Development of Substance Use Disorder in Chronic Kidney Disease Patients Experiencing Uremic Pruritis

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Introduction

- Uremic Pruritus (UP) is a distressing and life-changing symptom that is estimated to occur in nearly half of patients with end-stage renal disease (ESRD) who require maintenance dialysis.[1]
- The diagnosis of UP typically requires the presence of near-daily itching across large and bilaterally symmetrical skin regions.[2]
- The mechanism is thought to involve systemic inflammation from kidney failure that inflames the skin and nerves, and recent evidence shows μ-opioid receptor activity to play a large role.[2]
- Common therapies include gabapentin, phototherapy, and topical creams (calcineurin inhibitors, anesthetics, anti-itch creams, corticosteroids). κ-opioid receptor antagonists are an emerging treatment with promising preliminary data.[1]
- Despite these therapeutic options, many patients fail to receive sufficient remission of their pruritus and subsequently experience diminished quality of life and mental health burden.
- Thus, this study aims to assess the development of substance use disorders in patients with ESRD who experience uremic pruritus.

Methods

- A retrospective cohort analysis was conducted using TriNetX, a federated health research network database. This report was generated on a subset network called US Collaborative Network and included 55 HCOs.
- Using validated ICD-10 codes, the experimental group, cohort 1, identified patients with ESRD or CKD stage 5 who experience uremic pruritis, while the control group, cohort 2, identified patients with ESRD or CKD stage 5 who are not experiencing uremic pruritis.
- A 1:1 matched propensity score analysis was conducted adjusting for demographics and comorbidities.
- The outcomes that were then studied in these cohorts were Alcohol Abuse or Dependence, Opioid Abuse or Dependence, Cannabis Abuse or Dependence, Sedative, Hypnotic, or Anxiolytic-Related Dependence, and Nicotine Dependence.
- Outcomes were assessed within 30 days, 90 days, 1 year, and 5 years after the diagnosis of uremic pruritis.
- Adjusted Risk Ratios (RR) with 95% CI were utilized to demonstrate the significance of the increased risks in the uremic pruritis cohort vs. those without uremic pruritis in ESRD or CKD stage 5 patients.

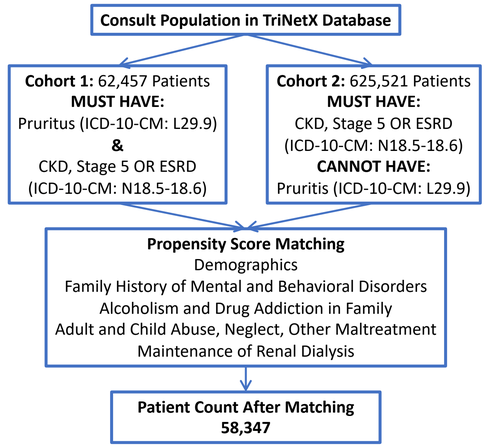

Figure 1. Flow diagram depicting the selection process in the creation of the cohorts for this retrospective cohort study

Substance Use Disorder	aRR at 30 Days	aRR at 90 Days	aRR at 1 Year	aRR at 5 Years
Alcohol Abuse or Dependence	**1.78**	**1.92**	**2.26**	**1.99**
Opioid Abuse or Dependence	**2.21**	**2.01**	**1.83**	**1.66**
Cannabis Abuse or Dependence	**1.94**	**1.65**	**1.59**	**1.41**
Sedative, Hypnotic, or Anxiolytic-Related Dependence	**2.66**	**2.33**	**2.43**	**1.96**
Nicotine Dependence	0.987	**1.18**	**1.45**	**1.29**

Table 1. Adjusted Risk Ratios (aRR) for the risk of developing substance use disorders in ESRD patients with uremic pruritis compared to ESRD patients without uremic pruritis. **Bold values indicate P < 0.05**

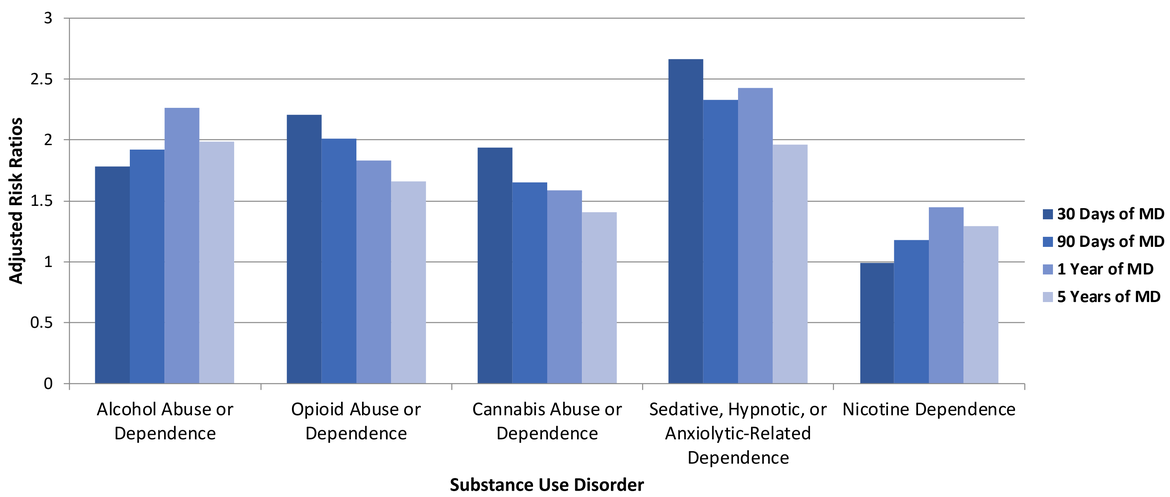

Figure 2. Risk of developing a specific substance use disorder at 30 days, 90 days, 1 year, and 5 years after the onset of uremic pruritis compared to control

Results

- Increased risk for alcohol abuse or dependence was observed at 30 days (aRR [95% CI])=(1.78[1.51,2.10]), 90 days(1.92[1.68, 2.20]), 1 year (2.26[2.05, 2.49]), and 5 years (1.99[1.84, 2.15]).
- Opioid abuse or dependence demonstrated greater risk at 30 days (1.53, 3.18), 90 days(2.01[1.55, 2.61]), 1 year (1.83[1.54, 2.17]), and 5 years (1.66[1.47, 1.88]).
- Increased risk for cannabis abuse or dependence was significant at 30 days (1.94[1.28, 2.93]), 90 days(1.65[1.23, 2.22]), 1 year (1.59[1.30, 1.94]), and 5 years (1.41[1.20, 1.63]).
- Sedative-hypnotic-anxiolytic abuse or dependence had increased risk at 30 days (2.26[1.44, 4.92]), 90 days(2.33[1.50, 3.59]), 1 year (2.43[1.80, 3.29]), and 5 years (1.96[1.58, 2.44]).
- Increased risk for nicotine dependence was observed at 90 days(1.18[1.07, 1.30]), 1 year (1.45[1.35, 1.55]), and 5 years (1.29[1.22, 1.35]).

Discussion

- 19 out of 20 risk ratios in this study were significantly increased in the uremic pruritis cohort versus control.
- The alcohol abuse and nicotine dependence disorder risk ratios increased over time. This was expected as these are by far the most accessible and common substances. Alcohol and cigarettes can be purchased without prescription, are prominently used, more socially accepted, and may be perceived by the public as a safer alternative to the other substances in this study.
- Cannabis abuse, opioid abuse, and sedative, hypnotic, or anxiolytic-related dependence all demonstrated decreasing risk ratios as time progressed. This may be explained by how difficult it is to obtain a legal prescription of these substances, social influences, and higher costs compared to alcohol and cigarettes.
- In all SUD diagnoses, there was a drop off at year 5. The average life expectancy of ESRD patients on dialysis is 5-10 years,[3] thus, this may be explained by significant progression of disease.

Conclusions

- ESRD patients with uremic pruritis demonstrated significantly higher risk of developing each SUD versus ESRD without UP.
- Increased risk over time was observed for alcohol abuse and nicotine dependence, and risk decreased in the other disorders.
- This highlights the alarming psychiatric complications of uremic pruritis and calls for mental health monitoring in this group.

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