

Gene Mutations and Steroid-Resistant Nephrotic Syndrome

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Glomerulopathies are the known cause of end-stage renal disease in 10% of cases in Iran. Furthermore, 8.6% to 11.4% of the end-stage renal disease population from 1996 till 2006 has been younger than 25 years.¹ Idiopathic nephrotic syndrome is the most common cause of nephrotic syndrome in children, and it is estimated that 20% of them are steroid resistant and half of this population develop ESRD in 6 to 8 years. It leads clinicians to look for different treatment options to prevent such an outcome.²⁻⁴

It has been well documented that nephrotic syndrome is related to different mutations in podocyte proteins. The *NPHS2* gene, which encodes podocin (a main constituent of the slit diaphragm), has drawn so much attention. Many studies have shown a strong correlation between the *NPHS2* gene mutations and steroid-resistant nephrotic syndrome (SRNS) in children.⁵⁻⁷ In 2009, Otukesh and colleagues did not find *NPHS2* mutations in exons 5 and 7 in 20 Iranian children with SRNS. Therefore, they did not recommend *NPHS2* (exons 5 and 7) mutation screening in Iranian children with SRNS.⁸ Abid and colleagues looked for mutations in the *NPHS1* and *NPHS2* genes in 145 patients with nephrotic syndrome. All mutations in the *NPHS1* gene were found in the early-onset cases and homozygous p.R229Q mutation in the *NPHS2* gene was found in 2 children with childhood-onset nephrotic syndrome. They concluded a low frequency of mutation of these two genes in children with nephrotic syndrome in Pakistan.⁹ Similarly, Vasudevan and coworkers who examined *NPHS2* mutations in 25 Indian children with sporadic SRNS found only 4% pathogenic mutation.¹⁰ As it was expected, no mutation of the *NPHS2* gene was found in 50 Czech adult patients with focal and segmental glomerulosclerosis/minimal change

disease, either.¹¹

However, there is a wide spectrum of the *NPHS2* mutations and Lipska and coworkers showed a 14% detection rate of *NPHS2* mutations in Polish patients, and it was advocated to test the whole gene coding sequence.¹² Carrasco-Miranda and colleagues analyzed a third exon of *NPHS2* and found missense mutation of *L142P* in SRNS patients.⁵

The different results may be due to varieties in design of studies: enrolled patients with different features, severity or familial background, and the mutations which were looked for. On the other hand, genetic variations in populations should not be overlooked, which shows the importance of genetic testing in different races.

It seems that testing for *NPHS2* mutations may help clinicians to make the decision to administer drugs with a high rate of side effects or not.⁵ However, the first necessity is to know the prevalence of different mutations in each race and region.

In this issue of the Iranian Journal of Kidney Diseases, two articles have addressed gene mutations in SRNS. Basiratnia and colleagues,¹³ in their study on 49 SRNS and 50 steroid-sensitive nephrotic syndrome in southwest of Iran, found a higher frequency of *NPHS2* gene mutation in SRNS cases in comparison with steroid-sensitive nephrotic syndrome (31% versus 4%) and also in familial forms, which is totally different from findings neighborhood countries like Pakistan and India.^{9,10} Their study emphasized the fact that the histologic features and clinical finding are not helpful to differentiate between those with or without mutation.¹³ Additionally, another study by Fotouhi and coworkers paid attention to this topic from northwest of Iran.¹⁴ They studies on 25 adult patients with focal and segmental

glomerulosclerosis, and similar to Reiterova and colleagues,¹¹ found no R229Q polymorphism.¹⁴ It would seem that we still need such studies to have a better scheme for our practice.

CONFLICT OF INTEREST

None declared.

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Voiding Dysfunction in Children With Chronic Functional Constipation

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Urination and defecation are complex functions and often misunderstood. They involve the coordination of completely different muscle systems. Dysfunctional elimination syndrome (DES) refers to patients who have problems with both bladder and bowel control. The pattern of abnormal voiding seen in children can be quite variable. Some children hold their urine for extensive periods, overstretching

their bladders and then urinate with perfectly normal coordination. Others have difficulty relaxing the sphincter during urination and void against the sphincter, straining the bladder extensively in the process. Finally, the outcome is inefficient voiding. All of these abnormal voiding patterns may also be associated with chronic constipation, which collectively is referred to as DES.