**Effects of smoking, alcohol, and coffee on female reproductive health**

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*In a recent study, female reproductive hormone concentration and age at menopause were impacted by smoking, alcohol, and coffee consumption.*

Smoking, alcohol, and coffee consumption are associated with impacts on women’s reproductive health, according to a recent study.

Smoking, alcohol, and coffee consumption are common habits, which have increased during the COVID-19 pandemic. This is associated with an increase in major health problems such as cardiovascular disease and immune function-related diseases.

Prior studies have reported adverse reproductive events in women from smoking, alcohol, and coffee consumption, along with potential impacts on fertility and pregnancy outcomes. There is also a risk of disturbances in sex hormones and menstrual health. About 26% of women reported suffering from menstrual abnormality with endocrine hormone-related changes in 2018.

To determine the association between smoking, alcohol, and coffee consumption with reproductive health, investigators conducted a 2-sample mendelian randomization (MR) analysis using publicly available genome-wide association study (GWAS) data.

Three hypotheses were met for the MR analysis, the first being a significant association between the genetic instrument and exposures. The second was the genetic instrument being selected independently from cofounders, and the third was the genetic instrument not affecting outcomes except through the exposure.

Genetic instrument collection was accomplished through extracting 378 single-nucleotide polymorphisms (SNPs) associated with smoking initiation and 99 SNPs associated with alcohol drinking. Data on coffee consumption was also collected through 10 SNPs.

Following data collection, adjustments were made based on sex, age, and major genetic principal components. Clumping procedural was performed to allow independence of all instrumental variants (IVs) and removal of linkage disequilibrium between SNPs. F-statistics of each genetic instrument were calculated to avoid weak instrument bias.

GWAS summary statistics for reproductive hormones in women were gathered from the United Kingdom Biobank. Genome-wide meta-analysis data was used to compile summary data for the anti-Mullerian hormone (AMH).

Other reproductive hormones analyzed included sex hormone-binding globulin (SHBG), total testosterone (TT), bioavailable testosterone (bio-T), and estradiol (E2). Outcomes also included abnormal menstrual phenotypes such as irregular menstrual cycle, age at menopause, and dysmenorrhea.

Lower SHBG concentration were seen in women who smoked, along with earlier age at menopause. Investigators identified 17 outlier SNPs which may have influenced the association with low SHBG concentration, and 4 which may have influenced the association with age at menopause.

A strong inverse association of smoking with SHBG concentration and age at menopause was found after outlier correction. A positive association was also found between smoking and bio-T levels, though a casual indication was not found for TT level during inverse-variance weighted (IVW) analysis, and smoking was not associated with E2 and AMH levels.

A positive association was made between alcohol consumption and higher TT levels and earlier menopausal age from the IVW MR. These results were supported by weighted median and weighted mode approaches. However, alcohol consumption was not associated with SHBG, bio-T, E2, and AMH levels or irregular menstrual cycle.

A significant inverse association between coffee consumption and SHBG concentrations was found in a random-effects IVW, which was supported by a weighted median approach. A positive casual effect from coffee consumption was also observed on bio-T levels. Earlier age at menopause, along with TT, E2, and AMH levels, were not associated with coffee consumption.

Overall, smoking, alcohol, and coffee consumption had significant associations with effects on the reproductive system and abnormal menstrual phenotypes. Investigators recommended further research to distinguish genetic instruments between male and female individuals.

Reference

Jiang Z, He R, Wu H, et al.The causal association between smoking initiation, alcohol and coffee consumption, and women's reproductive health: A two-sample Mendelian randomization analysis. *Front Genet.* 2023;14. doi:10.3389/fgene.2023.1098616