



**Abstract Type : Oral presentation**

**Abstract Submission No.: A-0741**

**Abstract Topic : Non-dialysis CKD**

## **Maternal kidney disease and Offspring Neurodevelopmental Outcomes: A Nationwide Population-based Study**

**Jeongin Song**<sup>1</sup>, Jeesun Lee<sup>4</sup>, Zio Kim<sup>5</sup>, Seung Hyun Han, Sehoon Park, Seung Mi Lee<sup>4</sup>, Hajeong Lee

<sup>1</sup>Department of Internal Medicine-Nephrology, Dongguk University Ilsan Hospital, Korea, Republic of

<sup>2</sup>Department of Obstetrics and Gynecology, Seoul National University Hospital, Korea, Republic of

<sup>3</sup>Department of Interdisciplinary Program in Bioengineering, Seoul National University College of Medicine, Korea, Republic of

<sup>4</sup>Department of Internal Medicine-Nephrology, Inje University Ilsan Paik Hospital, Korea, Republic of

<sup>5</sup>Department of Internal Medicine-Nephrology, Seoul National University Hospital, Korea, Republic of

**Objectives :** Maternal immune activation, triggered by acute and systemic chronic inflammation, is considered a predisposing factor for offspring neurodevelopmental conditions. This study aims to investigate the potential impact of maternal chronic kidney disease (CKD) on offspring neurodevelopmental outcomes.

**Methods :** We analyzed data on pregnant women from the National Health Information Database from 2008 to 2017 in South Korea. Subjects were categorized into four groups: healthy control, CKD, ESKD (end-stage kidney disease), and kidney transplantation (KT) according to their pre-pregnancy kidney function. The primary outcome was the incidence of offspring neurodevelopmental diseases, including motor and cognitive developmental delay, autism spectrum disorders, attention deficit hyperactivity disorder, tics, stereotypic behavior, and seizures, based on ICD-10-CM codes.

**Results :** A total of 3,794,031 children were born to 2,680,092 mothers during the study period. After excluding multiple pregnancies, we included 487,477 healthy controls, 47,099 mothers with CKD, 51 mothers with ESKD, 200 mothers with KT, and 3,637,903 children. As expected, mothers with kidney disease had a higher likelihood of adverse pregnancy outcomes, such as preeclampsia, preterm birth, and placenta previa/abruption. In addition, offspring from mothers with kidney disease had a higher risk for neurodevelopmental disorder compared to those of healthy controls. (13.4%, 15.6%, 36.2%, and 21.5% in healthy control, CKD, ESKD, and KT mothers, respectively). Mothers with CKD (adjusted HR 95% CI: 1.09 (1.07–1.11),  $p < 0.001$ ), and ESKD (1.98 (1.33–2.93),  $p < 0.001$ ) showed a higher risk of offspring neurodevelopmental diseases even after adjusting for maternal age, parity, underlying hypertension, diabetes, gestational diabetes, preeclampsia, neonatal sex, preterm birth, place of residence, and income level. Interestingly, KT mothers did not exhibit an elevated risk of neurodevelopmental outcomes in their offsprings (adjusted HR [95% CI]: 1.24 [0.94–1.65]).

**Conclusions :** In this nationwide cohort study, we found that maternal pre-pregnancy kidney function was associated with offspring's adverse neurodevelopmental diseases in dose-responsive manners.

Neuro\_Tables\_1.jpg



Risk of neurodevelopmental outcomes in offspring according to maternal kidney disease status

Neurodevelopmental outcomes (n)	Cumulative incidence (N, %)				Unadjusted HR (Hazard ratios, 95% CI)			*Adjusted HR (Hazard ratios, 95% CI)		
	Healthy control (713,776)	CKD (69,648)	ESKD (69)	KT (242)	CKD (69,648)	ESKD (69)	KT (242)	CKD (69,648)	ESKD (69)	KT (242)
Any neurodevelopmental outcome	95,459 (13.4%)	10,836 (15.6%)	25 (36.2%)	52 (21.5%)	1.09*** (1.07 – 1.12)	2.70*** (1.04 – 3.45)	1.67*** (1.27 – 2.19)	1.09*** (1.07 – 1.11)	1.98*** (1.33 – 2.93)	1.24 (0.94 – 1.65)
Motor developmental delay	10,416 (1.5%)	1,191 (1.7%)	3 (4.4%)	7 (2.9%)	1.06 (1.00 – 1.12)	2.40 (0.78 – 7.46)	1.85 (0.88 – 3.89)	1.07 (1.00 – 1.13)	1.45 (0.47 – 4.52)	1.19 (0.56 – 2.50)
Cognitive developmental delay	7,433 (1.0%)	1,024 (1.5%)	4 (5.8%)	3 (1.2%)	1.24** (1.16 – 1.32)	4.28*** (1.61 – 11.42)	1.07 (0.35 – 3.33)	1.17*** (1.10 – 1.25)	2.06 (0.77 – 5.52)	0.66 (0.21 – 2.06)
Autism spectrum disorders / ADHD	5,662 (0.8%)	841 (1.2%)	4 (5.8%)	7 (2.9%)	1.21*** (1.13 – 1.30)	4.62** (1.73 – 12.30)	2.92** (1.39 – 6.14)	1.16*** (1.07 – 1.25)	1.63 (0.61 – 4.37)	1.58 (0.75 – 3.35)
Tics / stereotypic behavior	4,197 (0.6%)	564 (0.8%)	1 (1.5%)	3 (1.2%)	1.13** (1.04 – 1.24)	1.62 (0.23 – 11.49)	1.71 (0.55 – 5.32)	1.17 (1.07 – 1.28)	1.27 (0.18 – 9.05)	1.56 (0.50 – 4.87)
Epilepsy/Febrile seizure	76,536 (10.7%)	8,475 (12.2%)	19 (27.5%)	41 (16.9%)	1.08*** (1.06 – 1.11)	2.50*** (1.60 – 3.92)	1.65** (1.22 – 2.24)	1.08*** (1.06 – 1.10)	1.92** (1.23 – 3.02)	1.28 (0.93 – 1.76)
Epilepsy	7,624 (1.1%)	1,021 (1.5%)	4 (5.8%)	10 (4.1%)	1.27*** (1.19 – 1.36)	4.71*** (1.77 – 12.54)	1.27*** (1.19 – 1.36)	1.23*** (1.15 – 1.31)	2.47 (0.92 – 6.62)	1.80 (0.89 – 3.63)
Febrile seizure	74,892 (10.5%)	8,241 (11.8%)	18 (26.1%)	35 (14.5%)	1.08*** (1.05 – 1.10)	2.39*** (1.51 – 3.80)	1.08*** (1.05 – 1.10)	1.07*** (1.05 – 1.10)	1.87** (1.18 – 2.97)	1.17 (0.83 – 1.64)

\*Adjusted for age, neonatal sex, parity, hypertension, diabetes, gestational diabetes, preterm birth, low birth weight, preeclampsia, place of residence, income level

p-values are indicated by asterisks (\*p<0.05, \*\*p<0.01, \*\*\*p<0.001)