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Testing the Effect of Acetaminophen Overdose on the Liver and the Role of Biomarkers to Predict Death or Survival

Christine Brasic[1,*], Aditi Ghosh[1]

[1]*Department of Mathematics, University of Wisconsin Whitewater, Whitewater, WI 53190*

brasiccs23@uww.edu

In the United States, acetaminophen (APAP) overdose is the leading cause of acute liver injury, with a third of cases being unintentional. The current model for assessing liver health, The King's College Criteria (KCC), cannot predict APAP dosage or time of overdose—crucial information for selecting treatment in the case of APAP overdose. The Model for APAP-Induced Liver Damage (MALD), however, uses dynamic system of differential equations to model liver injury. By utilizing the three bio-markers aspartate aminotransferase, alanine aminotransferase, and international normalized ratio, MALD estimates the dose of APAP and the time of overdose in order to assess whether treatment with N-acetylcysteine is sufficient or if survivability is contingent on a liver transplant. These biomarkers are indicative of hepatocyte death but are not specific to APAP. In our work we have modeled a fourth biomarker, APAP-protein adduct—specific to APAP—to the existing model, MALD. We validated our model using 59 cases from the Acute Liver Failure Study Group. The inclusion of APAP-protein adducts in the model improved the ROC curve of MALD by 13.63%. When patients with reported alcohol use were removed from the analysis, the addition of APAP-protein adducts improved the ROC curve of MALD by 34.22%. We also performed sensitivity analysis of the important parameters associated with the updated model. We found the addition of APAP-protein adducts increases the predictive quality for the model.