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Global Nephrology: Genetic mutation in Egyptian children with steroid-resistant nephrotic syndrome - Manal M Thomas - National Research Centre

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Nephrotic syndrome is that the commonest etiology of proteinuria in children. Steroid-resistant nephrosis (SRNS) is defined by resistance to plain steroid therapy, and it continues to be one among the foremost intractable etiologies of kidney failure . Molecular studies discovered specialized molecules in podocytes that play a task in proteinuria. Mutations in NPHS2 that encodes for podocin constitute a frequent explanation for SRNS worldwide. This study aimed to screen for podocin mutations in SRNS Egyptian children and their parents. Our study included patients from 10 unrelated Egyptian families diagnosed with SRNS. Mutational analysis of the NPHS2 gene was performed by polymerase chain reaction amplification of the entire coding region of the gene and direct sequencing. Positive consanguinity was detected in five cases, and 4 of them had a positive case history of SRNS during a loved one . Mutational analysis of NPHS2 revealed pathogenic mutations in four cases (40%) including a completely unique missense in one patient (c.1A>T; p.M1L). Our study concluded that mutations of NPHS2 gene are common among Egyptian children with SRNS. We support a model where ethnicity plays a crucial role in specific NPHS2 mutations since a completely unique mutation was found in one patient during this study. Future study on an outsized number of Egyptian patients with SRNS is warranted to spot the particular genetic contribution of this gene within the development of SRNS in our population, which could help in patients' prognosis and management.

Nephrotic syndrome (NS) is one among the most typical primary kidney diseases, and its progressive forms can find yourself in chronic renal disorder . NS is that the results of an injury to the glomerular filtration barrier and presents clinically with heavy proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Most patients with NS show an honest response to steroid therapy and have an honest prognosis. On the contrary, approximately 10%of children and 40% of adults are steroid-resistant [steroid-resistant nephrosis (SRNS)], showing no response to steroid therapy and having a poor prognosis. The progressive fate of SRNS to end-stage renal disease(ESRD) is seen in 50e70% of patients. Inherited structural defects of the glomerular filtration barrier are detected in isolated also as familial cases of SRNS. The pathological picture of focal segmental glomerulosclerosis (FSGS) is revealed in approximately 63-73% of patients with childhood-onset SRNS.

Recent molecular studies involving children with sporadic primary SRNS have described mutations in many genes encoding proteins liable for the integrity of the glomerular filtration barrier. These genes include nephrin (NPHS1), podocin (NPHS2), alpha-actinin 4 (ACTN4), CD2-associated protein (CD2AP), Wilms' tumor 1 gene (WT1), transient receptor potential cation channel 6 (TRPC6), and Laminin-beta-2(LAMB2). Proteins encoded by these genes (nephrin, podocin, alpha-actinin-4, an adapter protein anchoring CD2, and others) alter the function of the podocytes. Mutations of NPHS1, NPHS2,or WT1 could also be the explanation for severe sorts of NS in children, getting to ESRD. Of them, NPHS2 mutations are considered the foremost common and are observed in 10-30% of sporadic cases of SRNS with FSGS.8Theclinical scope of NPHS2 mutations has widened, with the proof that mutations within the corresponding gene podocin may cause NS at birth, in childhood, or in adulthood. it's recommended to see for NPHS2 mutations in parallel or before starting steroid therapy in NS patients to guage treatment benefits. NPHS2 mutations were first identified in children with SRNS diagnosed before the age of6 years who reached ESRD during the first decade of life.11This study aims to screen for podocin mutations in Egyptian patients with SRNS and compare it with other published series.

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