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CHARACTERISTICS OF PATIENTS WITH AND WITHOUT DIALYSIS DEPENDENT CHRONIC KIDNEY DISEASE AND ANEMIA RECEIVING BLOOD TRANSFUSIONS AND INTRAVENOUS IRON: A REPORT FROM THE DISCOVER CKD RETROSPECTIVE COHORT:

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Many patients experiencing anemia in CKD remain untreated until dialysis. We describe characteristics of patients with/without dialysis dependent CKD and anemia receiving a transfusion or IV iron in DISCOVER CKD.

Data for patients (aged >18 y) with CKD and anemia were taken from UK CPRD, Japan JMDV and US LCDB databases. Index: first Hb <12/13 g/dl (female/male) or an anaemia therapy (iron, ESA or transfusion) prescription on/after: dx code for CKD (stage 3A+) or dialysis or 2nd of two eGFR measures <60 mL/min/1.73m2 >90 days apart between Jan 2008 and Mar 2020.

In total, 27% of 72,429 patients were treated with anemia therapies during follow-up, of which 25% was transfusion or IV iron. Patients from the US and Japan had a higher proportion of comorbidities compared to patients from the UK.

Median Hb ranged 7.9-8.9 for those receiving a transfusion and 8.9-10.5 for those receiving IV iron, Table 1. There were clear country differences observed in the routine clinical care of anemia in patients with CKD. Transfusion and IV iron were commonly used as rescue therapies despite their invasive nature and well-recognized associations between transfusions and adverse reactions such as allo sensitization and infection.

ASSOCIATION OF WILLINGNESS TO SEEK CARE IN THE ED WITH FEAR AND ATTITUDES CONCERNING COVID-19 IN INNER-CITY KIDNEY PATIENTS:

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Fear of contracting COVID-19 and misinformation may contribute to reluctance to seek care in the ED. We studied the association of concerns of safety going to the ED with attitudes toward COVID-19 in a cohort of inner-city kidney disease patients.

A random sample of patients attending CKD (20) and transplant (40) clinics were interviewed by phone. Questions about COVID-19 and willingness to seek emergency medical care were assessed by an attitudinal survey. There were no differences between clinics so they were analyzed together.

Mean age was 58.7 ± 12.1 with 28 (47%) males, 32 (53%) females, 42 Black, 6 Hispanic, 3 White, and 4 others. 10 (18%) were employed, 4 (7%) were unemployed, 18 (33%) were retired, and 23 (42%) were receiving disability/SSI. 33 (72%) people reported they would seek care in the ED if they had a medical emergency but 16 people (40%) did not feel it would be safe (UNSAFE) and these pts were less likely to go to the ED (100% vs 0%, p = 0.004). Individuals who felt safe going to the ED (SAFE) were less likely to be afraid of COVID-19 (71% vs 29%, p = 0.019). UNSAFE were more likely to be afraid of public places (93% vs 7%, p = 0.001) and getting infected from a family member (77% vs 21%, p = 0.014). UNSAFE were more likely to feel unsafe going to eat at a restaurant (100% vs 0%, p = 0.027), avoid leaving their home (94% vs 0%, p = 0.001), and leave their house less since the pandemic (100% vs 0%, p = 0.021). There was no difference between the groups in frequency of hand washing hands, use of soap and water, or sanitizing surfaces regularly.

In our population: 1. Almost a third of pts surveyed would not go to the ED for emergency care and almost half did not feel safe. 2. Patients who did not feel safe were less likely to be willing to seek care in the ED. 3. Patients who felt unsafe in the ED also felt unsafe eating out, feared going to public places, avoided leaving their home, were more afraid of COVID-19 in general and of contracting it from a family member. 5. It is important that CKD/KTx pts be educated regarding safety of emergency care during the pandemic as avoidance of care could have deleterious effects.

A CASE REPORT OF THIN BASEMENT MEMBRANE WITH PROTEINURIA ASSOCIATED WITH COMPLEMENT 5 AND APOLIPOPROTEIN L1 VARIANTS IN THE HETEROZYGOS STATE:

Daniel Duyang, Nikhil Kasarla, Noah Panitch, Dinah Clark, Hossein Tabriziani, Ernie Yan, SUNY Downstate Health Sciences University, Brooklyn, NY, United States; Natera, Inc., San Carlos, CA, United States; Homozygous or compound heterozygous inheritance of high-risk APOL1 alleles is associated with increased risk of kidney disease among African Americans (AA). Individuals, heterozygous for recessive APOL1 alleles are not at risk for deleterious kidney effects. Additionally, C5 variants are not known to be nephropathic. Here, we present a case of thin glomerular basement membrane (GBM) with dual heterozygotic inheritance of APOL1 and C5 variants. A 39-year-old AA female presented with a 3-month history of foamy urine. She is positive for sickle cell trait and has no other pertinent triggers or medical history. Urinalysis revealed microscopic hematuria and proteinuria with urine protein/creatinine within 1.5-3 g/g range. Kidney biopsy showed preserved foot processes and GBM measuring 176-339 nm without laminated areas, and no detection of immune complex deposits. DNA sequencing of COL4A3, COL4A4, COL4A5 and multiplex ligation-dependent probe amplification of COL4A5 were negative for variants of significance. Genetic testing using Renasight, a 382 gene panel associated with chronic kidney disease yielded a heterozygous C5 variant c.754G>A (p.Ala252Thr), a heterozygous APOL1 risk allele c.1024A>G;1152T>G (p.[Ser342Gly;Ile384Met]) (G1 allele), and a heterozygous HBB variant c.200A>T (p.Glu67Val).

Heterozygosity for high-risk APOL1 variants is associated with protection against trypanosomiasis. Homozygosity for the C5 c.754G>A p.A252T variant can lead to C5 deficiency-related meningococcal disease. Homozygous and heterozygous individuals have <4% and 45% of the total levels of C5, compared to controls, respectively. Although dysregulation of the complement system could lead to glomerulonephritis, the implications of the heterozygous state of this C5 variant are unknown. Possible interaction of this C5 variant with heterozygous high-risk APOL1 variants on the GBM warrants further investigation.

Testing with a broad renal genetic panel could help uncover multiple genetic variants with potentially pathogenic interactions that lead to defects in the GBM.

ACUTE KIDNEY INJURY AND COLLAPSING GLOMERULOPATHY IN PATIENT WITH COVID-19 AND APOLIPOPROTEIN L1 GENE VARIANTS:

Sunil Shercan, Ammar Mohamed, Thy Vo, Neeta D’Souza, Dinah Clark, Hossein Tabriziani, Ernie Yan, SUNY Downstate Health Sciences University, Brooklyn, NY, United States; Natera, Inc., San Carlos, CA, United States; African Americans (AA) with high-risk APOL1 alleles are at an increased risk of developing early onset focal segmental glomerulosclerosis (FSGS) and rapid progression of chronic kidney
disease. In some cases, severe COVID-19 pneumonia is associated with kidney injury known as COVID-19-Associated Nephropathy, the exact mechanisms of which are unclear.

A 25-year-old AA female presented with mild respiratory symptoms and positive for SARS-CoV-2 and was admitted to Emergency in March 2020. Her serum creatinine (sCr) was 1.4 mg/dL, albumin 2.92 g/dL, she recovered clinically and was discharged. She returned to hospital 25 days later with severe kidney failure, sCr of 28 mg/dL, potassium of 5.6 mmol/L and uric acid/protein/creatinine (uPCR) of 10355 mg/g. She was initiated on hemodialysis. Kidney biopsy showed CG with acute tubular necrosis with direct invasion of the glomerular cells by particles resembling coronavirus. Hemodialysis was discontinued and she was discharged home on oral prednisone at 1mg/kg/day. After 5 months, she was tapered off of prednisone and her sCr improved to 2.6 mg/dL with uPCR of 3133 mg/g. Genetic testing with Renasight, a 382 renal gene panel was performed, yielding homozygosity for the APOL1 risk allele (c.1024A>G;1152T>G) (p.[Ser342Gly;Ile384Met]) (G1 allele).

High-risk APOL1 risk variants occur in 13% of AA. These individuals have an estimated 4% lifetime risk for incurring FSGS. However, a ‘2nd hit’ is necessary for kidney disease to develop. COVID-19 may lead to kidney injury due to tissue ischaemia, cytokine storm, hypercoagulability or direct viral-mediated mechanisms. In COVID-19 related kidney biopsies, CG is often described. Although glucocorticoid sensitivity in such well-defined cases is not well-defined, our patient showed response to oral prednisone.

This case adds to growing evidence that SARS-CoV-2 infection contributes to CG. The dual effect of high-risk APOL1 variants and SARS-CoV-2 in effecting CG remains to be elucidated. Testing with a broad renal genetic panel could help define genetic variants that promote complications from SARS-CoV-2 infection.

313 HOMOZYGOUS HIGH-RISK APOL1 ALLELE AND HETERozygOUS COL4A4 MUTATION IN AN AFRICAN AMERICAN PATIENT WITH COLLAPSING FOCAL SEGMENTAL GLOMERULONEPHRITIS:

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Homozygous inheritance of high-risk APOL1 alleles is associated with the development of focal segmental glomerulosclerosis (FSGS) amongst African Americans (AA). However, an additional genetic or environmental ‘2nd hit’ is required to promote onset of kidney disease. Mutations within the COL4A4 gene promote FSGS associated with Alport syndrome (AS). However, kidney implications of pathogenic COL4A4 variants combined with homozygous high-risk APOL1 variants are unknown. We describe a patient with early onset FSGS, who was found to have pathogenic variants in both APOL1 and COL4A4.

A 31-year-old AA male with a history of uncontrolled hypertension was referred to the Renal Service for management of progressive chronic kidney disease (CKD). Kidney biopsy disclosed collapsing FSGS with arteriolosclerosis with hyalinosis, with 80% fibrosis. Homodialisys was initiated and genetic testing with Renasight, a 382 renal gene panel test associated with CKD was performed. Renasight results yielded a heterozygous COL4A4 gene variant c.3451 G>A p.Gly1151Arg and homozygous APOL1 risk alleles c.1024 A>G;1152 T>G p.Ser342Gly;Ile384Met (G1 allele).

The concomitant inheritance of these variants have not been previously reported. However, another COL4A4 variant at the same amino acid, p.Gly1151Ala, was previously reported in an individual with AS. This amino acid lies in the collagen triple helix repeat domain (6S-1459) and variants at this site disrupt the Gly-X-Y motif. Other similar amino acid changes within the highly conserved Gly-X-Y motif of the COL4A4 protein have also been reported in individuals with AS. Heterozygous COL4A4 mutations underlie the clinical spectrum of AS that includes thin basement membrane nephropathy (TBMN) associated with COL4A4. In this individual, both abnormal COL4A4 and APOL1 alleles may have a synergistic effect in promoting a progressive form of kidney injury.

Testing with a broad renal genetic panel uncovered a previously unreported variant combination that may further our current understanding of the genetic underpinnings of FSGS.

314 MEDICARE COVERAGE FOR OUTPATIENT DIALYSIS FOR ACUTE KIDNEY INJURY (AKI): INITIAL UPTAKE AND OUTCOMES:

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Past Medicare policy prohibited payment to ESRD facilities for AKI dialysis services for patients with acute kidney injury who require dialysis (AKI-D). Beginning in 2017, new legislation allowed Medicare to pay ESRD facilities for AKI-D.

The study includes fee-for-service Medicare beneficiaries. Data sources include Medicare claims, enrollment and CROWNWeb files. AKI-D was defined by HCPCS code G0491.

The number of patients with claims for AKI-D increased each year: 9,740 patients treated at 4,002 facilities in 2017, 13,879 patients at 4,778 facilities in 2018 and 15,615 patients at 5,142 facilities in 2019. The number of ESRD patients who recovered kidney function steadily declined from 7,037 in 2016 to 5,754 in 2019. AKI-D patient characteristics were consistent with the underlying Medicare population (age 70 years, 56% male, 16% Black, 6% Hispanic). A prior index hospitalization was identified for 86% of patients, distributed as 63% medical and 37% surgical. On average patients received 20 outpatient AKI-D treatments with average Medicare payment of $186/session. The table shows patient outcomes after hospital discharge. At one year, the most common outcomes were death and ESRD but AKI-D claims continued for 6% of patients. Among deaths, 15% reached ESRD status first.