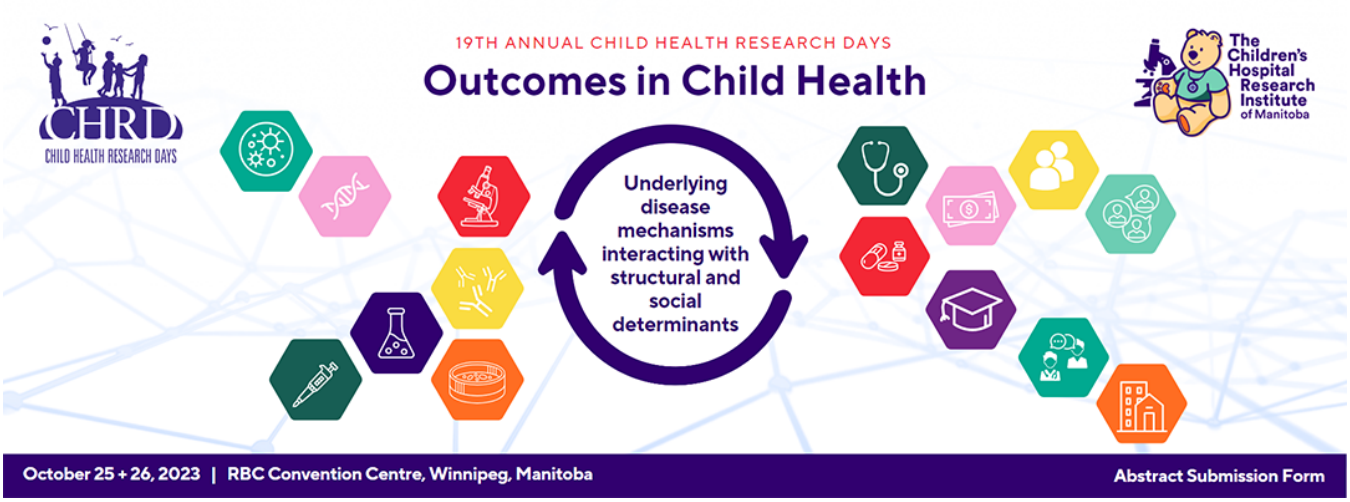

CHRD 2023: Abstract Submission Form

Submitter Name
Sriyani Ranatunga

Presenter Name
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Presenter Status
Masters Student

Research Category
Basic Science

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Title
Prenatal and early-life exposure to maternal diabetes as a risk factor for future COPD (Chronic Obstructive Pulmonary Disease): A study from a mouse model

Background
COPD ranks third globally and fifth in Canada for causes of death. Primarily caused by smoking, early-life exposure to environmental factors may also increase COPD risk by impairing lung development and altering response to cigarette smoke (CS). Prenatal diabetes (GDM) is linked with prematurity and childhood asthma, which are risk factors for COPD development. However, the direct impact of GDM on offspring susceptibility towards COPD remains unexplored.

Objective
To understand whether the GDM will worsen CS induced lung dysfunction and inflammation in offspring, information that might suggest changes to COPD risk.

Methods
Six-week-old C57BL/6NJ female mice were fed a high-fat diet (HF-45% kcal) to induce diabetes or low-fat (LF-10% kcal) control diet for 6-weeks. Diets continued throughout pregnancy and weaning. Weaned offspring were fed with standard research chow-diet until 8-weeks of age, at which point they were exposed to CS/Room air for 50 mins, twice/day, for four days. Lung function and cell counts (flow-cytometry) were assessed on day five. Data analyzed in Prism GraphPad using two-way ANOVA.

Results

Control dams had larger litter (8.0±1.8) than GDM (5.5±3.1), but all litter were culled to a maximum of 6 pups. GDM offspring were significantly heavier (14.8±2.5g male and female 12.8±1.6g) than controls (11.0±1.2g male and 10.8±1.0g female), at 3-weeks, but not 8-weeks of age. CS exposure significantly increased total lung resistance (12.8%) and airway resistance (14.2%) in male GDM offspring compared to control. GDM influenced offspring immune cell infiltration in a sex-specific manner. Female GDM-CS offspring had significantly decreased neutrophils and CD4+ T-cells compared to control smokers. Interestingly GDM-CS males had significantly elevated B-cells compared to control smokers.

Conclusion
Prenatal exposure to GDM promotes offspring susceptibility towards CS-induced lung dysfunction and inflammation, in a sex-specific manner. GDM may modulate response to cigarettes in early adulthood, suggesting a propensity to future COPD.

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