European Journal of Molecular & Clinical Medicine (EJMCM)
ISSN: 2515-8260 Volume 09, Issue 03, 2022

Nephrotic Syndrome and Single Nucleotide Polymorphisms in Tumor Necrosis Factor Alpha-863 C/A

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Abstract

The NS is a kidney disease caused by an immunological response. It's linked to T-cell dysfunction and a secondary B-cell condition that causes abnormalities in immunoglobulin scales. This systemic disruption of T cell activity causes the generation of humoral factors or lymphokines, which cause the glomerular basement membrane to become more permeable.This study aims to identify the link between tumour necrosis factor-alpha single nucleotide polymorphisms (TNF-SNP) (-863 C/A) and the development of NS and their impact on TNF levels in the blood and steroid medication responsiveness.A total of 65 NS patients (42 males and 23 females, with a mean age of 7.23 3.15 years) and 30 healthy controls were included in the current study. They sought treatment at Al-Ima main Al-Kadima Medical City's Central Child Teaching Hospital in India's nephrology consultation clinic. Using a kit from Promega Company in India, DNA was extracted from whole blood samples according to the manufacturer's instructions. PCR-RFLP was used to find 863 C/A SNPs in the promoter of the TNF gene.In terms of age and sex, both cases and controls are comparable. Patients and controls had similar mean ages of 6.952.86 and 7.52 3.42 years (p = 0.516). Patients had 42 men and 23 females, while controls had 23 males and ten females (p = 0.624).This finding implies that, at least in confident NS children, illness activity is linked to TNF-serum levels. The lack of a drop in serum TNF- levels in patients with SRNS supports this hypothesis. Furthermore, the current findings show that the -863 SNP does not influence TNF- levels in the blood.

Key Words: Nephrotic Syndrome, Single nucleotide, Polymorphisms, TNF gene

Introduction:

The NS is a kidney disease caused by an immunological response. It's linked to T-cell dysfunction and a secondary B-cell condition that causes abnormalities in immunoglobulin scales. This systemic disruption of T cell activity causes the generation of humoral factors or lymphokines, which cause the glomerular basement membrane to become more permeable. Children are more typically afflicted, with a lower quality of life, and they are more likely to be exposed to significant problems linked to high morbidity and mortality rates. According to many studies, cytokines are important mediators of inflammation and are regarded as key candidates

for mediating nephrotic syndrome development.The pro-inflammatory cytokine TNF- is linked to the establishment and progression of the inflammatory response.TNF is involved in kidney injury, inflammation, glomerular permeability barrier disruption, and albuminuria formation.The reasons underlying the differences in responsiveness to steroid therapy in NS are unknown. However, hereditary factors are thought to play a role.The promoter of the TNF gene could influence these mechanisms has been studied for various SNPs. By controlling TNF production, these SNPs affect circulating TNF levels.

Aim and Objective:

This study aims to identify the link between tumour necrosis factor-alpha single nucleotide polymorphisms (TNF-SNP) (-863 C/A) and the development of NS and their impact on TNF levels in the blood and steroid medication responsiveness.

Material and Methods:

A total of 65 NS patients (42 males and 23 females, with a mean age of 7.23 3.15 years) and 30 healthy controls were included in the current study. They sought treatment at Al-Ima main Al-Kadima Medical City's Central Child Teaching Hospital in India's nephrology consultation clinic. Using a kit from Promega Company in India, DNA was extracted from whole blood samples according to the manufacturer's instructions. PCR-RFLP was used to find 863 C/A SNPs in the promoter of the TNF gene. Table 1 shows the primer sequence for SNP.

Table 1: Primer Sequence of -863C/A		
Polymorphism	Primer 5'» 3'	Fragment length
-863	F: gGCTCTGAGGATGGGTTAC R; CCTCTACATGGCCCTGTCTAC	126 bp

A thermal cycler (Cleaver Scientific Thermal CyclerTC32/80-) was used for PCR amplification. The PCR was carried out in accordance with the protocol. Restriction enzymes were used to digest the PCR products. The fragments were then electrophoresed in a 2.5 per cent agarose gel with a 50-bp marker, stained with ethidium bromide, and seen with a UV transilluminator. The Statistical Package for Social Science (SPSS) software version 20 was used to conduct the statistical analysis. The level of significance was set at a p 0.05.

Results and Discussion:

In terms of age and sex, both cases and controls are comparable. Patients and controls had similar mean ages of 6.952.86 and 7.52 3.42 years (p = 0.516). Patients had 42 men and 23 females, while controls had 23 males and ten females (p = 0.624). The sociodemographic and clinical features of steroid-sensitive and steroid-resistant patients are shown in Table 32

Table 2: Socio-Demographic and Clinical Characteristics of steroid sensitive and steroid resistant patients with nephrotic syndrome			
Variables	Steroid sensitive patients (n= 32)	Steroid resistant patients (n= 33)	P value
Age, years (mean±	6.95 ±2.86	7.52 ±3.42	

SD)			0.516
Sex, no (%) Male Female	 21 (65.6%) 11 (34.37%)	 22 (65%) 10 (30.30%)	 0.782
Family history,No (%) No family history Nephrotic syndrome Asthma Dermatitis	 22 (68.75%) 5(15.65%) 4 (12.5%) 1 (3.12%)	 25 (75.7%) 3 (9.09%) 1 (3.12%) 3 (9.09%)	 0.314
Blood urea, mg/dL (mean ±SD)	25.12±11.60	25.15±10.52	0.934
Serum creatinine, mmol/L (mean±SD)	1.69±0.63	2.30±0.95	0.514
Serum albumin , g/dL (mean±SD)	165±82.52	130.52±81.25	0.003

All of the characteristics were not substantially different between the two groups, except serum album, which was considerably greater in steroid-resistant patients (22 65%g/dL) than steroidssensitive individuals (2165%) (p = 0.003). The Hardy Weinberg equilibrium was seen in the distribution of different genotypes of the SNP (HWE). This polymorphism had three genotypes, CC, CA, and AA, in NS patients and controls. According to the digestion pattern of TNF-863 PCR products in patients and controls, the frequency of different genotypes and alleles of this polymorphism. There were no significant variations in genotype or allele frequencies between the two groups.

TNF promoter SNPs are likely to be linked to other genes in the human leukocyte antigen locus, altering disease resistance, susceptibility, and severity, irrespective of TNF gene expression. However, this investigation found no significant link between a TNF-863 polymorphism (regardless of genotype or allele) and NS. Youssef et al. found an insignificant connection between TNF—863 and NS, similar to the current finding. On the other hand, a prior study found no link between this polymorphism and inflammatory diseases such as ulcerative colitis and Chron's disease in Indians. In contrast, the current investigation found that serum TNF- among nephrotic syndrome patients was higher than the control group. TNF- levels were also lower in children with steroid-sensitive NS than in steroid-resistant kids

Conclusion:

This finding implies that, at least in confident NS children, illness activity is linked to TNF- serum levels. The lack of a drop in serum TNF- levels in patients with SRNS supports this

hypothesis. Furthermore, the current findings show that the -863 SNP does not influence TNF- levels in the blood.

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