Researchers demonstrate how genetics play a role in the development of hypertension

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Hypertension or high blood pressure is known to be more prevalent in men than in women. The reasons for this difference are not completely understood. Researchers at the University of Alabama at Birmingham

Marnix E. Heersink School of Medicine reviewed nationwide data encompassing more than 200,000 individuals from diverse racial and ethnic backgrounds to assess the role of genetics in the sex differences in hypertension in a recent study published in *Circulation: Genomic and Precision Medicine*.

Hypertension affects approximately half of the United States population. It is the strongest risk factor for the development of cardiovascular diseases such as coronary heart disease, heart failure and stroke. Management of hypertension is associated with an annual health care spending of nearly $200 billion. Researchers say that predicting the development of hypertension may help establish preventive strategies to reduce the risk of heart disease.

In the current study, the investigators conducted genome-wide association studies for systolic blood pressure (SBP) using the U.K. Biobank data, which included more than 486,000 individuals from diverse ancestry groups. A genome-wide association study, or GWAS, is an analytical method that helps identify the risk factors that impact SBP.

"The GWASs were conducted for each sex individually, which allowed the team to account for the varying effects of genetic variants on SBP by sex," said Naman Shetty, M.D., a research fellow in the UAB Division of Cardiovascular Disease and first author of the study. "The variants identified in the GWAS were combined together to construct sex-specific polygenic risk scores, also known as PRS, for systolic blood pressure. The PRS reflects the genetic predisposition of developing hypertension."

Shetty and his team then applied the sex-specific PRS to the All of Us cohort, a research program that recruits individuals of diverse backgrounds from across the nation to promote precision medicine. The investigators conducted a sex-specific analysis of the association of the

PRS with hypertension in approximately 200,000 individuals.

"We found that the PRS was more profoundly associated with hypertension in females compared to males," Shetty mentioned. "Females with a high PRS had a higher risk of hypertension compared with males with a high PRS, and females with a low PRS had a lower risk of hypertension than males with a low PRS."

Furthermore, Shetty says the study revealed that the association between genetic risk and hypertension varied before and after menopause. Pre-menopausal women with a high genetic risk had a higher risk of hypertension compared to men, but the risk of hypertension became similar post-menopause.

"This comprehensive study highlights the role of genetics in the sex differences in hypertension," said Pankaj Arora, M.D., the senior author of the manuscript and associate professor in the UAB Division of Cardiovascular Disease.

Arora says further studies should focus on the genetic variants that were exclusively associated with SBP in each sex. Analysis of the functions of these genetic variants will advance the understanding of sex-specific mechanisms of regulation of SBP and the possibility of sex-specific responses to medications.

"For years, we have been aware of gender disparities in cardiovascular disease," Arora said. "Studies like these highlight a biological foundation for comprehending these differences. Such efforts will help in the development of precision medicine approaches to treating hypertension to reduce the gender disparities in the burden of cardiovascular disease."

More information: Naman S. Shetty et al, Sex Differences in the Association of Genome-Wide Systolic Blood Pressure Polygenic Risk

Score With Hypertension, *Circulation: Genomic and Precision Medicine* (2023). DOI: 10.1161/CIRCGEN.123.004259