KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Abstract Submission No. : 2558

Utility of whole exome sequencing in evaluation of genetic causes of adult chronic kidney disease of unknown origin

Ji Hye Kim[1], Eunjeong Kang[2], Kyung Chul Moon[3], Hee Kyung Kang[4], Hajeong Lee[1]
[1]Department of Internal Medicine, Seoul National University Hospital, Korea, Republic of
[2]Department of Internal Medicine, Ewha Womans University Medical Center, Korea, Republic of
[3]Department of Pathology, Seoul National University Hospital, Korea, Republic of
[4]Department of Pediatrics, Seoul National University Hospital, Korea, Republic of

Objectives: Whole exome sequencing (WES) has diagnostic yield of approximately 10-25% and is useful in identifying unknown causes of familial CKD, genetic FSGS and selecting unaffected family members for kidney donation. This study was conducted to identify causative genetic variants in familial CKD-UO and FSGS adults and evaluate diagnostic utility of WES in clinical practice.

Methods: WES was performed on buccal swab or blood samples from fourteen CKD or FSGS of unknown origin (UO) patients who visited Seoul National University Hospital nephrology clinic. Patient inclusion criteria were: over 20 years of age, familial history of CKD-UO without significant diagnosis from laboratory examination or kidney biopsy or suspected genetic FSGS with negative target gene panel for glomerular diseases.

Results: WES identified genetic variations in 7 of 14 patients (age range 30-75 years, male 50%, 9 CKD-UO patients and 5 FSGS patients). All nine CKD-UO patients had family history and variants were found in UMOD, PKD1, MUC1, WFS1 and GCGR genes. Likely pathogenic variants were found in two patients (WFS1, PKD1) and three patients had variant of uncertain significance (VUS). Additionally two patients' relatives received WES and same variants (WFS1, UMOD) they shared with primary patients were found. Among FSGS patients, three patients had family history and two VUS were found in MAFB and LAMA5 genes. WES was also used to exclude potential risky donor candidate by predicting diabetes development in candidate whose parents both had genetic variants in WFS1 and GCGR associated with diabetes.

Conclusions: WES had diagnostic yield of 14% in identifying likely pathogenic variants in CKD-UO and genetic FSGS patients with family history. It can aid physicians in unbiased, accurate diagnosis and prediction of CKD-UO. It is also helpful in transplantation field by identifying donor candidates who need to be excluded due to high likelihood of developing such diseases.