Metabolic Acidosis is Underdiagnosed and Undertreated in Patients with Chronic Kidney Disease

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BACKGROUND

- Metabolic acidosis is common in patients with stage 3-5 chronic kidney disease (CKD) and it is associated with adverse bone, muscle and kidney outcomes.[1]
- CKD treatment guidelines suggest treatment of metabolic acidosis[2-3] but a previous study indicated that the majority of patients are left untreated.[4]
- We sought to investigate the current diagnosis and treatment rates for metabolic acidosis in a large population-based cohort of patients with CKD and definitive laboratory evidence of chronic metabolic acidosis.

METHODS

- We integrated laboratory data from ~35.7 million US adults with de-identified longitudinal claims and prescription data from 280 million individuals included in the Symphony Health Solutions IDV® (Integrated Dataverse).
- Patients who met stringent laboratory criteria indicative of CKD and chronic metabolic acidosis were included: ≥ 2 eGFRs < 60 mL/min/1.73 m^2 with no intervening eGFR ≥ 60 mL/min/1.73 m^2; ≥ 2 serum bicarbonates ≥ 12 to < 22 mEq/L with no intervening bicarbonate < 12 or ≥ 22 mEq/L; qualifying values ≥ 28 days apart.
- No patients with a diagnosis of acute kidney injury (AKI) within 28 days prior to either qualifying bicarbonate value were included.
- A physician diagnosis of metabolic acidosis was based on administrative claims.
- Treatment of metabolic acidosis was defined as a prescription for oral alkali therapy.

RESULTS

Table 1. Baseline Characteristics of the Study Population

	Total Unique Patient Count (N)	Serum Bicarbonate (12 – 18 mEq/L)	Serum Bicarbonate (≥ 18.1 - 20 mEq/L)	Serum Bic30arbonate (≥ 20.1 – 22 mEq/L)
Age (y), %				
19 - 68	28,942	30	40	30
69 - 79	29,362	25	41	34
> 80	28,475	24	42	34
Gender, %				
Male	40,914	26	41	32
Female	45,868	26	41	33
Insurance, %				
Commercial	18,910	26	41	33
Medicaid	5,877	30	40	30
Medicare	35,363	25	41	33
Other	26,517	27	41	32
eGFR (mL/min/1.73 m^2), %				
< 20	15,144	41	38	21
20 - 40	35,084	27	42	32
40.01 - 60	36,554	20	42	38
Nephrology Visit, %	35,944	31	40	29
Comorbidities, %				
Atrial Fibrillation	8,841	27	42	32
Coronary Artery Disease	12,693	27	42	32
Digestive Heart Failure	9,705	29	42	29
Diabetes Mellites	41,956	28	42	30
Hypertension	60,497	28	42	31
Peripheral Vascular Disease	9,358	28	42	30
Medication Use, %				
ACE Inhibitors	25,616	27	42	31
ARBs	19,038	26	42	32
Diuretics	21,844	27	42	31
Statins	38,204	26	42	32

References

1. Kraut JA and Madias NE. *Adv Chronic Kidney Dis.* 24: 289-297, 2017.
2. KDIGO. *Kidney int.* Suppl 3: 1-150, 2013.
3. Eknoyan G, Levin A, Levin NW. *Am J Kidney Dis.* 42: 1-201, 2003.
4. Dobre M, Yang W, Chen J, Drawz P, Hamm LL, Horwitz E, et al. *Am J Kidney Dis.* 62: 670-678, 2013.

Figure 1. Flow Chart of Patient Selection

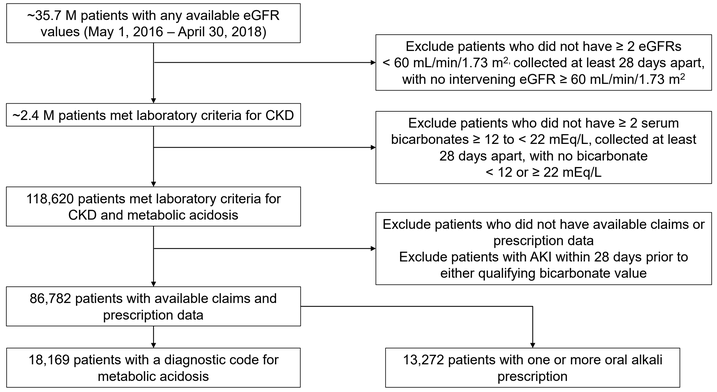
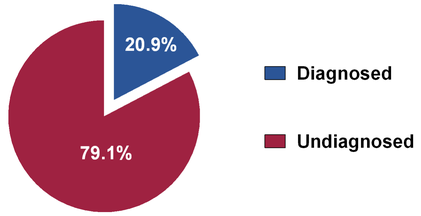
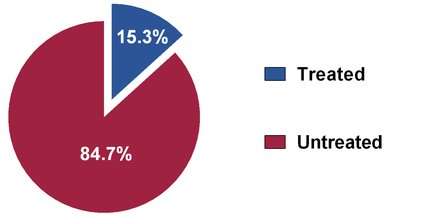


Figure 2. Metabolic Acidosis Is Underdiagnosed



Approximately 21% of patients with stage 3-5 CKD and metabolic acidosis are currently diagnosed (**Figure 2**).

Figure 3. Metabolic Acidosis Is Undertreated

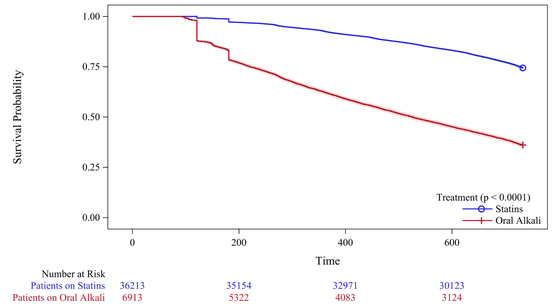


Approximately 15% of patients with stage 3-5 CKD and metabolic acidosis currently receive treatment (**Figure 3**).

Table 2. Factors Associated with Diagnosis or Treatment

Factors Associated with Diagnosis	Odds Ratio	P Value	Factors Associated with Treatment	Odds Ratio	P Value
Age	0.99	<0.001	Age	0.98	<0.001
Gender	0.93	0.001	Gender	1.19	<0.001
Payer - Medicaid	1.11	0.010	Payer - ASST	2.10	<0.001
Payer - Medicare	1.06	0.028	Payer - CASH	2.55	<0.001
Payer - Commercial	0.86	<0.001	Payer - Medicaid	1.66	<0.001
eGFR Value	0.98	<0.001	Payer - Medicare	1.65	<0.001
Nephrology Visit	3.93	<0.001	Payer - Commercial	1.76	<0.001
Atrial Fibrillation	1.22	<0.001	eGFR Value	0.95	<0.001
Coronary Artery Disease	1.15	<0.001	Nephrology Visit	2.18	<0.001
Congestive Heart Failure	1.46	<0.001	Atrial Fibrillation	0.91	0.030
Diabetes Mellites	1.12	<0.001	Congestive Heart Failure	0.83	<0.001
Hypertension	1.41	<0.001	Peripheral Vascular Disease	0.92	0.069
Peripheral Vascular Disease	1.11	0.001	Diuretics	1.13	<0.001
ACE Inhibitors	0.87	<0.001	Statins	1.16	<0.001
ARBs	0.79	<0.001	Second Serum Bicarbonate	0.89	<0.001
Statins	0.89	<0.001			
Second Serum Bicarbonate	0.90	<0.001			

Figure 4. Adherence to Oral Alkali Treatment Compared with Statin Treatment in Patients with CKD and Metabolic Acidosis



- Adherence to oral alkali therapy was significantly worse when compared to statins (**Figure 4**).
- At two years, only 36% of patients remained on oral alkali as compared to 74% on statins.
- There was an early and pronounced discontinuation of oral alkali in the first 180 days of use.

CONCLUSION

Metabolic acidosis is underdiagnosed and undertreated in patients with CKD.

Older age and higher eGFR are associated with a lower likelihood of diagnosis, and a nephrology visit and higher rates of comorbid conditions are associated with a higher likelihood of diagnosis.

Treatment rates are low (approximately 15%) and health insurance status and nephrologist visits are associated with a higher likelihood of treatment.

Discontinuation rates for oral alkali therapy are high and nearly double the rates of statin discontinuation in the same patient population.

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