THE GRADUATE COLLEGE OF THE UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

Wei-Jen Chen

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE

GRADUATE COLLEGE

Biostatistics and Epidemiology

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Evaluation of Associations between Environmental Chemical Exposures, the Urinary Microbiome, and Gestational Diabetes Mellitus

COMMITTEE IN CHARGE: Jennifer D. Peck, Ph.D. (Chair), Tabitha Garwe, Ph.D., Amanda E. Janitz, Ph.D., Chao Xu, Ph.D., Jooyeon Hwang, Ph.D.

ABSTRACT: Gestational diabetes mellitus (GDM) is an increasing health burden that affects approximately 6.0 to 9.2% of pregnancies every year in the United States. Pregnant women with a diagnosis of GDM are more likely to experience adverse pregnancy complications. Furthermore, the long-term impact of GDM is well recognized as GDM increases the risk of developing type 2 diabetes later in life in both the mothers and their offspring. Evidence suggests that exposure to environmental chemical contaminants may alter glucose homeostasis and increase the risk of insulin resistance. As pregnancy is a critical window of susceptibility to diabetes, further epidemiological studies are needed to advance our understanding of the role of multiple environmental toxicants involved in GDM development. In addition, the human microbiome during gestation may be associated with physiological changes in pregnancy; thus, investigation of the association between microbial profiles and GDM is warranted.

The specific aims of this dissertation research are to analyze data obtained from an existing clinic-based case-control study of an obstetric population at the University of Oklahoma Medical Center to 1) investigate the relationships between urinary inorganic arsenic concentrations, arsenic methylation capacity, and GDM 2) evaluate the relationships of urinary concentrations of phenol, paraben, and phthalate mixtures with GDM and 3) characterize the urinary microbiome of pregnant women with and without GDM, and to explore the association between microbial profiles and GDM.
Our study did not observe evidence of a positive association between inorganic arsenic exposure and GDM while taking into account non-toxic organic arsenic species. However, our assessment of relative measures of arsenic methylation capacity indicates that detoxification capacity may be an important aspect of arsenic exposure assessment when evaluating associations with GDM. For the study of multiple phenols, parabens, and phthalate metabolites, benzophenone-3 was positively associated with GDM when analyzing models for individual phenols. In contrast, bisphenol-A was negatively associated with GDM. In the mixtures analysis using probit implementation of Bayesian kernel machine regression, we observed that an increase in z-score transformed log urinary concentrations of benzophenone-3 from the 10th to 90th percentile was associated with an increase in the estimated difference in the probability of GDM, holding other phenols and parabens fixed at their medians. However, no statistically significant association was found between the other chemical measures and GDM in the mixture analysis. In addition, we observed a diverse microbial community with 27 genera in the pregnancy urinary microbiome among the study participants. The urinary microbial composition may differ according to GDM status with a relatively higher richness of genus Veillonella and a lower richness of genus Aerococcus in women with GDM than in those without GDM.

The findings of this research contribute evidence regarding the understudied effects of exposure to environmental factors and the microbiome on GDM. Our application of advances in laboratory and statistical methodologies reveals that arsenic metabolism, chemical mixtures, and the urinary microbiome may be important considerations when assessing environmental risk factors for GDM. This dissertation research may inform evidence for future public health interventions that aim to reduce the adverse effects of environmental factors on pregnant women.