

# Population-Specific Pharmacogenetics of Hypertension: Toward Culturally Tailored Therapy

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## ABSTRACT

Essential (primary) hypertension is a multifactorial disorder shaped by genetic and environmental factors, with prevalence rising worldwide. Interethnic variability strongly influences drug response. Genome-wide association studies (GWAS) have highlighted loci such as AGT, ACE, PLEKHA7, CYP4A11, UMOD, ATP2B1, and CACNA1C in blood pressure regulation. Pharmacogenetic variants—including CYP2D6 with  $\beta$ -blockers, CYP2C9 with losartan, ACE I/D with ACE inhibitors, and UMOD with loop diuretics—affect efficacy, adverse reactions, and dosing. However, most evidence derives from European, Asian, or African cohorts, leaving a major gap for Middle Eastern populations. Saudi data indicate reduced CYP2D6\*4 frequency and higher CYP2C9\*2/3 allele prevalence, potentially impacting therapeutic outcomes. This review synthesizes GWAS, meta-analyses, and emerging biomarkers such as non-coding variants, microRNAs, epigenetics, and polygenic scores. Yet, translation into clinical practice is limited by insufficient prospective validation, infrastructure gaps, and ancestry-specific data. Future multi-ethnic studies are critical to enable precision antihypertensive therapy and equitable personalized care.

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