Does Diabetic Ketoacidosis Increase Risk of Diabetic Nephropathy?

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Introduction

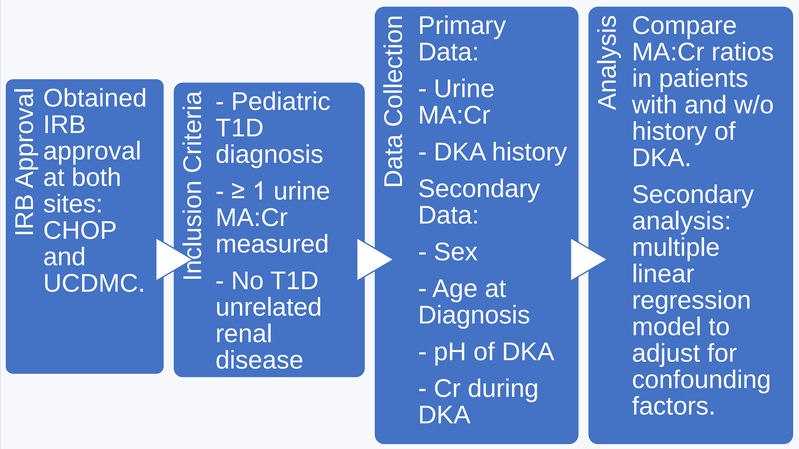
Diabetic nephropathy is the most common cause of death in patients with type 1 diabetes (T1D).[1]

- T1D patients hospitalized with Diabetic Ketoacidosis (DKA) are more likely to experience acute kidney injury (AKI)[2,3]
- In other disease states, AKI increases risk of developing chronic kidney disease.[2]
  - Proposed pathophysiology: AKI induces endothelial dysfunction, T cell activation, fibrosis, and tubular injury.[4]
- Mechanism suggests that DKA induced AKI may increase risk of diabetic nephropathy.
- To date, association between DKA and future diabetic nephropathy has not previously been investigated in children.
- Microalbuminuria is one of the earliest markers of diabetic nephropathy.[1] and can be used to track if there is an increased risk of diabetic nephropathy in T1D pediatric patients with ≥ 1 episode of DKA.

Hypothesis

T1D patients with a history of DKA have higher urine microalbumin levels, suggesting an increased likelihood of developing diabetic nephropathy.

Methods



Demographics

Total Participants		2394
Age		
	At Diagnosis of Diabetes Mellitus*	9.5 ± 4.4 years
	At Study Enrollment*	16.8 ± 5.1 years
Sex		
	Female	1087 (45.4%)
	Male	1307 (54.6%)
DKA at Diagnosis, Yes		841 (35.1%)
	pH*	7.18 ± 0.1
DKA after Diagnosis, Yes		413 (17.3%)
	pH*	7.17 ± 0.11
	1 DKA episode	257 (10.7%)
	2 DKA episodes	66 (2.8%)
	3 DKA episodes	27 (1.1%)
	> 3 DKA episodes	63 (2.6%)
HbA1C*		8.4% ± 1.5
Patients Diagnosed with Microalbuminuria		62 (2.6%)
	Age at Diagnosis of Microalbuminuria*	15 ± 4.4 years
Patients with Possible Microalbuminuria		128 (5.3%)

*Mean (SD)

Cr levels collected to calculate AKI stages. Data not yet available.

Preliminary Results

	Developed Microalbuminuria	No History of Microalbuminuria	Total
History of DKA	121	964	1085
No History of DKA	69	1240	1309
Total	190	2204	2394

The evidence cannot reject the null hypothesis. This suggests that there is a significant association between a history of DKA and developing microalbuminuria. X^2 (1, N = 2394) = 28.08, p < 0.0001.

Discussion

Preliminary analysis suggests a significant association between having an episode of DKA and developing microalbuminuria. Analyses involving multivariable models are needed to adjust for possible confounding variables: age, diabetes duration, and glycemic control (HbA1c). In addition, comparisons of patients with and without AKI during DKA are needed to determine whether effects of DKA on future risk of microalbuminuria are related to DKA per se or to the occurrence of AKI during DKA.

Other Limitations:

- Lapses in medical history of patients whose records are not fully in the UC Davis or CHOP system.
- "Possible history of microalbuminuria" are patients with one urinalysis showing elevated MA:Cr but were lost to follow up, resulting in lack of diagnosis.

Future studies should explore the mechanisms upon which we can act to either slow or prevent the progression of DKA induced AKI to diabetic nephropathy.

Understanding this risk would help better inform our current practices in the prevention of DKA and early prophylaxis against AKI. Doing so may help slow the progression to diabetic nephropathy following DKA episodes.

References

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