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Exploring the Role of Hyperuricemia in Anemia Worsening in Chronic Kidney Disease Patients

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Objectives : Both anemia and hyperuricemia are associated with chronic kidney disease (CKD) progression. However, the relationship between uric acid levels and anemia remains complex, with studies reporting positive, inverse, or U-shaped associations. There is a lack of research specifically examining the impact of uric acid concentration on anemia progression in CKD patients. This study aimed to investigate the effect of serum uric acid levels on anemia worsening in CKD patients.
Methods : This study included 3,858 CKD patients from 14 medical centers and communities in Taiwan between October 2008 and February 2016. Demographic characteristics and lifestyle factors were collected through structured questionnaires. Participants were stratified into quartiles based on serum uric acid concentration. Anemia worsening was defined as a progression in anemia severity by at least one category during follow-up, based on hemoglobin levels classified according to World Health Organization (WHO) criteria. Cox proportional hazards models were used to assess the association between serum uric acid levels and anemia worsening.
Results : The mean age of participants was 63.33 ± 13.71 years, and 58.45% were male. In the adjusted analysis, each 1 mg/dL increase in serum uric acid was associated with a higher risk of anemia worsening (HR: 1.06, 95% CI: 1.02–1.11). Patients with hyperuricemia had a significantly increased risk compared to those without hyperuricemia (HR: 1.18, 95% CI: 1.02–1.37). When categorized into quartiles, the third (HR: 1.31, 95% CI: 1.07–1.60) and fourth quartiles (HR: 1.34, 95% CI: 1.09–1.65) had a significantly higher risk compared to the first quartile.
Conclusions : Higher serum uric acid levels are associated with an increased risk of anemia worsening in CKD patients. These findings highlight the need for monitoring and managing uric acid levels to potentially mitigate anemia progression among patients with CKD.

Table 1.png

Table 1. The baseline characteristics by uric acid quartile among chronic kidney disease (n=3858)

	Overall n (%)	Q1: 1.80-5.80 mg/dL (n=987)	Q2: 5.81-6.90 mg/dL (n=1,034)	Q3: 6.91-8.00 mg/dL (n=909)	Q4: 8.01-16.50 mg/dL (n=928)	p-value
Baseline anemia severity [a], %						<.001[b]
No Anemia	1883 (48.81)	623 (63.12)	508 (49.13)	402 (44.22)	350 (37.72)	
Mild Anemia	914 (23.69)	189 (19.15)	260 (25.15)	224 (24.64)	241 (25.97)	
Moderate Anemia (8–10.9 g/dL)	983 (25.48)	161 (16.31)	240 (23.21)	271 (29.81)	311 (33.51)	
Severe Anemia (6.5–7.9 g/dL)	66 (1.71)	10 (1.01)	23 (2.22)	9 (0.99)	24 (2.59)	
Life threatening (less than 6.5g/dL)	12 (0.31)	4 (0.41)	3 (0.29)	3 (0.33)	2 (0.22)	
Follow-up period (month)	33.35±15.44	33.71 ± 15.86	34.33±16.14	32.93±14.88	32.30±14.67	0.022
Anemia worsen						0.001
No	2880 (74.88)	780(79.35)	775(75.17)	657(72.52)	668(72.14)	
Yes	966 (25.12)	203(20.65)	256(24.83)	249(27.48)	258(27.86)	
Sex, %						<.001
Female	1603 (41.55)	546 (55.32)	436 (42.17)	318 (34.98)	303 (32.65)	
Male	2255 (58.45)	441 (44.68)	598 (57.83)	591 (65.02)	625 (67.35)	
Age (years)	63.33±13.71	62.80 ± 13.80	64.46±12.99	63.09±13.80	62.87±14.27	0.020
Education, %						0.333
≤ 6	1398 (40.9)	354 (38.48)	401 (43.07)	310 (39.54)	333 (42.53)	
7-12	1275 (37.3)	351 (38.15)	329 (35.34)	302 (38.52)	293 (37.42)	
≥13	745 (21.8)	215 (23.37)	201 (21.59)	172 (21.94)	157 (20.05)	
Family income, NT dollars (month)						0.535
<40000	2903 (75.54)	729 (74.16)	778 (75.39)	684 (75.66)	712 (77.06)	
≥40000	940 (24.46)	254 (25.84)	254 (24.61)	220 (24.34)	212 (22.94)	
Hypertension	2907 (75.41)	643 (65.21)	784 (75.9)	711 (78.3)	769 (82.87)	<.001
Diabetes mellitus	1539 (39.92)	354 (35.90)	390 (37.75)	373 (41.08)	422 (45.47)	<.001
Dyslipidemia	1310 (33.98)	345 (34.99)	323 (31.27)	323 (35.57)	319 (34.38)	0.177
Gout	1161 (30.12)	166 (16.84)	269 (26.04)	287 (31.61)	439 (47.36)	<.001
Stroke	328 (8.51)	71 (7.2)	98 (9.49)	79 (8.7)	80 (8.62)	0.322
Cardiovascular disease	1060 (27.5)	263 (26.67)	273 (26.43)	265 (29.19)	259 (27.94)	0.509
Physical examination						
Uric acid (mg/dl)	6.95±1.76	4.87±0.75	6.39±0.31	7.48±0.31	9.28±1.18	<.001
Hemoglobin/Hb (g/dl)	12.35±2.45	12.82±2.74	12.39±2.27	12.25±2.30	11.89±2.34	<.001
Serum creatinine (mg/dl)	2.15±1.75	1.49±1.34	2.09±1.79	2.29±1.75	2.77±1.82	<.001
Baseline eGFR (ml/min per 1.73 m^2)	42.65±25.43	57.03±26.33	43.82±24.77	38.26±22.77	30.37±19.24	<.001
Systolic blood pressure (mmHg)	132.55±17.80	128.95±17.23	132.29±18.24	134.01±17.06	135.34±17.98	<.001
Diastolic blood pressure (mmHg)	75.91±11.76	75.03±11.17	76.19±11.62	76.06±11.73	76.38±12.55	0.075

[a] World Health Organization (WHO) criteria: no anemia (Hb ≥12 g/dL in women and Hb ≥13 g/dL in men), mild anemia (Hb 11–11.9 g/dL in women and Hb 11–12.9 g/dL in men), moderate anemia (Hb 8–10.9 g/dL), severe anemia (Hb 6.5–7.9 g/dL), and life-threatening anemia (Hb <6.5 g/dL); [b] Monte Carlo method.

Table 1.png

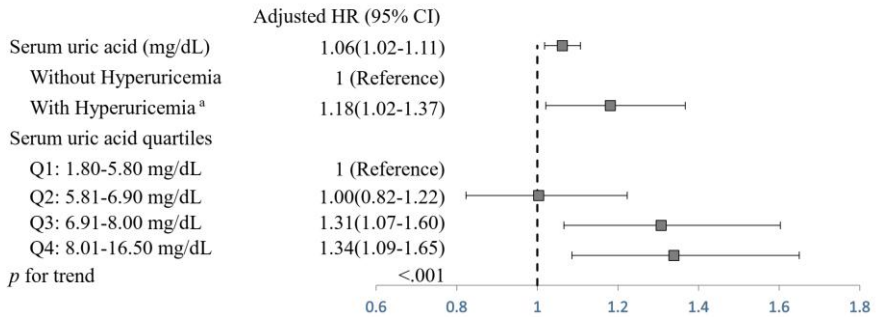

Figure 1. Adjusted hazard ratios serum uric acid and anemia worsen among patients with CKD

Note: Adjusts for age, sex, serum creatinine, education, family income, hypertension, diabetes mellitus, dyslipidemia, gout, stroke, cardiovascular disease. Abbreviations: HR, hazard ratio; CI, confidence interval; Q, quartile.

[a] Hyperuricemia was defined as serum uric acid levels ≥7.0 mg/dL in men and ≥6.0 mg/dL in women.