

## Thyrotropin Suppression during Intoxication Mediates a Positive Effect of Alcohol on Kidney Function in Males

Despite a well-established direct toxic effect on renal cells by alcohol, there is a dose-dependent positive effect of alcohol consumption salutary to common laboratory parameters related to kidney performance. Alcohol also impacts thyroid hormones, and thyroid status modulates kidney function. The modulation of kidney parameters with thyrotropin (TSH) and thyroid status indicates a possible interaction between alcohol, kidney, and thyroid functions.

This retrospective study was conducted to test the hypothesis that some portion of the positive correlation between alcohol use and estimated glomerular filtration rate (eGFR) is mediated indirectly via alcohol's effect on thyroid hormones. We reviewed the electronic medical record of 767 hospitalized adult patients free of thyroid disorders who received medical care in the Mayo Clinic Health System from June 2019 through June 2022 and had blood alcohol concentration (BAC), serum TSH, and serum creatinine measured during the hospitalization. We calculated the eGFR using both the Isotope-Dilution Mass Spectrometry (IDMS)-traceable Modification of Diet in Renal Disease (MDRD) study equation and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Creatinine equation. We found in both males and females a positive correlation between BAC and eGFR and a negative correlation between BAC and TSH and between TSH and eGFR. Using mediation analysis, we found a direct effect of BAC on eGFR in both males and females (using MDRD equation: males vs. females:  $b=0.047$ ,  $P<0.001$  vs.  $b=0.026$ ,  $P=0.02$ ) (using CKD-EPI equation: males vs. females:  $b=0.018$ ,  $P<0.001$  vs.  $b=0.032$ ,  $P=0.007$ ). However, we found that TSH mediates an indirect effect of BAC on eGFR only in males (using MDRD equation: males vs. females:  $b=0.01$ ,  $P=0.004$  vs.  $b=0.0026$ ,  $P=0.189$ ) (using CKD-EPI equation: males vs. females:  $b=0.0035$ ,  $P=0.03$  vs.  $b=0.003$ ,  $P=0.18$ ). Our results demonstrate a positive direct effect of alcohol use and kidney performance. In males, this effect is partially mediated by TSH.