Abstract: 45O

Metabolic syndrome in pregnancy causes fetal growth restriction and attenuates placental leukocyte populations.

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Metabolic syndrome (MetS) is a combination of metabolic disturbances (i.e., obesity, hypertension, high blood glucose or dyslipidaemia) that occurs in up to 25% of women of reproductive age. MetS increases the risk of maternal and fetal complications in pregnancy, but the mechanisms that drive this are poorly understood. Thus, this study aimed to characterise fetal growth and placental function and inflammation in a mouse model of metabolic syndrome. At 5 weeks of age, C57BL/6 female mice were randomly assigned to either a high fat sugar salt diet (HFSS, 42% kcal fat content) or a normal chow diet (NCD) for 10 weeks (n = 8-9 per diet). Females were then mated with male C57BL/6 mice for conception. Bodyweight, systolic blood pressure (SBP), blood lipids and glycaemic status were measured regularly throughout the diet regimen and following conception. HFSS significantly ($P < 0.05$) increased maternal bodyweight, fasting blood glucose and blood cholesterol, indicating that the diet induced MetS. Mice were culled on day 18.5 of pregnancy, each pup's sex was identified, and maternal, fetal, and placental weights and dimensions were recorded. Placental tissues were processed for flow cytometry to characterise infiltrated immune cell populations within the maternal decidua basalis and labyrinth layers. HFSS significantly reduced pup weight and pup crown-rump-length compared to pups from NCD mothers ($P = 0.01$ and $P = 0.02$, respectively). HFSS did not affect placental weight. Interestingly, pup weight or size was not affected by sex, but placental weight was significantly reduced in female pups ($P= 0.001$) compared to male pups. *Post hoc* analyses revealed that this sex effect was specific to female pups from HFSS mice but not NCD mice. Neither maternal diet nor pup sex affected leukocyte populations in the labyrinth layer of the placenta. However, myeloid-derived leukocytes (CD11b+) were significantly reduced ($P = 0.03$) in the basalis layer of the placentas of male pups from HFSS mothers (compared to that of male pups from NCD mothers). Subpopulations of myeloid-derived leukocytes were further explored, and there was a trend for reduced patrolling monocytes in the basalis layer from male pups of HFSS mothers ($P = 0.09$; compared to male pups from NCD mothers). In conclusion, diet-induced MetS caused fetal growth restriction and reduced placental myeloid-derived leukocytes in a sex-specific manner. Female pups were protected from the reductions in myeloid-derived cells and further studies (histopathology and qPCR and immunohistochemistry) are currently underway to better understand the physiological relevance of these effects.