STUDY OF NR1I2 GENE POLYMORPHISM (A7635G) AND STEROID RESISTANCE IN EGYPTIAN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

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Introduction

Nephrotic Syndrome (NS) is chronic disorder, characterized by alterations of the permeability of the glomerular capillary wall, resulting in its inability to restrict the urinary loss of protein.

Idiopathic nephrtic syndrome (INS) (also called nephrosis) is defined by the combination of a nephrotic syndrome (proteinuria, hypoalbuminemia, hyperlipidemia, and edema) and non-specific histological abnormalities of the kidney including minimal changes (MC), focal and segmental glomerular sclerosis (FSGS), and diffuse mesangial proliferation. As INS response to treatment with steroids varies ,several studies was done to analyze the association between patient genetic profile and the response to steroid treatment, which help in predicting the treatment response of children with INS..

Nowadays it is clear that *NR1I2 gene* is also involved in regulation of steroid metabolism through trans-activation and trans-repression of genes controlling glucose, lipid, cholesterol, bile acid, and bilirubin homeostasis.

Aim of the work

The aim of this work was to study association between NR1I2 gene polymorphism (A7635G) rs6785049 and steroid resistance in Egyptian children with idiopathic nephrotic syndrome.

Subjects

After approval of the Alexandria ethics committee, 100 INS patients and 50 healthy individuals were included in the current study. INS patients were enrolled consecutively from Nephrology Units in Alexandria Children Hospital, and were further subdivided into two groups. The first group included 50 nephrotic sensetive patients and the second group included 50 nephrotic resistant patients.

Methods

Genotyping for *NR1I2* polymorphism (rs6785049) was done using stratagene Mx3000P Q PCRsystem.

Results

Table 1: Comparison between nephrotic sensetive and nephrotic resistant groups according to genotype and allele frequency

	NS		NR		χ^2	p
	No.	%	No.	%		
Gene	**(n = 50)**		**(n = 50)**			
AA®	14	28.0	4	8.0		
AG	30	60.0	30	60.0	10.101*	0.006*
GG	6	12.0	16	32.0		
Allele frequency	**(n = 100)**		**(n = 100)**			
A®	58	58.0	38	38.0	8.013*	0.005*
G	42	42.0	62	62.0		

χ^2: **Chi square test** p: p value for comparing between the studied groups

*: Statistically significant at $p \leq 0.05$

NS: Nephrotic sensitive , NR: Nephrotic resistant

®: Reference type

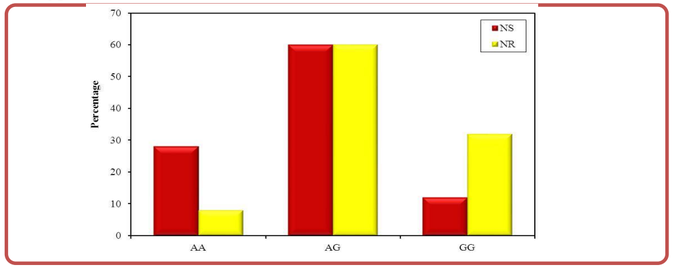

Figure1comparison between NS and NR according to genotype .

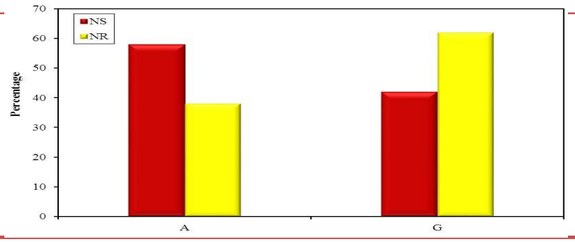

Figure2:comparison between NS and NR according to allelo frequency .

Table 2: Comparison between nephrotic sensetive and nephrotic resistant s regarding NR1I2 gene SNP rs6785049 genotypes

	NS®		NR		χ^2	p	OR	95%C.I
	No.	%	No.	%				
Gene	**(n = 50)**		**(n = 50)**					
AA®	14	28.0	4	8.0				
AG	30	60.0	30	60.0	4.345*	0.037*	3.50	1.032 – 11.867
GG	6	12.0	16	32.0	10.101*	0.001*	9.33	2.180 – 39.96
Allele frequency	**(n = 100)**		**(n = 100)**					
A®	58	58.0	38	38.0				
G	42	42.0	62	62.0	8.013*	0.005*	2.253	1.279 – 3.970

χ 2 : Chi square test p: p value for comparing between the studied groups *: Statistically significant at $p \leq 0.05$ OR: Odds ratio CI: Confidence interval LL: Lower limit UL: Upper Limit ®: Reference

Conclusion

NR1I2 single nucleotide polymorphism (rs6785049) is associated with the development of steroid resistance in INS patients. Nephrotic syndrome patients with GG genotype were 9.33 times are prone develop nephrotic resistance