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### GENETIC STUDIES OF DIABETIC NEPHROPATHY IN THE MALAYSIAN POPULATION: A REVIEW

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#### INTRODUCTION

Malaysia is reported to have the world's second fastest growing rate of kidney failure. The 2018 Annual Data Report of the United States Renal Data System noted that the incidence rate of treated end-stage renal disease in Malaysia increased by an average of 13.2% per year from 2003 to 2016. Diabetes is cited as the most common cause of end-stage renal disease in Malaysia. This article aims to review genetic studies conducted among patients with diabetic nephropathy in the Malaysian population.

#### METHODOLOGY

This review was conducted by searching PubMed, MEDLINE and Google Scholar databases to identify all relevant papers published in English from March to April 2022, using the following keywords: diabetes, type 2 diabetes, diabetic nephropathy, diabetic kidney disease and Malaysia.

#### RESULTS

The case-control study of patients with and without diabetic nephropathy showed a significant association of CNDP1, NOS3, and MnSOD genes with diabetic nephropathy. Ethnic subgroup analysis showed significant differences in terms of diabetes duration ( $\geq 10$  years) in CCL2 rs3917887, CCR5 rs1799987, ELMO1 rs74130, and IL8 rs4073. IL8 rs4073 was found to have significant association only in Indians, while CCR5 rs1799987 was significantly associated with the Chinese ethnic group. In Malays, SLC12A3 Arg913Gln polymorphism and ICAM1 K469E (A/G) polymorphism were found to be associated with diabetic nephropathy. No significant difference was observed in the I/D polymorphism of the ACE gene, regardless of ethnicity and gender. Studies on gene-environment interactions have suggested significant genetic and environmental factors for eNOS rs2070744, PPARGC1A rs8192678, KCNQ1 rs2237895 and KCNQ1 rs2283228 with kidney disease.

#### CONCLUSION

The contributions of genetic variants differed across ethnic groups. Further studies on the relationship of genetic variants and phenotypes are important because of the different complication profiles and susceptibility to diabetic nephropathy among Malaysians.