
A multicenter, descriptive cross-sectional study was performed in 77 children (73% male) in Eastern India. Children less than 18 years with clinically suspected tubulopathy were enrolled in the study and whole exome sequencing (WES) was performed in all the cases. Sanger sequencing and Multiplex ligation-dependent probe assay (MLPA) were also done when indicated. The variants were classified as pathogenic/likely pathogenic (P/LP) in accordance with American College of Medical Genetics and Genomics, 2015. Fifty five (24 novel) P/LP variants were identified and genetic diagnosis was established in 54 children (70%). Clinically, distal renal tubular acidosis (32.4%) was the most commonly identified tubular disorder but the diagnostic yield of WES was highest for nephrogenic diabetes insipidus (100%). Barakat syndrome and Renal cyst with diabetes syndrome were the rare disorders identified. WES led to revision of clinical diagnosis in 14 children (26% of those with a confirmed genetic diagnosis and 18% of the overall cohort) and detection of unidentified co-morbidities (sensorineural deafness n=5, hemolytic anemia n=2, dental changes n=1). The authors suggested that WES is an essential tool in the diagnosis and management of inherited tubulopathies in India.

Evaluation of daily low-dose prednisolone during upper respiratory tract infection to prevent relapse in children with relapsing steroid-sensitive nephrotic syndrome - The PREDNOS 2 randomized clinical trial (JAMA Pediatr. 2022;176:236-43)

A number of studies including, randomized controlled trials, have established that increasing the maintenance dose of corticosteroids during upper respiratory tract infections (URTI) for 5-7 days can reduce the risk of relapse in nephrotic syndrome. PREDNOS 2 is a phase 3, double blind, placebo-controlled randomized clinical trial which evaluated the efficacy of daily (for 5-7 days) low dose prednisolone (15 mg/m²/day) during an episode of URTI in reducing the risk of relapse among 365 children with or without background immunosuppressive treatment in the United Kingdom. The primary outcome was the incidence of first upper respiratory tract infection-related relapse (URR). Secondary outcomes were overall rate of relapse, changes in background immunosuppressive treatment, cumulative dose of prednisolone, rates of serious adverse events, incidence of corticosteroid adverse effects, and quality of life. In intention to treat analysis, the number of patients experiencing URR was 56 of 131 (42.7%) in the prednisolone arm and 58 of 131 (44.3%) in the placebo arm (adjusted risk difference, 0.02; 95% CI, 0.14 to 0.10; P=0.70). No significant differences were observed in secondary outcomes as well between the treatment arms. It was concluded that daily short course of low dose prednisolone at the time of URTI does not reduce the risk of relapse in children with nephrotic syndrome.


Membranoproliferative glomerulonephritis (MPGN) is a histopathological entity characterized by increased mesangial matrix and cellularity along with thickening of glomerular capillary walls, resulting from dysregulation of the alternative complement pathway. It is broadly classified into C3 glomerulopathy [C3 glomerulonephritis (C3GN) and Dense deposit disease (DDD)] and immune complex MPGN. This multicenter observational cohort study enrolled 80 pediatric (2-15 years) patients with MPGN/C3 glomerulopathy to determine the phenotype and were followed up for a median of 5.18 (IQR, 2.13-8.08) years within the National Registry of Rare Kidney Diseases (RaDaR). C3GN was more common than immune complex MPGN (39 vs 31 patients) while 10 patients were identified with immune complex GN. Acquired (anticomplement autoantibodies) alternate pathway dysregulation was detected in 46% patients across all groups while genetic alterations contributed to only 9% of patients. Hematuria was the most common presentation (91%) and low estimated glomerular filtration rate (eGFR) was detected in 44% patients at recruitment. Importantly, severe kidney dysfunction (eGFR <30 mL/min per 1.73 m²) was observed only in patients with C3GN. On follow up, complete or partial remission was observed in 28 patients (71%) with C3GN and 36 patients (88%) with immune complex MPGN. Eleven patients (14%) progressed to renal failure and histopathologic evidence of >50% crescents was found to be the only risk factor for renal failure in multivariate analysis (hazard ratio, 6.2; 95% confidence interval, 1.05 to 36.6; P<0.05). Nine transplants were performed in eight patients but 2 of these failed due to recurrent disease. The authors concluded that presenting eGFR and crescentic disease are important prognostic markers of C3GN in pediatric patients, and even though acquired complement pathway abnormalities are common among these patients, they do not contribute to renal failure.

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