

# Increased mortality associated with uncontrolled diabetes mellitus in patients with pulmonary cryptococcosis: a single US cohort study

## Abstract

**Background:** Diabetes mellitus is an established risk factor for bacterial infections, but its role in cryptococcosis is unclear. The study aimed to determine whether uncontrolled diabetes (HbA1c >7%) was an independent risk factor for mortality in cryptococcosis.

**Methods:** A retrospective case-control study partially matched by age and gender was performed in patients tested for *Cryptococcus* infection at the University of Colorado Hospital from 2000 to 2019. A multivariable logistic regression model was used to identify mortality predictors. Cox proportional hazard model was used for survival analysis.

**Results:** We identified 96 cases of cryptococcosis and 125 controls. Among cases, cryptococcal meningitis (49.0%) and pneumonia (36.5%) constituted most infections. Cases with pulmonary cryptococcosis with uncontrolled diabetes had a higher mortality at 10 weeks (50% versus 7%,  $p = 0.006$ ) and 1 year (66.7% versus 13.8%,  $p = 0.005$ ) compared to pulmonary cases with controlled or no diabetes. Unadjusted Cox proportional hazard model found an increased rate of death for uncontrolled diabetes at 10 weeks [hazard ratio 8.4, confidence interval (CI): 1.4–50.8,  $p = 0.02$ ] and 1 year (hazard ratio 7.0, CI: 1.7–28.4,  $p = 0.007$ ) among pulmonary cryptococcosis cases. Multivariable analysis showed a significantly increased odds of 10 weeks [odds ratio (OR) = 4.3, CI: 1.1–16.5,  $p = 0.035$ ] and 1 year (OR = 5.0, CI: 1.4–18.3,  $p = 0.014$ ) mortality for uncontrolled diabetes among pulmonary cryptococcosis cases. After adjustment for gender, age, and case/control, for every 1% increase in HbA1c levels, the odds of pulmonary cryptococcosis mortality at 1 year increased by 11% (OR = 1.6, CI 95%: 1.1–2.3,  $p = 0.006$ ).

**Conclusion:** Uncontrolled diabetes is associated with worse outcomes in pulmonary cryptococcosis, including a 4-fold and 6-fold increased odds of death at 10 weeks and 1 year, respectively. Glucose control interventions should be explored to improve clinical outcomes in patients with pulmonary cryptococcosis.