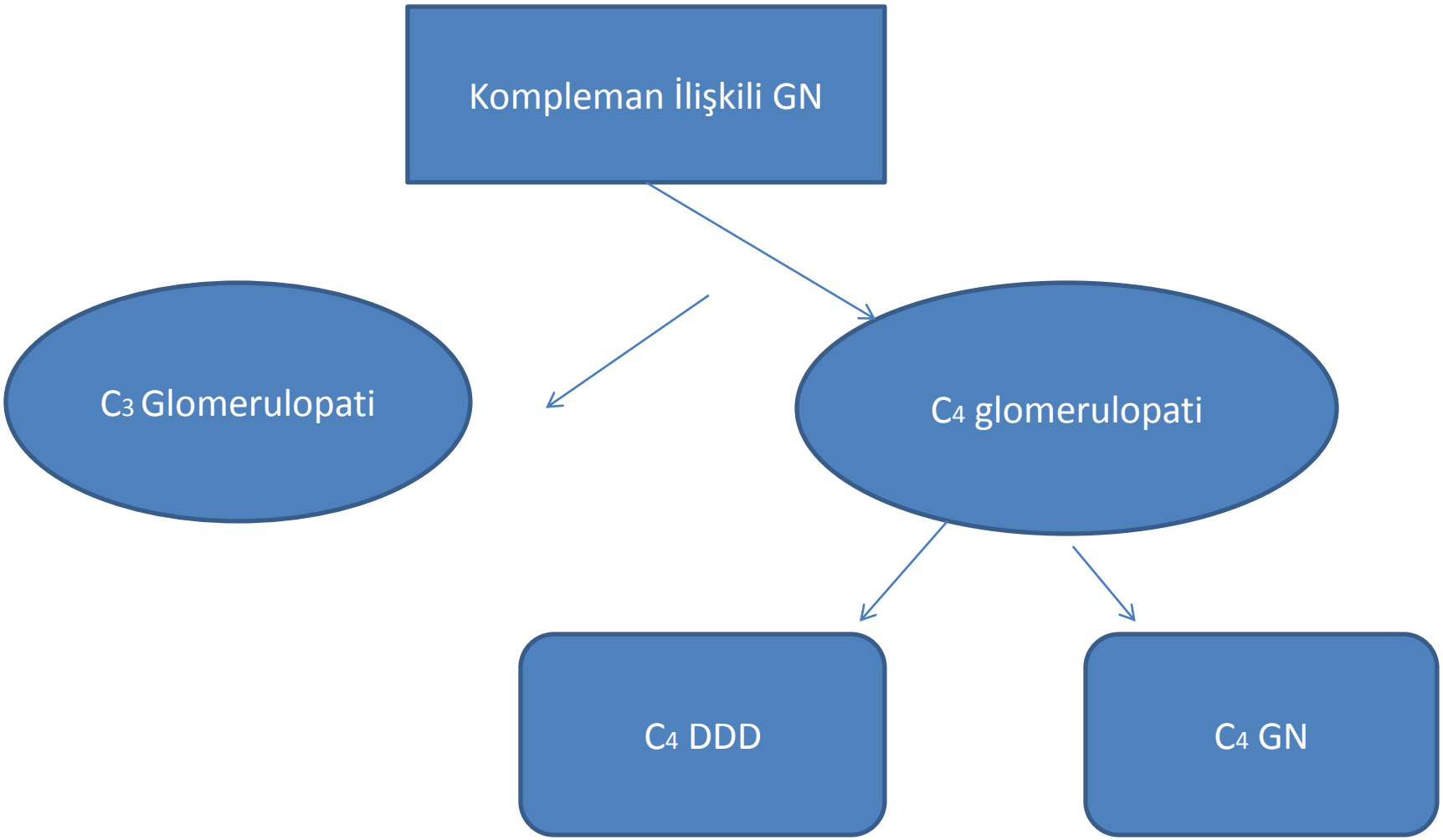
Sanjeev Sethi, MD, PhD,[1] Patrick S. Quint, PhD,[1] Conall M. O'Seaghdha, MD,[2] Fernando C. Fervenza, MD, PhD,[3] Vanesa Bijol, MD,[4] Anthony Dorman, MD,[5] Surendra Dasari, PhD,[6] Richard J.H. Smith, MD,[7] Paul J. Kurtin, MD,[1] and Helmut G. Rennke, MD[4]

Complement-mediated glomerulonephritis, which includes C3 glomerulopathy, is characterized by dominant staining of C3 with minimal or no immunoglobulin deposits on immunofluorescence studies. We describe a new entity of complement-mediated glomerulonephritis that is characterized by bright C4d staining but with no

C4 Glomerulopati; C4 DDD ve C4 glomerulonefrit
C4 seviyesi düşük olabilir.
Renal biyopside immunfloresan boyamada C4d pozitif ve immunglobulin ve C3 boyama negatif veya minimal.
C4 DDD: C4d boyama ve glomeruler bazal mmbran boyunca dens depozit
C4 GN: C4d boyama ve mesangial elektron dens depozit (nadiren elektron intramembranöz dens depozit olabilir)

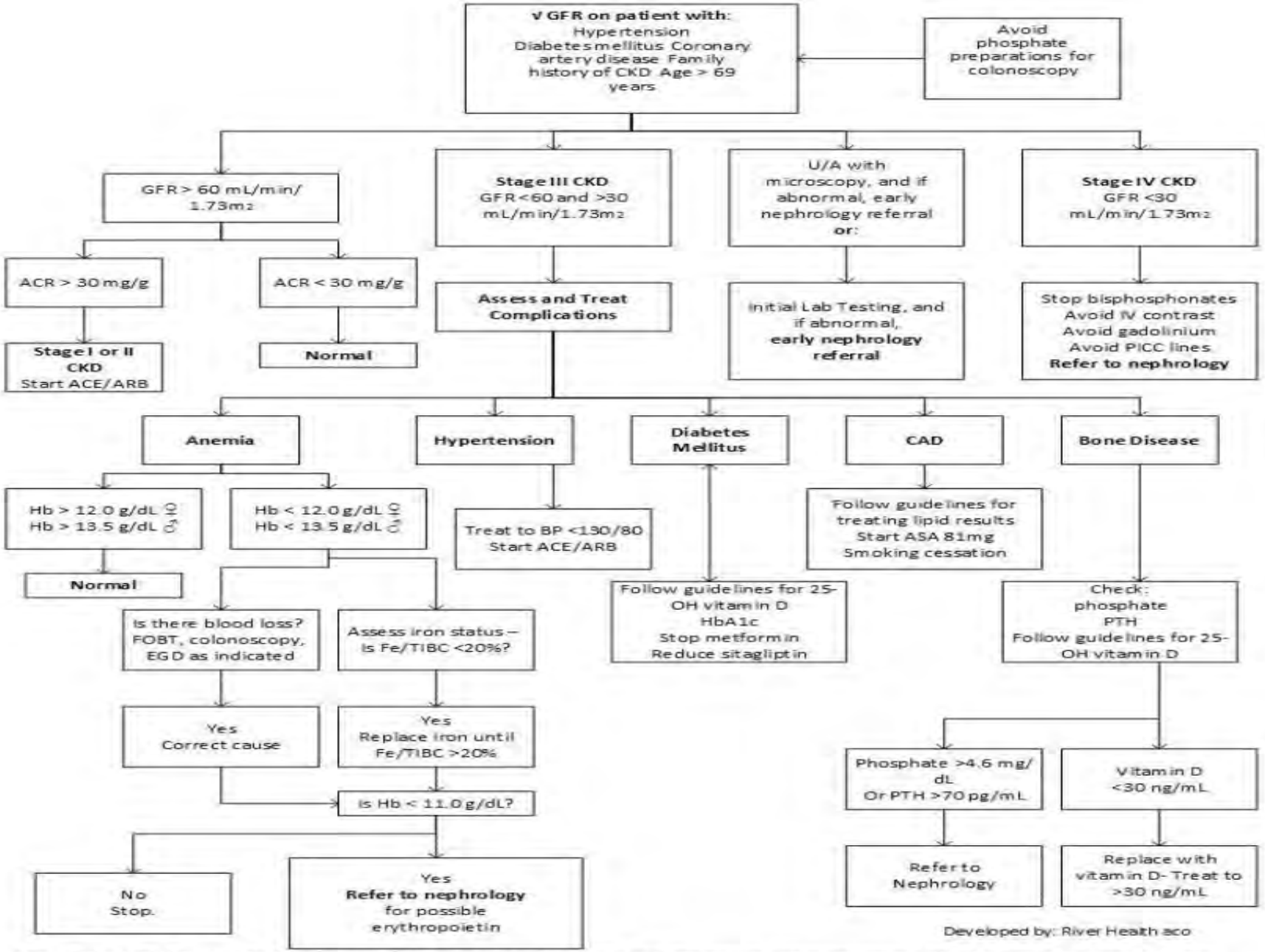
Am J Kidney Dis. 67(6):949-953. © *2016 by the National Kidney Foundation, Inc.*

INDEX WORDS: C4 glomerulopathy; C4 glomerulonephritis; C4 dense deposit disease; C4d deposition; membranoproliferative glomerulonephritis (MPGN); complement; proteinuria; kidney biopsy; renal pathology.


Kompleman İlişkili GN
C3 Glomerulopati
C4 glomerulopati
C4 DDD
C4 GN

Bardet Biedl sendromu

- Otozomal resesif geçişli
- Renal malformasyon
- Obezite
- Hipogonadizm
- Öğrenme güçlüğü
- Retinal distrofi,
- Mental retardasyon



Abbreviations: GFR, glomerular filtration rate; ACR, albumin/creatinine ratio; ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; U/A, urinalysis; PICC, peripherally inserted central catheter; Hb, hemoglobin, PTH, parathyroid hormone; FOBT, fecal occult blood testing; EGD, esophagogastroduodenoscopy; Fe/TIBC, iron/total binding capacity.

KAHRAMANMARAŞ NECİP FAZIL ŞEHİR HASTANESİ

Sabrınız İçin Teşekkürler