

# Alcohol Withdrawal Syndrome: Does Sex Matter?

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## Introduction

Alcohol Withdrawal Syndrome (AWS) occurs after an individual significantly reduces or completely stops consuming alcohol after a period of constant consumption. Existing literature plentifully describes social factors that contribute to lower likelihood of development of alcohol dependence among women. Physiological differences make alcohol dependent women more likely to develop alcohol-related hepatic complications. Animal studies suggest that ovarian hormones are neuroprotective and lead to lower incidence of seizures and allow for quicker recovery from AWS.

## Methods

Available data on all eligible patients admitted to Maricopa Integrated Health System with a discharge diagnosis of AWS 2010 and 2014 was obtained. Data sources included electronic medical records for collection of gender, age, total hospital length of stay (LOS), medical intensive care unit (MICU) LOS, non-MICU LOS, comorbidities, non-MICU benzodiazepine requirements, and mortality. Patients with diagnoses of trauma, burns, or other surgical diagnoses were excluded from this study. Male MICU patients were compared with female MICU patients. A randomized selection of male non-MICU admissions equal to the total number of non-MICU female admissions was performed. Benzodiazepines given at initial presentation while patients were receiving care in the Emergency Department (ED) as well as those administered while patients were admitted to non-MICU care were documented. Total amount of Benzodiazepines given in the ED were converted to mg/kg for both men and women. Total amount of Benzodiazepines administered during non-MICU admission were converted to mg/kg/day. Length of Benzodiazepine therapy, in days, was also recorded.

## Results

1496 patient charts were identified. 437 were analyzed. 220 male and 19 female patients were admitted to the MICU. MICU women were younger than MICU men, 41.2 (SD 9.5) vs. 46.2 (SD 9.8). Men had a longer total LOS, 9.36 days (SD 6.1) vs 7.31 days (SD 5.0). Men had longer MICU LOS, 5.23 days (SD 4.8) vs 4.05 days (SD 4.9). Men required intubation more often, 89 (40.5%) vs 7 (36.8%). Men and women had similar ventilator requirements, 2.5 days (SD 4.8) for men vs 2.3 days (SD 5.4) for women. Men developed pneumonia and sepsis more often; 90 men (40.9%) vs 4 women (21.1%) and 12 men (5.5%) vs no women (0%), respectively. Women developed seizures, hepatitis, and pancreatitis more frequently than men; 6 women (31.6%) vs 48 men (21.8%), 6 women (31.6%) vs 42 men (19.1%), and 4 women (21%) vs 13 men (5.9%), respectively. 1 man (0.45%) and no women perished in the MICU.

| Characteristics            | Overall<br>N=437<br>(mean, SD) | Females<br>N=118<br>(mean, SD) | Males<br>N=319<br>(mean, SD) | P-Value |
|----------------------------|--------------------------------|--------------------------------|------------------------------|---------|
| Age, Years                 | 45.6 (10.2)                    | 43.9 (10.8)                    | 46.2 (9.8)                   | 0.05    |
| Total Length of Stay, Days | 6.9 (5.4)                      | 4.5 (3.1)                      | 7.7 (5.8)                    | <0.001  |

**Table 1: Overall Age and Length of Stay. P-values calculated using the Wilcoxon Rank Sum Test.**

| Characteristics            | Overall<br>N=239<br>(mean, SD) | Females<br>N=19<br>(mean, SD) | Males<br>N=220<br>(mean, SD) | P-Value |
|----------------------------|--------------------------------|-------------------------------|------------------------------|---------|
| Age, Years                 | 45.8 (9.8)                     | 41.2 (9.5)                    | 46.2 (9.8)                   | 0.03    |
| Total Length of Stay, Days | 9.20 (6.1)                     | 7.31 (5.0)                    | 9.36 (6.1)                   | 0.1     |
| ICU Length of Stay, Days*  | 5.14 (4.8)                     | 4.05 (4.9)                    | 5.23 (4.8)                   | 0.06    |
| Intubation Length of Stay* | 2.50 (4.9)                     | 2.26 (5.4)                    | 2.52 (4.8)                   | 0.6     |
|                            | N (%)                          | N (%)                         | N (%)                        |         |
| Seizure (yes, %)           | 54 (22.6)                      | 6 (31.6)                      | 48 (21.8)                    | 0.32    |
| Hepatitis (yes, %)         | 48 (20.1)                      | 6 (31.6)                      | 42 (19.1)                    | 0.23    |
| Pancreatitis (yes, %)      | 17 (7.1)                       | 4 (21.0)                      | 13 (5.9)                     | 0.03    |
| Sepsis (yes, %)            | 12 (5.0)                       | 0 (0.0)                       | 12 (5.5)                     | 0.6     |
| Death (yes, %)             | 1 (0.42)                       | 0 (0.0)                       | 1 (0.45)                     | 1       |
| Intubation (yes, %)*       | 96 (40.2)                      | 7 (36.8)                      | 89 (40.5)                    | 0.75    |
| Pneumonia (yes, %)         | 94 (39.3)                      | 4 (21.1)                      | 90 (40.9)                    | 0.14    |

**Table 2: ICU Demographics. P-values calculated using the Wilcoxon Rank Sum Test.**

## Results (cont)

99 female and 99 randomly selected male patients admitted to non-MICU care were compared. Women were younger, 44.4 years (SD 11) vs 46.1 years (SD 10.1). Men had longer LOS, 4.21 days (SD 2.86) vs 3.96 days (SD 2.2). 14 women (14.1%) developed seizures vs 15 men (15.1%). Hepatitis and pancreatitis occurred more frequently in women; 21 women (21.2%) vs 16 men (16.2%) and 6 women (6.1%) vs 4 men (4.1%), respectively. 1 woman (1.1%) and no men were diagnosed with sepsis.

| Characteristics            | Overall<br>N=198<br>(mean, SD) | Females<br>N=99<br>(mean, SD) | Males<br>N=99<br>(mean, SD) | P-Value |
|----------------------------|--------------------------------|-------------------------------|-----------------------------|---------|
| Age, Years                 | 45.3 (10.6)                    | 44.4 (11.1)                   | 46.1 (10.1)                 | 0.3     |
| Total Length of Stay, Days | 4.09 (2.5)                     | 3.96 (2.2)                    | 4.21 (2.86)                 | 0.64    |
|                            | N (%)                          | N (%)                         | N (%)                       |         |
| Seizure (yes, %)           | 29 (14.7)                      | 14 (14.1)                     | 15 (15.1)                   | 0.84    |
| Hepatitis (yes, %)         | 37 (18.7)                      | 21 (21.2)                     | 16 (16.2)                   | 0.36    |
| Pancreatitis (yes, %)      | 10 (5.1)                       | 6 (6.1)                       | 4 (4.1)                     | 0.51    |
| Sepsis (yes, %)            | 1 (0.51)                       | 1 (1.1)                       | 0 (0.0)                     | 1       |
| Death (yes, %)             | 0 (0.0)                        | 0 (0.0)                       | 0 (0.0)                     | N/A     |
| Pneumonia (yes, %)         | 4 (2.02)                       | 0 (0.0)                       | 4 (4.1)                     | 0.12    |

**Table 3: Ward Demographics. P-values calculated using the Wilcoxon Rank Sum Test.**

|                             | Overall<br>N=198 | Females<br>N=99 | Males<br>N=99  | Coefficient<br>(95% CI)  | P-Value |
|-----------------------------|------------------|-----------------|----------------|--------------------------|---------|
| All Drugs, mg/kg (mean, SD) | 0.26 (0.52)      | 0.30 (0.68)     | 0.21 (0.30)    | -0.12 (-0.26, 0.02)      | 0.1     |
| Ativan, mg/kg (mean, SD)    | 0.03 (0.06)      | 0.04 (0.07)     | 0.02 (0.03)    | -0.01 (-0.03, 0.003)     | 0.11    |
| Valium, mg/kg (mean, SD)    | 0.22 (0.49)      | 0.26 (0.63)     | 0.18 (0.31)    | -0.003 (-0.12, 0.12)     | 0.96    |
| Xanax, mg/kg (mean, SD)     | 5.3e-5 (0.0007)  | 0 (0.0)         | 0.0001 (0.001) | 0.0001 (-0.0001, 0.0003) | 0.3     |

**Table 4: Emergency Department Medications. Multiple Linear Regression used to ascertain Coefficients (95% CI).**

|                             | Overall<br>N=239 | Females<br>N=19 | Males<br>N=220 | Coefficient<br>(95% CI)    | P-Value |
|-----------------------------|------------------|-----------------|----------------|----------------------------|---------|
| All Drugs, mg/kg (mean, SD) | 0.55 (0.71)      | 0.60 (0.71)     | 0.49 (0.69)    | -0.05 (-0.23, 0.12)        | 0.57    |
| Ativan, mg/kg (mean, SD)    | 0.34 (0.44)      | 0.32 (0.37)     | 0.35 (0.49)    | 0.04 (-0.08, 0.15)         | 0.55    |
| Valium, mg/kg (mean, SD)    | 0.08 (0.26)      | 0.12 (0.33)     | 0.04 (0.14)    | -0.08 (-0.14, -0.02)       | 0.009   |
| Xanax, mg/kg (mean, SD)     | 0.0004 (0.003)   | 0.0004 (0.003)  | 0.0003 (0.003) | -9.5e-5 (-0.00009, 0.0008) | 0.82    |
| Klonopin, mg/kg (mean, SD)  | 0.0002 (0.003)   | 0.0005 (0.005)  | 0 (0.0)        | 0.0002 (-0.0007, 0.001)    | 0.64    |
| Temazepam, mg/kg (mean, SD) | 0.002 (0.02)     | 0.004 (0.03)    | 0 (0.0)        | -0.004 (-0.01, 0.002)      | 0.16    |

**Table 4: Ward Medications . Multiple Linear Regression used to ascertain Coefficients (95% CI).**

## Results (cont)

In the Emergency Department, women required more overall benzodiazepines than men did; 0.30 mg/kg (SD 0.68) vs 0.21 mg/kg (SD 0.30). Women also required more of each individual benzodiazepine than men with the exception of Xanax, 0.0 mg/kg (SD 0.0) vs 0.0001 mg/kg (SD 0.001). Of the patients admitted to non-MICU care, women required more overall benzodiazepines than men did; 0.60 mg/kg (SD 0.71) vs 0.49 mg/kg (SD 0.69). Women required more Valium, Xanax, Klonopin, and Temazepam; 0.12 mg/kg (SD 0.33) vs 0.04 mg/kg (SD 0.14), 0.0004 mg/kg (SD 0.003) vs 0.0003 mg/kg (SD 0.003), and 0.0005 mg/kg (SD 0.005) vs 0 mg/kg (SD 0.0), respectively. Men required more Ativan than women did during admission, 0.35 mg/kg (SD 0.49) vs 0.32 mg/kg (SD 0.37).

## Discussion/Conclusions

To our knowledge, there are no studies currently available that directly compare men and women with AWS. Demographic data support existing literature stating women are less likely to develop alcohol dependence, more likely to develop alcohol-related hepatic complications, and recover from AWS sooner than men. Our data refutes animal study suggestions that ovarian hormones exert a neuroprotective effect against seizures. Our study shows that women admitted to the MICU have shorter MICU and overall LOS. Women admitted to non-MICU care presented with more advanced symptoms of AWS. Despite the presenting with more severe symptoms, women admitted to non-MICU care were also shown to have shorter LOS. Women admitted to non-ICU care required shorter duration of benzodiazepine administration compared to men. Future studies would benefit from larger sample size consisting of multiple sites.

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