

Title of the project:	
Non-invasive urinary biomarkers of kidney injury in children with sickle cell disease – the BIODREPA study	
Principal investigator	Year of award
Rute Baeta Baptista	2022
Please provide an overall summary of the project (max 500 words)	
Sickle cell nephropathy (SCN) affects up to one third of adults with sickle cell disease (SCD) and accounts for 16–18% of SCD-related mortality, with 12% of patients progressing to end-stage renal disease. SCN may manifest in childhood, with tubular injury often preceding the alterations detectable by traditional markers such as reduced glomerular filtration rate (GFR) or increased albuminuria. Non-invasive urinary biomarkers – specifically alpha-glutathione S-transferase (α-GST), neutrophil gelatinase-associated lipocalin (NGAL), and kidney injury molecule-1 (KIM-1) – have shown promise in adults for earlier diagnosis of SCN, but had not previously been studied concurrently in a paediatric population. The BIODREPA study is a prospective, longitudinal, observational cohort study designed to characterise the natural history of SCN in children and adolescents aged 2–18 years. Participants were recruited at a scheduled outpatient visit in steady-state, after informed consent. Patients with intercurrent illness in the preceding 30 days, regular transfusion, prior bone marrow transplant, pregnancy, or comorbidities independently associated with kidney disease were excluded. Baseline assessment included demographic, clinical, and laboratory data, kidney ultrasound, and measurement of urinary α-GST, NGAL, and KIM-1 normalised to urinary creatinine by ELISA. Longitudinal follow-up visits are conducted at least annually, capturing hypertension, hyposthenuria, creatinine- and cystatin-C-based GFR, kidney ultrasound findings, and urinary biomarkers. A composite renal outcome was defined as GFR <90 mL/min/1.73 m², albuminuria (uACR >30 mg/g), or abnormal kidney ultrasound findings. Preliminary results are available for 65 patients. The prevalence of SCN at baseline was 60% (composite renal outcome present in 37/65 patients): no patient had GFR <90 mL/min/1.73 m²; 6% had albuminuria (uACR >30 mg/g); and 57% had abnormal kidney ultrasound findings. Patients with SCN had significantly higher urine albumin-to-creatinine ratios (15.1 ± 9.8 vs. 10.5 ± 3.5 mg/g, $p = 0.019$) and lower diastolic blood pressure compared to those without SCN. Among the three biomarkers studied, urinary NGAL showed the most clinically relevant association: levels were significantly elevated in patients with albuminuria compared to those without (12.0 vs. 3.0 ng/mL, $p = 0.035$), suggesting its potential value for early detection of glomerular involvement. Alpha-GST and KIM-1 did not differ significantly between groups, though a trend towards higher α-GST levels was observed in patients with albuminuria. Longitudinal follow-up is ongoing and statistical analysis of follow-up data has not yet been completed. These findings confirm that SCN is common in children with SCD, frequently manifesting as structural kidney abnormalities on ultrasound before measurable declines in GFR. Urinary NGAL appears to be the most promising non-invasive biomarker for identifying early glomerular injury in this population. The completion of longitudinal follow-up analysis will enable assessment of whether baseline biomarker levels predict future progression of SCN, which may have important implications for timely initiation of nephroprotective strategies such as hydroxycarbamide in paediatric SCD patients.	
How was the grant used for the project? (max 200 words)	
The grant was used to cover ELISA kits to measure urinary NGAL, KIM-1, and α -GST and transportation of blood samples from the three participating centers to a common laboratory where the urinary biomarkers were measured.	

Please list all publications completed, with links to open access publications where available

Not applicable.

Are any other publications planned?

Since the baseline evaluation, patients have been followed up at least annually, and we expect to publish the results when we reach a 5-year follow-up by the end of 2026.

Please list all presentations relating to the project

Poster at ESPN 2022 Annual Meeting (baseline evaluation results).