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Research Article

THE RELATIONSHIP OF URINARY UROMODULIN LEVELS WITH SNP RS1333226 IN THE UMOD QUALITY IN PAKISTANI POPULATION

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Abstract:

Uromodulin, maximum plentiful protein in urine, stays manufactured in profuse climbing loop of Henle in addition distal intricate tubules. Cases through CKD were condensed urinary uromodulin stages subordinate to tubular injury. Genome extensive connotation researches recognized substantial single nucleotide polymorphism (SNP) relations through chronic kidney disease at uromodulin locus. Researchers observed suggestion of urinary uromodulin attentions through chronic kidney disease in addition through SNP rs1333228 in UMOD genetic factor. The research encompassed 72 Pakistani through hypertension-attributed chronic kidney disease through an eGFR \leq 65ml/minute/1.74m³, 53 first-degree relations, also 60 unconnected panels. Urinary uromodulin absorption remained unrushed experiencing Lumina_ multiplex kits. Urinary uromodulin stages remained expressively inferior in chronic kidney disease patients associated to mutually controls in addition first degree families in addition connected destructively through age, serum uric acid, serum creatinine, in addition systolic Blood Pressure in addition completely through chronic kidney disease -EPI eGFR. Our current research was conducted at Services Hospital, Lahore from May 2019 to April 2020. For individually 1-standard deviation rise in uromodulin level, multivariable-attuned odds proportion for chronic kidney disease remained 0.7 (96% Confidence Interval [0.49 to 0.82]; $p < 0.02$). Here remained not any substantial variances in slight allele occurrence among chronic kidney disease patients also controls ($p=0.58$) nor among first-degree relations in addition to controls ($p = 0.99$). Here remained not any substantial relations among genotype at rs1333227 also urine uromodulin levels ($p = 0.44$). Developed levels of urinary uromodulin remain related through inferior odds of hypertension-qualified chronic kidney disease. Researchers did not notice relations of genotype at rs1333227 through urinary uromodulin stages in the current sample people. Greater example extent researches from culturally different populaces remain indispensable to more categorize the current suggestion.

Keywords: Urinary Uromodulin Levels, SNP Rs1333226, UMOD, Pakistani Population.**Corresponding author:****Iram Munir,**

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INTRODUCTION:

Tamm-Horsfall protein (THP), the mucoprotein which constrains hem agglutination of worms, remained primary exposed in urine of fit grownups through Tamm also Horsfall in 1958 [1]. Thirty-two years in future, uromodulin, the glycol protein that constrains *in-vitro* examines of human T-cell also monocyte movement remained disinfected from urine [2]. By means of description of balancing DNA also genomic clones, Tamm-Horsfall protein also uromodulin remained originate to remain identical glycoprotein. Changes in uromodulin gene source to autosomal leading kidney illnesses, medullary cystic kidney illness 3, also ancestral juvenile FJHN, that current through juvenile beginning of polyuria, hyperuricemia, gout, also liberal nephropathy [3]. The primary genome wide association study (GWAS) on CKD recognized solitary nucleotide polymorphisms (SNPs) in important connotation through chronic kidney disease at the UMOD locus. 4 loci remained recognized in connotation by eGFR creak, of those one of the solidest connections remained for SNP rs129177075, by negligible T allele related through the 21% decrease in danger of CKD [4]. In the GWAS on hypertension, negligible G allele of rs13333229 in UMOD gene stayed related by the inferior danger of hypertension, condensed urinary uromodulin excretion, and better renal purpose. The purpose of the current research remained to examine association also reminder of urinary uromodulin levels by polymorphisms rs1333228 in UMOD genetic factor in Pakistani population [5].

METHODOLOGY:

Our existing research was conducted at Mayo Hospital Lahore Pakistan from September 2017 to June 2018. 75 unconnected Pakistani respondents by medically identified hypertension-qualified CKD (age \geq 19 years at illness start) remained employed. Our current research was conducted at Services Hospital, Lahore from May 2019 to April 2020. The analysis of hypertension-accredited CKD remained the medical judgement grounded on distinctive geographies as measured through doctor (occurrence of hypertension before usage of antihypertensive mediators, minor or else not any proteinuria [proteinuria \leq 3.3 g/24h]) otherwise characteristic histological variations of hypertensive nephrosclerosis uncertainty the kidney operation was existing. Cases having DM, additional recognized reasons of CKD, also/before seropositivity for HIV remained excepted. Cases remained measured as "Pak" Pakistani populace hesitation they self-reported overall 5 antecedents as being Pakistani. Altogether accessible first-degree relations (cases, sisters, also, children) remained involved. The over-all

of 55 first-degree families from 44 relations remained employed, including 6 cases, 19 brothers, also 20 offspring. Also encompassed remained physically also ethnologically harmonized healthy regulars, by regular kidney working, undesirable HIV serology, in addition standard BP.

Uromodulin Measurements: Another morning urine example remained together (mid-stream) in disinfected vessels also aliquoted into 1.5ml tubes directly afterwards gathering also deposited at -81°C beforehand examination. Long-lasting medicines remained suspended till subsequently specimen gathering.

Genomic DNA Withdrawal: Genomic DNA remained removed from entire blood by means of salting out process also Maxwell automated nucleic acid withdrawal platform from Promega, rendering to producer's teaching.

PCR Intensification also Arrangement Study: Genotyping of rs13333227 remained achieved while experiencing TaqMan SNP genotyping assesses (Practical Biosystems). The arrangement for reader remains by way it trails:

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GTCATAGCACAGAAGAGGTAGCAGACTCCTC
TTCCAGCTGTAGG[A/G]
ATATTGACTCCTCTTCCCAAACAGC
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Statistical Analysis: Information remained examined experiencing STATA v13. The Shapiro-Wilk's trial remained exercised to assess for regularity resultant in uromodulin levels being demonstrated by means of the logarithmic alteration to recover ordinariness. Unceasing variables remained articulated as means \pm SD or else as middles also IQR also separate variables described as proportions. Genotype delivery remained examined underneath preservative inherited models experiencing Kruskal- Wallis trial. $P < 0.06$ remained measured statistically substantial.

RESULTS:

Starting point Features: Researchers employed the overall of 185 Pakistani applicants (73 cases having hypertension credited CKD, here mentioned to as CKD patients, 54 primary degree relations also 60 controls). Demographic also medical info of contributors remains exposed in Table 1. Of first-degree families, 25.6% remained recognized hypertensive, whereas the extra 18% remained identified by hypertension throughout employment period. First-degree families had pointedly advanced SBP in addition DBP associated to controls ($p = 0.003$ also $p = 0.007$, correspondingly).

Urinary Uromodulin Levels: Urine examples remained obtainable in 168 (93%) applicants (67 CKD patients, 48 first-degree families, also 54 regulars). The average log uromodulin ($\mu\text{g/ml}$) levels remained pointedly inferior in CKD patients (-1.5 ± 2.5) likened to controls (2.0 ± 2.5), ($p < 0.002$), as displayed in Table 1. The average log uromodulin levels remained identical once associating first-degree relations (1.1 ± 2.0) also controls (2.0 ± 2.8), ($p = 0.525$), together of whom had standard kidney purpose. Here remained not any variances in urinary creatinine levels among CKD patients also regulators, by suggestively inferior uromodulin-to-creatinine standards in CKD patients associated to controls, owing to inferior uromodulin heights in CKD patients. Here remained the weakly optimistic association among log uromodulin stages also CKD EPI eGFR ($r_s = 0.37$, $p < 0.002$). Between CKD respondents, here remained not any connection among uromodulin stages also urinary entire protein stages ($r = 0.09$, $p = 0.557$). For individually 1-standard nonconformity rise in uromodulin level, multivariable-attuned odds proportion for CKD

remained 0.7 (96% Confidence Interval [0.49 to 1.82]; $p < 0.002$; Table 2).

UMOD SNP rs13333227: The entire of 182 (98%) respondents remained positively genotyped. Allele also genotype incidences remain existing in Table 1. Researchers originate not any substantial variances in allele incidence (A, G) among CKD patients besides controls ($p = 0.593$), among first-degree families also controls, ($p = 0.984$), otherwise among CKD patients also first-degree families ($p = 0.626$).

SNP rs13333227 besides Log Uromodulin Levels: Solitary 167 respondents that got both urinary uromodulin heights also genotype information stood comprised in the examination. On pole hoc examination, amongst CKD respondents, researchers originate substantial variances in uromodulin stages grounded on genotype, by patients homozygous for inherited the allele with developed uromodulin stages associated to these homozygous for negligible G allele ($p = 0.06$). Here remained not any alterations detected amongst these by AA against AG or among GG Versace AG genotypes (altogether $p > 0.06$).

Table 1: Features of research populace.

Features	CKD PATIENTS First-	degree relations	Regulator	p-value*	p-value
Man, (%)	27 (25-33)	28 (24-32)	28 (24- 30)	0.634	0.853
Age	46 (65%)	17 (33%)	26 (45%)	0.023	0.193
BMI	30 (21-50)	48 (41-53)	41 (34-46)	<0.001	0.046
SBP	129 (120-149)	118 (113-130)	141 (132-168)	<0.001	0.003
DBP	76 (72-88)	74 (66-78)	86 (79-98)	<0.002	0.007
Serum creatinine	770 (483-1117)	74 (65-83)	76 (64-84)	<0.002	0.854
Serum uric acid	0.3 (0.3-0.3)	0.5 (0.4-0.6)	0.4 (0.4-0.5)	<0.002	0.106
UMOD/Cr ratio ($\mu\text{g/mg}$)	3.6 (1.2-8.1)	3 (1.0- 7.0)	0.6 (0.2-3)	<0.002	0.978
Rs13333228 genotype occurrences (AA, AG, GG), %	43, 35, 22	40,41,19	35, 44, 21	0.869	0.768
Rs13333228 allele occurrence %	58, 42	57, 43	59, 41	0.593	0.984

Table 2: Suggestion by hypertension-credited long-lasting kidney illness.

Distinctive	Unadjusted		Attuned*	
	Odds Relation (96% CI)	p-value	Odds Relation (97% CI)	p-value
Age				
Linear Tendency	2.07 (2.04 - 2.07)	<0.002	2.03 (2.01 - 2.07)	<0.002
Gender				
Man	2 (Ref)		2 (Ref)	
Woman	0.35 (0.19 - 0.65)	0.002	0.27 (0.11 - 0.64)	<0.002

Table 3: Association among rs13333227 polymorphisms in UMOD genetic factor also medical in addition demographic structures in CKD patients.

rs13333228	AA	AG	GG	p-value#
N (%)	32	16	26	
Sex (Male/Female)	19/12	12/3	15/10	0.379*
Age	49 (44-53)	47 (42-57)	44 (40-50)	0.158
SBP	151 (135-170)	138 (130-141)	141 (128-166)	0.328
DBP	90 (79-100)	82 (76-87)	87 (78-97)	0.334
Serum creatinine	638 (513-1054)	810 (462-1015)	823 (505-1141)	0.791
Uric acid	0.5 (0.4-0.6)	0.5 (0.4-0.5)	0.4 (0.4-0.6)	0.667
Urine PCR	0.1 (0.1-0.2)	0.1 (0.0-0.2)	0.1 (0.1-0.2)	0.316

DISCUSSION:

In our current research, researchers established that urinary uromodulin remains the indicator of kidney illness, by inferior levels in CKD patients associated to these by standard kidney working. Researchers established that urinary uromodulin relates damagingly by serum creatinine in addition absolutely by eGFR [6]. Through every 1-SD rise in urinary uromodulin, here remained inferior probabilities of CKD (OR = 0.7). In one research through Thorley et al. (1987), here remained the sturdy optimistic association among 20th hour uromodulin levels in addition creatinine permission, irrespective of kind of Chronic Kidney Disease [7]. In applicants by DM, urinary uromodulin levels remained suggestively inferior in these through DM nephropathy associated to these by standard kidney working. This remains primary research to describe urinary uromodulin attentions in the Pakistani people [8]. Urinary uromodulin levels in the current contributors of Pakistani grandparents remained inferior than these formerly described amongst peoples of European grandparents. In peoples of Australian ancestry, 1-day urinary uromodulin levels remained also linearly related by renal extent also capacity measured by means of ultrasonography, signifying that uromodulin might remain measured as the indicator for tube-shaped numbers replicated via tubular figure [9]. In previous effort, Brenner et al. Freshly, this remained exposed that 1-day urinary uromodulin levels connected by birth mass in peoples of European

ancestry, signifying that urinary uromodulin might remain experienced as the replacement of nephron figure [10].

CONCLUSION:

In deduction, advanced stages of urinary uromodulin remain related by inferior odds of hypertension-accredited CKD. Researchers did not notice relations of genotype at rs13333229 by urinary uromodulin stages, perhaps owing to early phase of the existing respondents. By way of UMOD was concerned in kidney meaning in addition Blood Pressure control, researches by greater example dimensions also from culturally dissimilar inhabitants remain important to additional classify in the current connotation.

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