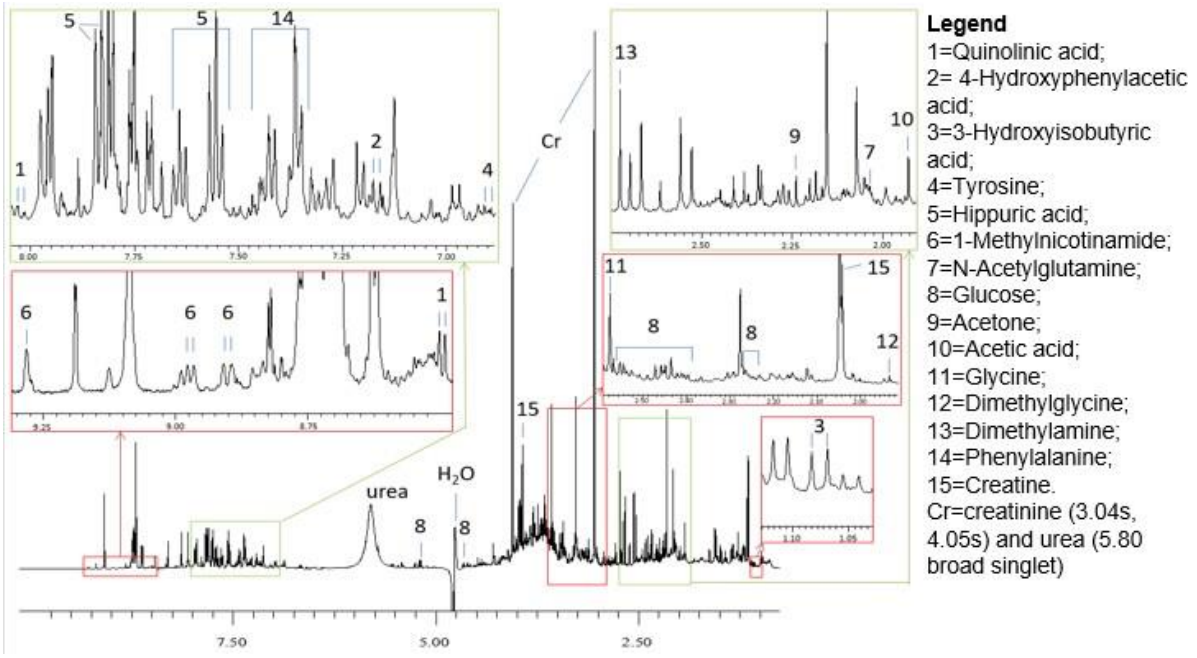
**Urinary metabolic characterization of stage 3 tuberculous meningitis in a South African paediatric population**

**Simon Isaiah**

North-West University, Potchefstroom, South Africa

Tuberculous meningitis (TBM) is a severe form of tuberculosis that causes a high rate of morbidity and mortality among paediatrics. Paediatrics (aged <12 years) are the most at risk group, and only one in three survive without long-term neurological sequelae. Existing diagnostic techniques for TBM are invasive, complex and time-consuming. Yet, there are still no clear biomarker(s), nor bio- signature, for TBM; let alone one from patient samples collected non-invasively. The goal of this study is to identify metabolites as characteristic markers that differentiate severe cases of TBM from healthy controls for paediatrics through non-invasive urine collection. Urine samples selected for this study were from two paediatric groups. Group 1: controls (n = 45): healthy paediatric patients from the same geographical region who had no neurological symptoms and without meningitis. Group 2: TBM cases (n = 13): were collected from paediatric patients that were admitted to Tygerberg Hospital on suspicion of TBM, most of them severely sick; with a later confirmation of stage 3 TBM. $^{1}$H NMR- based metabolomics data of urine was generated, statistical analyses via MetaboAnalyst (v5.0), and identification of important metabolites. Twenty-two metabolites were discovered, four of which were medications and three metabolites (*myo-inositol, methylmalonic acid and urea*) were identified but not quantifiable. Fifteen quantified metabolites were identified that differentiate severe TBM cases and healthy controls (*quinolinic acid, tyrosine, phenylalanine, glycine, 1-methylnicotinamide, glucose, hippuric acid, 4-hydroxyphenylacetic acid, 3-hydroxyisobutyric acid, N-acetylglutamine, dimethylamine, dimethylglycine, acetone, acetic acid, and creatine)*. All quantified metabolites, except *hippuric acid and phenylalanine,* showed statistical significance. This study provides an insight into a bio-signature of urinary metabolites that can be used to metabolically characterize paediatric TBM patients. This non-invasive metabolomics approach will be developed further to identify early diagnostic urinary markers in the initial stages of the disease and for monitoring of treatment strategies.




1H-NMR spectrum of urine from a TBM patient indicating the metabolites that characterize TBM.

Keywords: Tuberculous meningitis, Metabolites, Urine, $^{1}$H-NMR Metabolomics