APOL1 CKD Risk Alleles in New Mexico African American and American Indian Populations: Racial Disparity

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Abstract

Purpose/Background: Two haplotypes of human apolipoprotein L1 gene (gene: APOL1; protein: ApoL1) harboring three coding sequence mutations have been demonstrated as risk variants associated with non-diabetic chronic kidney diseases (CKD) in African Americans. The first one, termed G1, is a two non-synonymous SNP haplotype (rs73885319 (A>G; p.S342G) and rs60910145 (G>T; p.I384M). The second one, termed G2, is a two codon deletion haplotype rs71785313 (6-bp in frame deletion) These two coding-sequence variants have been discovered in CKD patients of African ancestry and linked to the pathogenesis of primary focal and segmental glomerulosclerosis (FSGS), hypertension-attributed kidney disease, and HIV-associated nephropathy (HIVAN), under a recessive inheritance pattern. Marked disparities exist in races, rates, and etiological classifications of CDK between African Americans (AAs) and European Americans. Sequencing and genotyping analysis of known APOL1 SNPs showed that only APOL1 G1 and G2 confer kidney risk, and other common and rare APOL1 missense variants, including the G3 haplotype, do not contribute to FSGS and HIVAN in the US population.

According to the report of US census bureau, African American and American Indian (AI) citizens in New Mexico make up nearly 2.5% and 10.9% of the state's entire population in 2018 (2). However, whether APOL1 G1 and G2 kidney-risk alleles are linked with hypertension-attributed CKD in AAs and AIs in New Mexico has not been investigated.

Materials & Methods: We analyzed the published results of a retrospective analysis of inpatient and discharge data from hospitals across the state of New Mexico, known as Hospital Inpatient and Discharge Dataset (HIDD; 3).

Results: A pattern persisted for all three years (2012-2014) that AAs had the highest rate of CKD followed by AIs per 10,000 population in New Mexico. AAs had the highest age adjusted rate of CKD with hypertension at 102.6 per 10,000 population (29.7% (102.6/345.7) of all CKD with hypertension patients) followed by American Indians at 91.9 (26.6% (91.9/345.7) of all CKD with hypertension patients). Interestingly, in terms of CKD with diabetes, AIs had the highest age adjusted rate at 79.9 per 10,000 followed by AAs at 66.5.

Discussion/Conclusion: The prevalence of CKD with hypertension in AA and AI populations is significantly high in New Mexico, To understand the etiology of CKD in AAs and AIs in New Mexico, genotyping the APOL1 G1 and G2 risk alleles in these two populations is warranted. Detection of APOL1 associations with CKD and delineation of injury pathways (autophagy, necroptosis and ferroptosis) would bring hope for effective treatment for these kidney diseases. In addition, modifier loci can influence APOL1 risk for the development of CKD. ‘Second hits’, for example viral and environmental, may alter the outcome of APOL1 risk variants.

Keywords

APOL1 CKD Risk Alleles; African Americans; American Indians

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Purpose/Background: Two haplotypes of human apolipoprotein L1 gene (gene: APOL1; protein: ApoL1) harboring three coding sequence mutations have been demonstrated as risk variants associated with non-diabetic chronic kidney diseases (CKD) in African Americans. The first one, termed G1, is a two non-synonymous SNP haplotype (rs73885319 (A>G; p.S342G) and rs60910145 (G>T; p.I384M). The second one, termed G2, is a two codon deletion haplotype rs71785313 (6-bp in frame deletion) These two coding-sequence variants have been discovered in CKD patients of African ancestry and linked to the pathogenesis of primary focal and segmental glomerulosclerosis (FSGS), hypertension-attributed kidney disease, and HIV-associated nephropathy (HIVAN), under a recessive inheritance pattern. Marked disparities exist in races, rates, and etiological classifications of CDK between African Americans (AAs) and European Americans. Sequencing and genotyping analysis of known APOL1 SNPs showed that only APOL1 G1 and G2 confer kidney risk, and other common and rare APOL1 missense variants, including the G3 haplotype, do not contribute to FSGS and HIVAN in the US population.

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References:

1. Hu et al (2015) How complicated can it be? The link between APOL1 risk variants and lipoprotein heterogeneity in kidney and cardiovascular diseases. Nephrol Dial Transplant.
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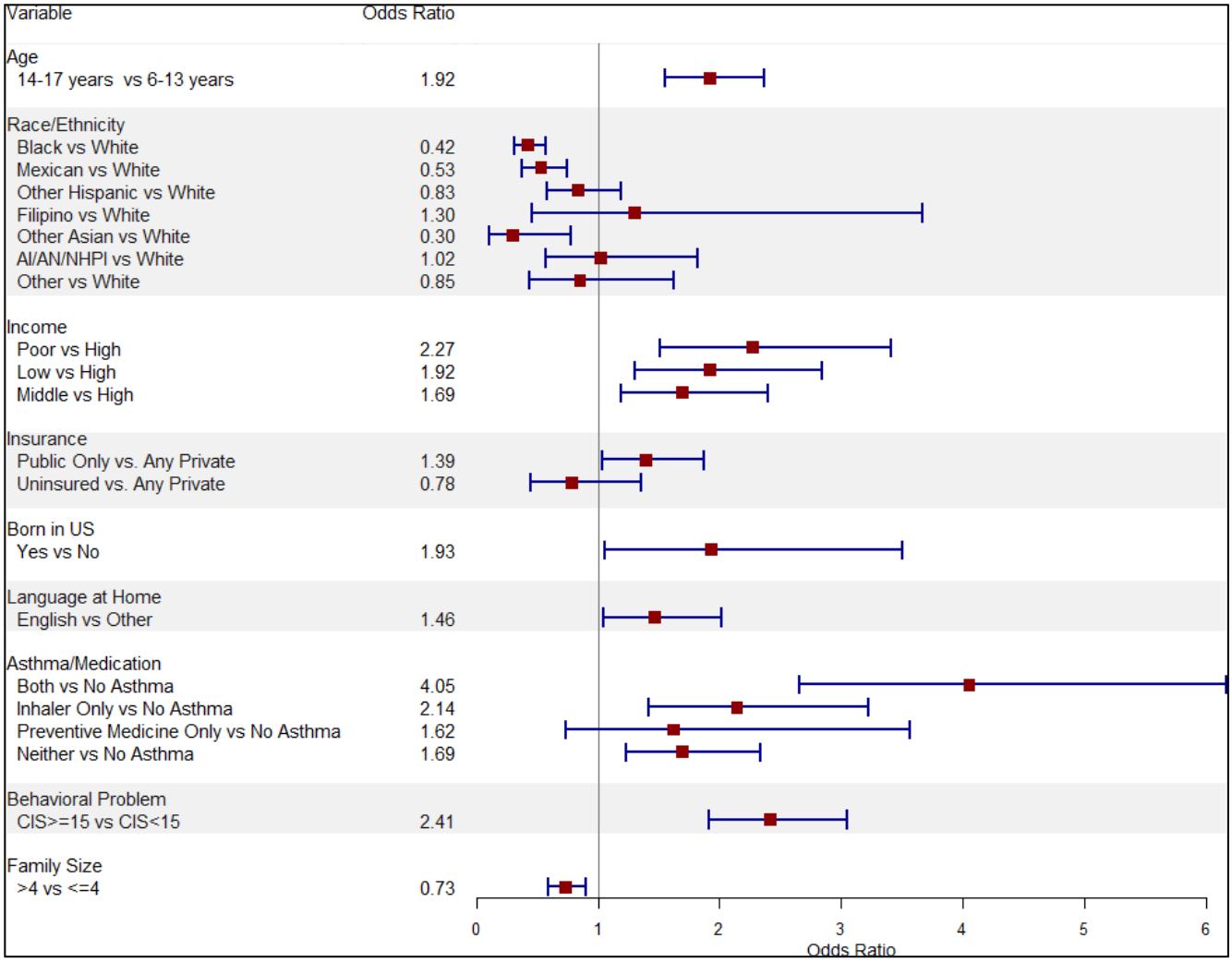
Table 1. Subject Chracteristics and Percentage of Chronic Absenteeism

Variable	Total		Chronic Absenteeism		Total		Chronic Absenteeism
	Unweighted N	Weighted % (SE)	Weighted % (SE)		Unweighted N	Weighted % (SE)	Weighted % (SE)
Socio-Demographic Variable				***Family Structure Variable***			
Age				Family Type			
6-13 yrs.	15,815	68.3 (0.4)	1.7 (0.1)	Two-parent	22,524	69.4 (0.8)	1.8 (0.1)
14-17 yrs.	6,696	31.7 (0.4)	3.1 (0.3)	Single-parent	12,236	27.9 (0.8)	3.0 (0.2)
Sex				No-parent	1,167	2.7 (0.2)	3.4 (0.8)
Boy	11,524	51.0 (0.5)	2.1 (0.1)	Family Size			
Girl	10,987	49.0 (0.5)	2.3 (0.2)	≤4	18,632	58.2 (0.9)	2.5 (0.2)
Race/Ethnicity				>4	17,295	41.8 (0.9)	1.7 (0.2)
White	7,342	56.4 (1.3)	2.6 (0.2)	# of Elderly (≥65 yrs.)*	35,927	0.05 (0.00)	0.08 (0.01)
Black	4,992	14.4 (0.8)	1.7 (0.3)	# of Preschool Children (≤5 yrs.)*	35,927	0.34 (0.01)	0.31 (0.03)
Mexican	5,762	14.8 (1.2)	1.4 (0.1)	# of Adult (≥18 yrs.)			
Other Hispanic	2,415	7.0 (0.4)	2.4 (0.3)	0-1	6,255	15.0 (0.5)	2.8 (0.3)
Filipino	275	1.0 (0.2)	2.1 (1.1)	2	19,585	60.2 (0.7)	1.9 (0.1)
Other Asians	979	3.4 (0.2)	0.5 (0.2)	≥3	10,087	24.8 (0.6)	2.5 (0.2)
AI/AN/NHPI	330	1.3 (0.3)	3.5 (0.8)	***Health/Behavior Variable***			
Other	416	1.8 (0.2)	2.1 (0.7)	Asthma & Medication			
Highest Education in Family				No Asthma	19,522	87.0 (0.3)	1.8 (0.1)
≤High School	9,828	31.7 (0.9)	2.6 (0.2)	Both Inhaler and Preventive Medicine	1,496	6.5 (0.2)	4.1 (0.7)
Some College	6,358	28.6 (0.6)	2.4 (0.2)	Inhaler Only	125	0.7 (0.1)	1.5 (0.9)
Bachelor's	3,689	21.8 (0.7)	1.8 (0.3)	Preventive Medicine Only	931	4.0 (0.2)	5.2 (1.3)
≥Graduate	2,622	17.9 (0.8)	1.5 (0.3)	Neither Inhaler nor Preventive Medicine	417	1.8 (0.1)	11.7 (2.2)
Income				ADHD			
Poor	8,815	25.0 (0.8)	3.1 (0.2)	Yes	2,194	10.7 (0.4)	2.0 (0.1)
Low	4,195	15.6 (0.4)	2.4 (0.3)	No	20,314	89.3 (0.4)	3.8 (0.4)
Middle	5,833	32.0 (0.7)	2.2 (0.2)	Obesity			
High	3,668	27.4 (0.9)	1.3 (0.2)	Normal	13,771	83.1 (0.5)	2.2 (0.1)
Insurance				Overweight	2,240	11.5 (0.4)	2.5 (0.3)
Any Private	10,168	61.0 (1.0)	1.8 (0.1)	Obese	1,197	5.4 (0.2)	4.8 (0.8)
Public Only	10,666	32.4 (1.0)	3.1 (0.2)	Behavioral Problem			
Uninsured	1,677	6.6 (0.4)	1.3 (0.4)	CIS<15	19,636	86.4 (0.4)	1.6 (0.1)
Born in US				CIS≥15	2,875	13.6 (0.4)	6.1 (0.5)
No	6,522	17.3 (0.9)	0.8 (0.2)	Number of Dental Care Visits*	22,511	1.38 (0.03)	1.53 (0.19)
Yes	15,981	82.7 (0.9)	2.3 (0.1)	Less Healthy Than Other Child			
Language at Home				No	20,720	93.0 (0.2)	1.6 (0.1)
Other	1,542	4.7 (0.2)	1.2 (0.1)	Yes	1,776	7.0 (0.2)	10.1 (0.8)
English	20,952	95.3 (0.2)	2.4 (0.1)				


Variable
Odds Ratio
Age
14-17 years vs 6-13 years
1.92
Race/Ethnicity
Black vs White
0.42
Mexican vs White
0.53
Other Hispanic vs White
0.83
Filipino vs White
1.30
Other Asian vs White
0.30
AI/AN/NHPI vs White
1.02
Other vs White
0.85
Income
Poor vs High
2.27
Low vs High
1.92
Middle vs High
1.69
Insurance
Public Only vs. Any Private
1.39
Uninsured vs. Any Private
0.78
Born in US
Yes vs No
1.93
Language at Home
English vs Other
1.46
Asthma/Medication
Both vs No Asthma
4.05
Inhaler Only vs No Asthma
2.14
Preventive Medicine Only vs No Asthma
1.62
Neither vs No Asthma
1.69
Behavioral Problem
CIS>=15 vs CIS<15
2.41
Family Size
>4 vs <=4
0.73
0
1
2
3
4
5
6
Odds Ratio