A successful bid to the National Commissioning Group in 2010 supported the development of designated clinics for patients with diagnosed or suspected Bardet-Biedl syndrome (BBS). The clinics are held over 4 centres, covering England, Scotland, Wales and Northern Ireland, providing a specialist service to both adults and children. Most patients with BBS in the UK are seen in one of these centres which have provided a unique opportunity to study this disease in depth.

Bardet-Biedl syndrome is a rare autosomal recessive, multisystem disease characterised by rod-cone dystrophy, renal malformations, learning difficulties, obesity, postaxial polydactyly, and hypogonadism. This is caused by mutations in the BBS genes. The genes code for proteins that localize to the primary cilia and are known to be involved in cilia function. Nineteen disease-causing genes have been identified and sequencing of known disease-causing genes confirms a clinical diagnosis of BBS in around 80% of patients.

Variable expressivity is a hallmark of BBS and both inter-and intrafamilial phenotypic variation is observed. Structural renal and urinary tract anomalies and renal dysfunction is a cause of considerable mortality and are reported to affect 53%-82% of patients with BBS. The primary renal phenotype is highly variable and the high frequency of renal disease in BBS causes heightened anxiety among patients and their carers due to the effects it has on quality of life, morbidity and mortality.

Through collaborative working between the four sites we were able to study the prevalence and severity of CKD in 350 patients with BBS-related renal disease attending the United Kingdom national Bardet-Biedl syndrome clinics, to further elucidate the phenotype and identify risk factors for CKD. Overall, 31% of children and 42% of adults had CKD; 6% of children and 8% of adults had stage 4-5 CKD. In children, renal disease was often detected within the first year of life.

Analysis of the most commonly mutated disease-causing genes revealed that, compared with two truncating mutations, two missense mutations were associated with less severe CKD in adults. Moreover, compared with mutations in BBS10, mutations in BBS1 were associated with less severe CKD or lack of CKD in adults. There appears to be both genotype and mutation-type correlations with CKD, with increased risk of developing CKD3b-5 for those patients who have truncating mutations and/or mutations in BBS10. Adults with missense mutations in BBS1, who have normal renal ultrasound scans, are unlikely to develop CKD3b-5. Patients with truncating mutations in BBS10, hypertension, and abnormal ultrasound scans are at significantly increased risk of CKD3b-5. Finally, 51% of patients with available ultrasounds had structural renal abnormalities, and 35% of adults were hypertensive. The presence of structural abnormalities or antihypertensive medication also correlates statistically with stage 3b-5 CKD.

This abstract describes the largest reported cohort of patients with renal disease in Bardet-Biedl syndrome. It maps the prevalence of renal disease in BBS and characterises the highly variable renal phenotype. We have identified risk indicators as well as potentially protective factors for renal disease.