**Variable phenotypic presentations of renal involvement in Fabry Disease**

**Abstract**

Fabry disease is an X-linked genetic deficiency in the alpha galactosidase enzyme resulting in intracellular accumulation of glycosphingolipids and multisystem organ dysfunction. Around 50% of males and 20% of affected females will have renal involvement, ranging from proteinuria, reduced renal function, renal parapelvic cysts and end stage renal disease (ESRD) requiring dialysis or renal transplantation. The phenotypic presentation of Fabry disease is incredibly varied and will even vary between family members with the same confirmed genetic mutation. However identification of an index case will typically lead to 3-4 cases being identified by cascade screening.

In a cohort of patients affected by Fabry disease in the North East of England we reviewed the different phenotypic presentations of 8 index cases with renal disease and the renal manifestations within their 29 affected family members. The mean age of presentation was 40yrs (range 23-59yrs) and 6 of the 8 index cases were male. Various multisystem manifestations were observed including cardiac, neurological, cerebrovascular and skin involvement. 2 of the male index patients reached ESRD requiring renal replacement therapy. 2 female index patients had only hypertension and proteinuria at presentation and the remaining patients had either stable or progressive chronic kidney disease at the time of diagnosis.

This significant phenotypic variation demonstrates the need for a high index of suspicion in order to consider Fabry disease as a diagnosis. Additionally we highlight the importance of cascade genetic screening to identify additional affected and at risk family members so that treatment can be initiated in a timely fashion.