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# P049 -Clinical and genetic characteristics of autosomal dominant tubulointerstitial kidney disease – a case series

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Background
Autosomal dominant tubulointerstitial kidney disease (ADTKD) (previously termed medullary cystic kidney disease or familial juvenile hyperuricaemic nephropathy) is a group of disorders characterised by slowly progressive renal disease, bland urinary sediment with minimal proteinuria and autosomal dominant inheritance. Imaging studies are non-diagnostic showing degrees of renal atrophy ± medullary cysts. Renal biopsy, if performed, shows tubular atrophy and interstitial fibrosis without any pathognomonic features. Diagnosis can be confirmed by identifying a pathogenic variant in one of three genes: UMOD, MUC1 or REN. UMOD and MUC1 account for the majority of ADTKD families. Analysis of MUC1 is technically challenging and only available in limited centres. Hyperuricaemia, a low fractional excretion of urate and gout is associated with UMOD variants.

ADTKD may be under-recognised and underdiagnosed. This report describes clinical and genetic characteristics of affected individuals across two regional renal services in England.

Methods
Retrospective collection of clinical and laboratory data from affected individuals identified with ADTKD via the regional Clinical Genetics Service. Data was collected by local teams and anonymised for analysis. Data are presented as mean±SD.

Results
Twenty four individuals were identified: 12 from three families with MUC1 variants and 12 from four families with UMOD variants. There were no REN families. Ten patients were deceased and phenotypic data was available for 21 patients.

At presentation, 4 of 21 (19%) patients reported a history of gout, however, 12 of 14 (86%) had elevated serum urate. The medical record of 9 of 21 (43%) patients did not have family history of renal disease recorded at presentation. Age at time of referral to renal services was 46.5±7.4 years, with baseline eGFR 31±18 ml/min/1.73m2. Three patients presented with end stage renal disease (ESRD) and 13 more progressed to ESRD, aged 49.9±6.8 years (range 38 – 59 years).

Pre-dialysis eGFR data was available for nine patients; rate of loss of eGFR ranged from 0 to -8 ml/min/1.73m2/year with mean±SD -4.4±2.5 ml/min/1.73m2/year.

Seven patients were labelled with “unknown aetiology” as their initial diagnosis, 2 with familial nephropathy, 1 with hypertensive nephrosclerosis, 1 with diabetic nephropathy and 1 with reflux nephropathy. Six patients were labelled as having ADTKD as their initial clinical diagnosis. Data was unavailable for 6 patients.

Genetic diagnosis was identified up to 20 years after initial presentation. Three of four families with UMOD variants had an indel variant that has previously been reported in other British families, and less likely to be

associated with gout. Two MUC1 families had the common Cytosine insertion but the third family had a rare Adenine insertion.

Conclusion
ADTKD is an uncommon cause of progressive renal failure that may be misdiagnosed at initial evaluation.

Genetic testing for UMOD and MUC1 (±REN) should be considered in patients with a family history of renal disease, minimal proteinuria and normal renal ultrasound.

Family history of renal disease was not ascertained in over 40% of patients at initial evaluation, despite most families having multiple affected individuals. The importance of taking a good family history in the renal clinic is emphasised.