

**DOES CHRONIC METABOLIC ACIDOSIS IMPACT THE PROGRESSION OF DIABETIC NEPHROPATHY?** Mark Cook and

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**BACKGROUND:** Chronic metabolic acidosis (CMA) is a feature of Chronic Kidney Disease (CKD) secondary to diminished ammoniogenesis within the kidney and diminished acid excretion. CMA has been associated with adverse consequences to protein and muscle metabolism, renal osteodystrophy, impaired insulin sensitivity, beta2-microglobulin accumulation, and inflammation. Despite this, conflicting data exist regarding CMA and progression of CKD. Therefore, the purpose of this study is to further define the relationship between CMA and CKD progression in patients with diabetic nephropathy (DN).

**PATIENTS AND METHODS:** 2149 patients with DN and CKD as defined by billing codes for DN and baseline serum creatinine (SCR) greater than or equal to 1.50 mg/dl were examined retrospectively over a 72 month period from January 2000 through December 2005. Patients with incomplete data during the review period were excluded. Inclusion criteria required no oral alkali therapy in the 72 month period of data collection. Only patients demonstrating a change of SCR less than 0.25 mg/dl per quarter year were included to eliminate artifact from acute kidney injury. Patient observations were then divided into two groups based upon average bicarbonate less than 20 mg/dl (n=410) or greater than 20 mg/dl (n=1739). SCR was observed quarterly determining change in SCR from the previous measurement. A binary outcome variable with 1 representing a worsening SCR and 0 representing a stable or improved SCR was created.

Generalized linear modeling with repeated measures and logit link function was used to adjust for SCR and estimate the odds ratio (OR) for worsening SCR as a function of bicarbonate greater than or less than 20 mg/dl.

**RESULTS:** After adjusting for SCR, the odds of increased SCR in subjects with average bicarbonate levels < 20 mg/dl was 2.45 times the odds of increased SCR in subjects with bicarbonate levels > 20 mg/dl (p<0.001).

**CONCLUSION:** After adjusting for SCR, patients with DN and CMA had a higher likelihood of progression of CKD as compared to patients with DN without CMA. This provides significant evidence of an adverse relationship between CMA and progression of CKD.