Heat Stress-Associated Intrauterine Growth Retardation is Mitigated by Preconception Nutritional Supplementation in Rural Pakistan

Kartik Shankar1, Puuee Jambal1, Meghan Ruebel1, Jennifer Kemp1, Jamie Westcott1, Sarah J. Borengasser2, K. Michael Hambidge1, Nancy F. Krebs1
1Department of Pediatrics, Section of Nutrition, University of Colorado Denver Anschutz Medical Campus, Aurora, CO, USA

OBJECTIVE & HYPOTHESIS

- Determine the influence of ambient heat and maternal nutritional status on fetal growth.
- We hypothesized that 1) excessive heat during early pregnancy impairs fetal growth; and 2) improving maternal nutritional status will mitigate heat-stress associated growth retardation.

METHODS

The Women First (WF) trial was an individually randomized, non-masked, multi-site, controlled trial (ClinicalTrials.gov NCT01883195) to determine the effect of a preconception small quantity lipid-based nutrition supplement (sqLNS) on birth length and other anthropometry outcomes in rural/suburban women. The trial included three arms: Arm 1 women consumed sqLNS 3 months prior to conception; Arm 2 women consumed the same sqLNS commencing at 12 wk gestation until delivery; or Arm 3 no sqLNS was administered and women followed local pregnancy standard of care. The WF trial was conducted in rural or semi-rural locations in India (Belagavi), Pakistan (Thatta), Guatemala (Chimaltenango), and the Democratic Republic of the Congo (Equateur). Findings presented here are from the Pakistan site since women here are susceptible to both poor nutrition and seasonal high ambient temperature.

Assessments:
- Maternal height and weight were obtained at enrollment, and maternal weight was obtained at -12 and 34 wk of gestation. Newborn anthropometry was obtained within 48 h of delivery by trained assessment teams. Newborn anthropology was adjusted for GA based on inter-trimester growth charts.
- Global placental gene expression analysis (RNA-seq) were done using term placenta tissues (n = 150).
- Daily maximum air temperature for the years 2014-2017 (which encompassed all birth dates) were acquired from the closest automated surface observation systems (ASOS) using the GSOOR package.

Statistical analyses were performed in R. Linear regression was utilized to assess the associations between temperature exposure and birth outcomes. Analysis of variance (ANOVA) and Student t-test were employed to ascertain differences between groups. Statistical significance was set at P < 0.05.

RESULTS

Maternal sqLNS improves fetal growth. Z-scores of gestation-age-adjusted birth length (LGAZ) and birth weight (BWG) in participants assigned to each arm of the 3-arm study were utilized to determine and test the impact of women randomized to sqLNS before pregnancy. In general, Z-scores from infants born from November to February were significantly lower for infants born between November and February. P values were derived using one-way ANOVA, (n = 146, 139 and 162, respectively).

Effects of heat stress on birth length. Growth restrictive effects of excessive heat exposure in the 1st trimester are mitigated by maternal nutritional supplementation. Presence of excess heat stress was defined as over 20 days with Tmax >39°C within 1 trimester. P values were derived using Student t-test.

SUMMARY & CONCLUSIONS

- Ambient heat stress in human populations has significant negative effects on intrauterine growth.
- In resource-limited settings exposure to high ambient temperature in the 1st trimester decreases linear growth in utero.
- Reduced heat exposure disrupts placental genes involved in protein translation.
- Improved maternal nutritional status provides resilience against heat-induced growth restriction.
- The mechanisms of heat-associated effects on child development require further study.

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University of Colorado Anschutz Medical Campus