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-308 G/A polymorphism in the TNF-alpha gene is associated with susceptibility to nephrotic syndrome in children: a systematic review and meta-analysis

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Objectives : NS or nephrotic syndrome is a disease commonly seen in children characterized by proteinuria, hyperlipidemia, hypoalbuminemia, and generalized edema. The pathogenesis of the disease is still unknown; however, studies show that genetics and immune dysregulation play a vital role in glomerular filtration disruption, but this is still poorly understood. Several studies have shown that the TNF-alpha and its gene variants are linked to the development of childhood NS. Still, the results are conflicting, which leads us to perform a meta-analysis to obtain more precise estimates.
Methods : The literature search concluded on January 9, 2024, and included ten eligible articles in which the -308 G/A polymorphism and its genotypes were determined among cases and controls. Pooled odds ratios (ORs) and 95% confidence intervals (95% CIs) were estimated in standard allelic, co-dominant, dominant, and recessive genetic models using Review Manager 5.4.
Results : The analysis using various genotypic models showed a significant association between the -308 G/A polymorphism and susceptibility to NS, favoring the development of the disease in the presence of the variant allele. Studies were subgrouped by geographic location and showed significant associations in the Asian subgroup compared to non-Asians. Moreover, removing studies that deviated from HWE (n=2) and studies conducted among Adults (n=1) yielded the same significant outcomes.
Conclusions : Results of the meta-analysis suggest that the -308 G/A polymorphism may affect the likelihood of NS development in children. Further large-scale and prospective studies must be conducted to verify these claims further.