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Sex-Specific Association of Parental Chronic Kidney Disease with Their Offspring's Kidney Function: A Population-Based Cohort Study

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Objectives: Although most kidney diseases are not hereditary, chronic kidney disease (CKD) has familial predispositions. The purpose of this study is to evaluate whether the presence of maternal and paternal CKD is differentially associated with their offspring's kidney function.

Methods: Using a database from the Korea National Health and Nutrition Examination Surveys between 2005 and 2018, we conducted a population-based cross-sectional study in 4,707 offspring who were aged 19-40 and their 7,318 parents. Considering age-specific threshold of decreased kidney function, parental and offspring CKD were defined as eGFR <60 and <75 ml/min/1.73m^2, respectively.

Results: The mean age was 25.6 years and 58.3% were men. There were 414 (8.8%) offspring with parental CKD. They were more likely to be smokers (38.9% vs. 29.3%), had higher proportion of dyslipidemia (30.9% vs. 18.8%), and diabetes (2.4% vs. 0.9%), and had lower eGFR (87.4 vs. 97.7 ml/min/1.73m^2) than those without parental CKD. Parental eGFR well correlated with their offspring's eGFR. In multivariable logistic analysis after adjustment of confounding factors, parental CKD was associated with 4.5-fold higher odds for offspring CKD (Odds ratio [OR], 4.50; 95% confidence interval [CI], 3.13-6.47). This association was more prominent in the presence of maternal CKD. The OR for CKD in offspring with maternal CKD was 5.60 (95% CI, 3.69-8.50) and the corresponding OR in those with paternal CKD was 2.62 (95% CI, 1.55-4.43). Moreover, the odds for offspring CKD was greatest when both maternal and paternal CKD were present (OR, 12.02; 95% CI, 4.22-34.20). There was a significant interaction for offspring CKD between offspring sex and maternal CKD; maternal CKD was more associated with daughter's decreased kidney function than son's.

Conclusions: Our study showed that parental CKD was significantly associated with offspring's kidney function and this association was stronger in the presence of maternal CKD.

Table 1. Baseline characteristics of offspring and parent according to parental CKD (eGFR <60 ml/min/1.73m²)

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	Offspring				Parent			
	Total (n=4,707)	Parent eGFR <60 (n=414)	Parent eGFR ≥60 (n=4,293)	P-value	Total (n=7,318)	Parent eGFR <60 (n=336)	Parent eGFR ≥60 (n=6,982)	P-value
Age (years)	25.6 (0.1)	27 (0.3)	25.5 (0.1)	<0.001	53.8 (0.1)	57.2 (0.4)	53.7 (0.1)	<0.001
Sex (Male, %)	2,313 (58.3%)	195 (60%)	2,118 (58.2%)	0.503	3,659 (57.1%)	175 (56.2%)	3,484 (57.1%)	0.755
BMI (kg/m²)	23 (0.1)	23.2 (0.2)	22.9 (0.1)	0.217	24.3 (0)	24.8 (0.2)	24.2 (0)	0.002
SBP (mmHg)	110.6 (0.2)	110.3 (0.7)	110.7 (0.2)	0.702	121 (0.2)	125.3 (1)	120.8 (0.3)	<0.001
DBP (mmHg)	73.1 (0.2)	73.6 (0.6)	73.1 (0.2)	0.309	79.5 (0.2)	80.5 (0.6)	79.4 (0.2)	0.093
Smoking history (%)				<0.001				0.511
Current Smoker	1,270 (30.2%)	127 (38.9%)	1,143 (29.3%)		1,694 (27.2%)	74 (25.1%)	1,620 (27.3%)	
Past smoker	402 (9.3%)	42 (10.8%)	360 (9.2%)		1,409 (21.3%)	65 (19.8%)	1,344 (21.4%)	
Non smoker	3,035 (60.5%)	245 (50.3%)	2,790 (61.5%)		4,136 (51.5%)	193 (55.1%)	3,943 (51.3%)	
Alcohol history (%)				0.444				<0.001
Heavy drinker	598 (13.5%)	42 (12%)	556 (13.6%)		900 (15.2%)	16 (6.1%)	884 (15.5%)	
Social drinker	3,546 (75.6%)	310 (75.2%)	3,236 (75.6%)		4,338 (60%)	209 (62.8%)	4,129 (59.9%)	
Non drinker	563 (10.9%)	62 (12.9%)	501 (10.7%)		1,990 (24.8%)	107 (31.2%)	1,883 (24.6%)	
Econimic status (%)				0.537				0.256
1st Quartile	266 (6.1%)	29 (8.4%)	237 (5.9%)		436 (5.8%)	25 (8.5%)	411 (5.7%)	
2nd Quartile	935 (20.9%)	88 (21.5%)	847 (20.8%)		1,510 (20.7%)	76 (21.4%)	1,434 (20.6%)	
3rd Quartile	1,496 (31.4%)	138 (30.6%)	1,358 (31.4%)		2,320 (31.6%)	109 (32.1%)	2,211 (31.6%)	
4th Quartile	2,010 (41.6%)	159 (39.5%)	1,851 (41.9%)		3,052 (41.9%)	126 (37.9%)	2,926 (42.1%)	
Hypertension (%)	251 (5.5%)	19 (4.7%)	232 (5.5%)	0.551	2563 (34.4%)	184 (56.3%)	2,379 (33.5%)	<0.001
Diabetes (%)	45 (1%)	8 (2.4%)	37 (0.9%)	0.049	902 (12.2%)	78 (24.6%)	824 (11.7%)	<0.001
Dyslipidemia (%)	862 (19.9%)	104 (30.9%)	758 (18.8%)	<0.001	3,382 (46.1%)	193 (57.7%)	3,189 (45.6%)	<0.001
Fasting glucose (mg/dL)	88.6 (0.2)	88.7 (0.6)	88.6 (0.2)	0.928	102.2 (0.3)	106.5 (2.1)	102.1 (0.3)	0.037
Total cholesterol (mg/dL)	174.9 (0.6)	173 (1.9)	175.1 (0.6)	0.743	195.3 (0.5)	193.2 (2.3)	195.4 (0.5)	0.337
HDL cholesterol (mg/dL)	51.9 (0.2)	49.1 (0.7)	52.2 (0.2)	<0.001	48.6 (0.2)	45.2 (0.7)	48.8 (0.2)	<0.001
Triglyceride (mg/dL)	105.2 (1.5)	113.1 (4.6)	104.5 (1.6)	0.048	150.8 (1.7)	158 (6.3)	150.5 (1.8)	0.251
Hemoglobin (g/dL)	14.6 (0.1)	14.6 (0.1)	14.6 (0)	0.710	14.3 (0.1)	13.9 (0.1)	14.3 (0)	0.001
BUN (mg/dL)	12.5 (0.1)	13 (0.2)	12.5 (0.1)	0.01	15.3 (0.1)	19.9 (0.6)	15.1 (0.1)	<0.001
Creatinine (mg/dL)	0.88 (0.01)	0.96 (0.01)	0.87 (0)	<0.001	0.88 (0.1)	1.42 (0.06)	0.86 (0)	<0.001
eGFR (ml/min/1.73m²)	96.8 (0.3)	86.6 (0.8)	97.8 (0.3)	<0.001	84 (0.2)	52.6 (0.6)	85.3 (0.2)	<0.001
eGFR <75 (%)	278 (6%)	92 (19.7%)	186 (4.7%)	<0.001	2,009 (27.3%)	336 (100%)	1,673 (23.4%)	<0.001
eGFR <60 (%)	3 (0.1%)	1 (0.2%)	2 (0.1%)	0.503	336 (3.9%)	336 (100%)	6,982 (100%)	
Proteinuria >1+ (%)	43 (1.1%)	4 (0.9%)	39 (1.2%)	0.695	124 (1.8%)	32 (10.3%%)	92 (1.4%)	<0.001

Mean (standard error) or number (weighted %)

Table 2. Multivariate logistic regression for offspring CKD (eGFR<75ml/min/1.73m²) and subgroup analysis according to offspring sex

Table 2 . Multivariate logistic regression for offspring CKD (eGFR<75ml/min/1.73m²) and subgroup analysis according to offspring sex

	OR	95% C.I.	P-value
Offspring † (n =4,707)			
Parental CKD	4.50	(3.13 - 6.47)	<0.001
Maternal CKD	5.60	(3.69 - 8.50)	<0.001
Paternal CKD	2.62	(1.55 - 4.43)	<0.001
Son ‡ (n=2,313)			
Parental CKD	2.13	(1.19 - 3.82)	0.011
Maternal CKD	1.59	(0.79 - 3.18)	0.194
Paternal CKD	3.16	(1.53 - 6.55)	0.002
Daughter ‡ (n=2,394)			
Parental CKD	11.16	(6.98 - 17.85)	<0.001
Maternal CKD	22.21	(12.10 - 40.76)	<0.001
Paternal CKD	2.66	(1.27 - 5.57)	0.010

† Adjusted for offspring factors (age, sex, obese, economic status and history of alcohol, smoking, hypertension, diabetes and dyslipidemia) + parental factors (obese and history of hypertension and diabetes)

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P value for interaction (offspring sex*maternal CKD) <0.001 , P value for interaction (offspring sex*paternal CKD) = 0.342