**POTENTIAL DIAGNOSTIC ROLE OF URINARY EXOSOMAL MIRNAS IN IGA NEPHROPATHY: A CLINICAL OBSERVATIONAL STUDY**

**Authors:**

Shankar M, Moorthy M, Shetty A

Introduction: IgA nephropathy is the most common primary glomerulonephritis worldwide and can progress to kidney failure. The current “gold standard” for diagnosis is kidney biopsy, which is invasive with risks of morbidity and mortality. miRNAs are small, non-coding endogenous RNA that may serve as non-invasive biomarkers, and that are found in urinary exosomes. Thus far, there is paucity of studies on the miRNA profile for the diagnosis of IgA nephropathy. Hence, we aimed to study the urinary exosomal miRNA signature of Indian patients with IgA nephropathy.

Methods: 50 biopsy-proven IgA nephropathy cases, 50 healthy controls & 24 disease controls which included biopsy proven diabetic nephropathy, hypertensive nephrosclerosis, lupus nephritis, membranous nephropathy, MCD and primary FSGS, were recruited over 4 years (2020–2024). Urinary exosomes were isolated from which miRNA was extracted. Analysis of urinary exosomal miRNA was done using the digital multiplexed nCounter® human v3 miRNA Expression Assay which contains 798 unique miRNA barcodes. Candidate miRNAs were identified using Lasso regression and CombiROC algorithm.

Results: 9 candidate miRNAs, hsa-miR-4532,hsa-miR-4488,hsa-miR-3158-3p,hsa-miR-151b,hsa-miR-3195,hsa-miR-1289,hsa-miR-20a-5p+hsa-miR-20b-5p,hsa-miR-32-5p,hsa-miR-525-3p differentiated IgA nephropathy cases from both healthy and disease controls with AUC values of >0.7. Additionally, a combination of just 2 miRNAs - hsa-miR-4532, and hsa-miR-548a-3p was found capable enough to diagnose IgA nephropathy from healthy controls and disease controls with an AUC of >0.8.

Conclusion: There was a significant difference in the urinary exosomal miRNA profile in IgA nephropathy cases when compared to healthy and disease controls, suggesting that miRNAs are valuable in the non-invasive diagnosis of IgA nephropathy.