KSN 2020
FULLY VIRTUAL MEETING

**Abstract Type : Poster**
**Abstract Submission No. : PO-1656**

# Placental Growth Factor Deficiency Aggravates Diabetic Nephropathy

**Ji Hee Lim[1]**, Yaeni Kim[1], Eun Nim Kim[1], Yongjie Jin[1], Hyung Duk Kim[1], Tae Hyun Ban[2], Bum Soon Choi[2], Cheol Whee Park[1]
[1]Department of Internal Medicine-Nephrology, The Catholic University of Korea, Seoul St. Mary's Hospital, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, The Catholic University of Korea, Eunpyeong St. Mary's Hospital, Korea, Republic of

**Objectives:**

Placental growth factor (PlGF) is a member of the vascular endothelial growth factor (VEGF) family. PlGF exerts favorable angiogenetic and lymphangiogenic activity by binding to VEGF-R1 and -R3, respectively. Due to its functional synergy with VEGF-A, it is required for a correct neovascularization during pathological conditions while inactivation of PlGF contributes to decrease of pathological angiogenesis. Because reduced angiogenesis and lymphagiogenesis that contribute to defective lipid drainage are implicated in the progression diabetic kidney disease, we investigated the role of PlGF in the development of diabetic nephropathy by using PlGF-knockout mice.

**Methods:** Diabetes was induced by a low-dose streptozotocin injection in 9-week-old male C57BL/6J PlGF-KO and wild-type mice and biochemical and morphological parameters were examined at 12 weeks later.

**Results:** In diabetic PlGF-KO mice, fasting blood glucose and HbA1c levels increased significantly and the development of glomerular sclerosis and mesangial area expansion were accompanied by albuminuria. Diabetic PlGF-KO mice exhibited increased expression of Col IV, TGF-β1 and glomerular IHC staining for nephrin, PECAM-1 and WT-1-positive cells and VEGF-R1,-R2,-R3 expression decreased, suggesting decreased endothelial cell and podocyte structure. Intrarenal expression of pLKB1, and pAMPK decreased and that of PPARα, PGC1α, ERRα, p-eNOS, and urinary Nox concentration decreased while iNOS increased, indicating disturbed lipid metabolism and endothelial dysfunction in the same group. Increased intrarenal FFA, TG, and cholesterol concentration represents presence of lipid accumulation. F4/80- and TUNEL-positive cells increased, suggesting increased inflammatory cell infiltration and apoptosis. CD68 and arginase-II increased indicating that macrophage subtype M1 polarization is involved in the inflammatory process. Expression of Bcl2/bax decreased and that of SOD1 and 2 decreased, indicating increased apoptosis and oxidative stress, respectively.

**Conclusions:**

Impaired angiogenesis and lymphangiogenesis are implicated in PlGF deficiency and this promotes lipotoxicity-induced inflammation, oxidative stress and deteriorates renal functional and phenotypic parameters in the diabetic kidney.