Bonell Ana (Orcid ID: 0000-0001-5981-762X)

# A feasibility study of the use of UmbiFlow™ to assess the impact of heat stress on fetoplacental blood flow in field studies.

Authors:
+Ana Bonell[1,2], Valerie Vannevel[3,4,5], Bakary Sonko[1], Nuredin Mohammed[1], Ana M. Vicedo-Cabrera[6,7], Andy Haines[2,8], Neil S Maxwell[9], Jane Hirst[*10], Andrew M Prentice[*1]

*joint last author

1. Medical Research Council Unit The Gambia at London School of Hygiene and Tropical Medicine, Banjul, The Gambia
2. Centre on Climate Change and Planetary Health, London School of Hygiene and Tropical Medicine, London, UK
3. Maternal and Infant Healthcare Strategies Unit, SAMRC, Pretoria, South Africa
4. Department of Obstetrics and Gynaecology, University of Pretoria, Pretoria, South Africa
5. Research Centre for Maternal, Fetal, Newborn & Child Healthcare strategies, University of Pretoria, Pretoria, South Africa
6. Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland
7. Oeschger Center for Climate Change Research, University of Bern, Bern, Switzerland
8. Department of Public Health, Environment and Society, Department of Population Health, London School of Hygiene and Tropical Medicine, London, UK
9. Environmental Extremes Laboratory, University of Brighton, Eastbourne, UK
10. Nuffield Department of Women's and Reproductive Health and the George Institute for Global Health, University of Oxford, Oxford, UK

+ Corresponding author: Ana Bonell, Medical Research Council Unit The Gambia at London School of Hygiene and Tropical Medicine, MRC Fajara, Atlantic Boulevard, Banjul, The Gambia. Ana.bonell@lshtm.ac.uk

**Keywords:** heat; pregnancy; fetoplacental circulation; climate change; Africa

**Synopsis:** Extreme heat exposure is increasing and a low-cost umbilical artery doppler device, UmbiFlow™, can aid understanding of fetoplacental function under heat stress conditions.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/ijgo.14480

**Type of article:** Clinical Article
Word count: abstract 198: main text 2476

**Abstract**

**Objective:** To evaluate the use of UmbiFlow™ in field settings to assess the impact of heat stress on umbilical artery resistance index (RI).

**Methods:** This feasibility study was conducted in West Kiang, The Gambia, West Africa; a rural area with increasing exposure to extreme heat. We recruited women with singleton fetuses who performed manual tasks (such as farming) during pregnancy to an observational cohort study. The umbilical artery RI was measured at rest, during and at the end of a typical working shift in women ≥ 28 weeks' gestation. Adverse pregnancy outcomes (APO) were classified as stillbirth, preterm birth, low birth weight, or small for gestational age, and all other outcomes as normal.

**Results:** A total of 40 participants were included; 23 normal births and 17 APO. Umbilical artery RI demonstrated a nonlinear relationship to heat stress, with indication of a potential threshold value for placental insufficiency at 32°C by Universal Thermal Climate Index and 30°C by Wet Bulb Globe Temperature.

**Conclusions:** The Umbiflow™ device proved to be an effective field method for assessing placental function. Dynamic changes in RI may begin to explain the association between extreme heat and APO with an identified threshold of effect.

**Funding:** The Wellcome Trust (216336/Z/19/Z)

## Introduction

With the ongoing climate crisis, global extreme heat exposure is progressively increasing with, for example, 30% of the world's population already exposed for 20 or more days annually to levels of heat sufficient to cause excess mortality and up to 74% predicted to be exposed by 2100.(1) Sub-Saharan Africa (SSA), South and South East Asia have been identified as regions at high risk of climate change related extreme weather events, despite contributing almost nothing to the problem.(2) In The Gambia, West Africa, extreme heat, defined as above the 90% centile compared to the average temperature for that region (>39.4°C), occurred on average for 50 days per year, from 2016-2019 (from local weather station data). The double burden of deadly heat exacerbated by climate change and existing health inequalities make this a critical location to study.

The burden of adverse pregnancy outcomes (APOs) are mainly felt in low middle income countries (LMICs), for example an estimated 15 million preterm births (PTB) occur per year, with greater than 80% occurring in Asia and SSA.(3) PTB is linked to high rates of both perinatal mortality (the cause of up to 24% of SSA neonatal deaths) and morbidity with long-term implications.(4) Triggers for preterm labour are complex and multifactorial, but recent environmental epidemiological studies demonstrate that maternal exposure to extreme heat increases the risk of PTB.(5, 6) Stillbirths, a neglected tragedy are again mainly felt in LMICs, with increasing rates and have also been linked to extreme heat exposure.(7)

The impact of heat on pregnancy depends on the intensity, duration and exposure window. First trimester exposure leads to increased embryonic death, cardiac and neurological anomalies.(8) In the second and third trimester, maternal exposure to ambient heat has been shown to increase the risk of PTB, stillbirths and low birth weight (LBW) in multiple settings.(6, 9, 10) Despite strong environmental epidemiological evidence of the association between heat and APO, there remains limited understanding of the pathophysiological mechanism associated with these poor outcomes.(11) One of the proposed hypotheses is that thermoregulatory changes to blood flow prioritise heat loss through cutaneous vasodilation over other homeostatic mechanisms. For example, in non-pregnant individuals during exertional heat strain, mesenteric and renal blood flow can be reduced to such an extent that gut permeability or acute kidney injury may occur.(12) In pregnancy, where blood flow to the uterus and placenta depends on cardiac output, with no autoregulation, there is evidence from animal studies that this occurs,(13) but human studies are lacking.(11) However, utero-placental insufficiency is implicated in the pathophysiological mechanisms of stillbirth, preterm birth and intrauterine growth restriction.(14) Heat stress could potentially impact on fetal wellbeing if the placenta is unable to buffer the effects of the reduction in blood flow leading to transient utero-placental insufficiency.

Direct measurement of blood flow to the placenta through the uterine arteries can be challenging as it requires highly specialised non-portable equipment in conjunction with fluid dynamic modelling.(15) However, the umbilical artery doppler waveform gives an indication of the fetoplacental circulation function, and so indicates how effectively the fetus is receiving oxygen, nutrients and removing waste products, and can be used as a surrogate for direct blood flow measurement. The UmbiFlow™ device, a low-cost portable continuous-wave doppler device was designed and developed in South Africa and has been validated for use to identify placental insufficiency based on the resistance index (RI) of the umbilical artery, with accuracy comparable to commercial units.(16, 17) It has not yet been used to explore dynamic changes in the RI under different physiological conditions. We hypothesise that heat stress will impact on umbilical artery RI, and those who have APO are more likely to have placental insufficiency under heat stress. Therefore, the following study objectives were defined:

- determine if UmbiFlow™ identifies a change in umbilical artery resistance index under heat stress; and
- determine the practical considerations needed to use UmbiFlow™ in the field.

**Materials and Methods**

This feasibility study follows the guidelines on reporting non-randomised pilot and feasibility studies (checklist can be found in the supplement).(18) It was part of a larger prospective cohort study on heat strain in pregnant subsistence farmers and the physiological impact on their fetuses.(11) The study was approved by the Gambia government/MRC Joint ethics committee and the London School of Hygiene and Tropical Medicine Ethics Advisory Board (ref: 16405) in accordance with the Declaration of Helsinki (2013).

Briefly, pregnant women living in West Kiang, The Gambia, participated in an observational cohort study of maternal heat strain and the assessment of the dynamic changes in maternal and fetoplacental blood flow during a day of field work from August 2019 to March 2020, with follow-up until December 2020.(19) Participants were identified through the antenatal clinic or the health and demographic surveillance system in place in West Kiang and were eligible if they were pregnant with a singleton, undertook farming or manual tasks during pregnancy and did not suffer with pre-eclampsia or eclampsia at the time of recruitment. Gestational age was determined by last known menstrual period when known, or if unknown, by biparietal diameter on ultrasound scan before 28 weeks' gestation. The feasibility study visits occurred in those with gestational age $\geq$ 28 weeks. Exposure to external environmental conditions (air temperature, relative humidity, solar radiation, wind speed) were measured hourly using the HT200: Heat Stress WBGT Meter, Extech® and the Extech® AN100 thermo-anemometer, NH, USA. Measurements were taken within 1 metre of participants to record exact exposure conditions. Two thermal indices were calculated from these measures – the Wet Bulb Globe Temperature (WBGT) and the Universal Thermal Climate Index (UTCI). These are composite measures of thermal stress taking into account heat, humidity, solar radiation and wind speed.(20)

UmbiFlow™ measures the blood flow velocity in the umbilical cord and calculates the RI = (systolic velocity – diastolic velocity)/systolic velocity. The hand-held probe attaches to a laptop/tablet, signal processing occurs within the specialised software to give both a waveform and audible umbilical artery blood flow. Validated reference values by gestational age indicate if the RI is within normal, intermediate or high-risk risk range (RI below 75$^{th}$ percentile, between 75$^{th}$-95$^{th}$ percentile and >95$^{th}$ percentile respectively for the gestational age). On a single occasion for each subject the RI was measured at baseline in an airconditioned environment with the participant supine at rest, and with abdominal lateral tilt, and then at two time points during her working day – determined based on the length of the work shift to correspond with a mid-point and end-point of the manual tasks. At each time point, two measurements were taken, assessed for quality (signal quality assessed by expert trained by the South African team), mean values taken when good/moderate quality and discarded if poor quality. The risk category was recorded at each reading as well as the exact value of the RI. FHR was measured concurrently, and average values over 5 mins taken. When FHR or umbilical artery RI was identified as high risk during the study and did not resolve in 30 minutes then participants were referred for urgent care. This involved being assessed by the rural antenatal clinic (staffed by a midwife and 4 doctors), with the option to be referred to a tertiary centre should they identify a clinical need. All participants were followed until after delivery and data on birth outcome collected. APOs were defined as follows: stillbirth = pregnancy > 20 weeks' gestation where the baby was born dead; PTB = live birth prior to completion of 37 weeks' gestation; LBW = birth weight ≤ 2.5 kg; small for gestational age (SGA) = birth weight < 10% expected at gestational age based on Intergrowth-21 standardised curves. To determine practical considerations, the study team recorded any issues with the software, the use of UmbiFlow™ in the field and the results generated.

All analyses were performed in R version 4.1.0. Descriptive characteristics are presented as mean +/- SD or median (IQR) by outcome, depending on distribution. The relationship between UTCI, fetal heart rate and umbilical artery RI were explored using linear and non-linear models. Non-linear models were tested across different spline definitions and different knots placed at the median and 90th percentile. The lowest AIC was used to determine best model fit. Change in fetal heart rate (FHR) by UTCI was best explained by a linear model. RI z-score (which is age adjusted) or change in RI by UTCI was best explained by a non-linear model with a cubic spline with one knot at the median.

A multilevel linear regression model, with individual as random effect, of the association between umbilical artery RI z-score and heat stress was explored both with and without cubic splines, with the best fit determined by AIC. The final model is shown:

$$\text{Z-score}_{ij} \sim \beta_0 + \beta_1 \text{*heat stress}_{ij}$$

z-score = umbilical artery RI z-score for individual *i* at time *j* heat stress = UTCI for individual *i* at time *j*

Multilevel model assumptions were assessed by examining normality of residuals and performing Levene's Tests for homogeneity of variance. The simr package was used to run a simulation-based power analysis on the multilevel model to give estimations of sample size requirements to detect a difference in umbilical artery RI z-score under heat stress.

**Results**

Full umbilical artery doppler was completed on 40 participants the field. Out of these 40 participants, 17 had APO and 23 did not. Of those with APO, 3 suffered with stillbirths, 7 delivered preterm (spontaneously), 6 were LBW and 8 had SGA. Descriptive characteristics of all participants are presented in Table 1, with detailed description of those with stillbirths in Table 2.

Environmental conditions and physiological parameters at baseline, during the work shift and at the end of the work shift are presented in Table 3 (full exposures can be found in the supplement Figure 1). All participants were exposed to "extreme heat stress" (based on the UTCI value), which has been shown to increase risk of mortality in other populations and settings.(21) Average physical energy expenditure for the working shift was equivalent to moderate intensity exercise such as a brisk walk.(22) There was no significant difference between working environmental conditions or estimated energy expenditure in those who went on to have an APO compared to those who did not.

Fetal heart rate demonstrated a linear relationship with heat stress, giving an increase of 10.7 (95% CI 7.5;13.8) BPM for each 10°C UTCI increase and 13.4 (95% CI 9.5;17.2) BPM for each 10°C WBGT increase (Figure 1). However, there was no clear linear or nonlinear relationship between fetal heart rate and maternal tympanic temperature. Change in RI from cool baseline to working conditions reduced with increasing heat stress exposure up to 32°C UTCI/30°C WBGT and then appears to begin to increase with rising heat stress (Figure 2). There was no statistical difference in association between RI and heat stress in those with APO versus without APO (see supplement Figure 2). Based on these findings several simulation-based power calculations are given in the supplement. Model diagnostics for normality of residuals and homogeneity of variance (using Levene's Test) did not indicate gross violation of model assumptions.

Practical considerations for use in the field included ensuring comfortable and private area to scan - which was provided by local vegetation or screens; protection from extreme weather – provided by portable shade/rain protector; and need for accurate gestational age to calculate RI z-scores. Several challenges were identified: software compatibility; delay in loading of the program when in the field; and interference with the signal when using windows 7. The programming for the software can only run on windows and is incompatible with Apple devices. It also required a laptop versus a tablet so requiring multiple electronic devices to be carried into the field as all study records were taken directly onto tablets. There was a delay in loading the software at each start up, which required planning for especially considering the need to capture dynamic changes. We also struggled with interference in the signal when using Windows 7, which resolved on upgrading to Windows 10, but made measurements difficult. All these issues were worked through and we were able to successfully record umbilical artery RI in the field at all required time points. Furthermore, the manufacturers of UmbiFlow™ are working to resolve many of the points raised.

**Discussion**

We show that the UmbiFlow™ device is highly suited to field work, being light and compact, that the measurement of umbilical artery doppler in field conditions is possible and shows promising evidence of potentially enhancing the understanding of the fetoplacental circulation response to heat stress. Under heat stress conditions below 32°C UTCI/30°C WBGT there was a reduction in the umbilical artery RI from baseline, which would indicate increased blood velocity within the fetoplacental circulation as we would expect. However, above these temperature thresholds there appears to be a trend towards increasing RI which would indicate insufficiency in the fetoplacental circulation. The response to heat stress may be different in those individuals that went on to have an APO, however the study was not powered to determine this with statistical significance.

There are few studies exploring the impact of heat on uterine or placental blood flow. A study from Sweden on sauna use (20 mins at 70°C) in late pregnancy found a reactive increase in fetal heart rate, but no change in umbilical artery blood flow.(23) This study is not immediately translatable to other settings due to both the inactivity and the extreme heat, but could be reassuring in terms of short bursts of unavoidable extreme heat exposure. Other studies have mainly focused on thermoregulation in pregnancy and there are several studies with encouraging evidence that thermoregulation is not compromised.(24, 25) Although there is clear evidence that moderate intensity exercise is of benefit in pregnancy,(26) these studies are in temperate conditions and so not transferable to our setting. Additionally in extreme cases (Olympic athletes exercising at > 90% maximum maternal heart rate) there can be compromised fetal wellbeing.(27) This extreme physiological strain may be similar to that experienced under extreme heat and warrants further investigation.

The study has several limitations. The sample size was reduced due to the covid-19 pandemic halting all field work activity from March 2020, limiting the scope of analysis available. Maternal core temperature could not be measured in the field (impractical to use rectal thermometer and lack of evidence on safety for core telemetry pills) and therefore the less accurate and less precise tympanic temperature was measured. Additionally, pregnancy and neonatal outcomes in the general population of The Gambia are worse than the global average which may impact on generalisability of the findings globally but could be reasonably representative of a rural SSA population. We found the number of participants with pre-eclampsia was higher in those without an adverse pregnancy outcome, but this is most likely due to chance. This study comes at a time where extreme heat exposure is becoming a reality for much of the global population. Despite this, those most commonly experiencing these extreme conditions are often missing from the medical literature. This study is set in a rural African setting, with a population that can be difficult to access but are often exposed to extreme environmental conditions. By exploring ways to improve the understanding of pathophysiological mechanisms in a real-life setting we highlight the need for future work. The simulation-based sample size calculations (see supplement) give an estimate of the sample size and conditions needed to progress understanding of this using the Umbiflow™ device. However, without expanding the work to include several key topic areas the impacts of this research will have little meaning to this population. Identifying at risk women will not be beneficial without clear management options to reduce the risk of these adverse outcomes. Health system strengthening in both facilities and human capacity in dealing with maternal health are urgently needed, especially in the face of the growing climate crisis and resultant impacts on healthcare. Additionally, identification of a dangerous heat exposure threshold will not have a real-world impact until evidence-based, effective, realistic, pragmatic and sustainable interventions for cooling both individuals and their environment are identified and enacted.

**Author contributions:**

AB: conceptualization, methodology, formal analysis, writing original draft.

VV: methodology, validation, editing.

BS: software, data curation, editing.

NM: formal analysis, editing.

AVC, AH, NM, JH, AP: conceptualization, methodology, supervision, editing

**Data availability:**

Anonymised data will be made available on reasonable request from the corresponding author.

**Conflict of interest:**

None declared

**Funding:**

This project was funded by the Wellcome Trust through the Wellcome Trust Global Health PhD Fellowship awarded to AB (216336/Z/19/Z). The funders had no role in study design, data collection, analysis, manuscript writing or decision to submit.

**References**

1. Mora C, Dousset B, Caldwell IR, Powell FE, Geronimo RC, Bielecki CR, et al. Global risk of deadly heat. Nature Clim Change. 2017;7(7):501-6.
2. Andrews O, Le Quéré C, Kjellstrom T, Lemke B, Haines A. Implications for workability and survivability in populations exposed to extreme heat under climate change: a modelling study. The Lancet Planetary Health. 2018;2(12):e540-e7.
3. Chawanpaiboon S, Vogel JP, Moller A-B, Lumbiganon P, Petzold M, Hogan D, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. The Lancet Global health. 2019;7(1):e37-e46.
4. Population-based rates, timing, and causes of maternal deaths, stillbirths, and neonatal deaths in south Asia and sub-Saharan Africa: a multi-country prospective cohort study. Lancet Glob Health. 2018;6(12):e1297-e308.
5. Bekkar B, Pacheco S, Basu R, DeNicola N. Association of Air Pollution and Heat Exposure With Preterm Birth, Low Birth Weight, and Stillbirth in the US: A Systematic Review. JAMA Network Open. 2020;3(6):e208243-e.
6. Chersich MF, Pham MD, Areal A, Haghighi MM, Manyuchi A, Swift CP, et al. Associations between high temperatures in pregnancy and risk of preterm birth, low birth weight, and stillbirths: systematic review and meta-analysis. BMJ. 2020;371:m3811.

7. Khodadadi N, Dastoorpoor M, Khanjani N, Ghasemi A. Universal Thermal Climate Index (UTCI) and adverse pregnancy outcomes in Ahvaz, Iran. Reprod Health. 2022;19(1):33.
8. Edwards MJ, Saunders RD, Shiota K. Effects of heat on embryos and foetuses. International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group. 2003;19(3):295-324.
9. Basu R, Malig B, Ostro B. High ambient temperature and the risk of preterm delivery. American journal of epidemiology. 2010;172(10):1108-17.
10. Strand LB, Barnett AG, Tong S. Maternal exposure to ambient temperature and the risks of preterm birth and stillbirth in Brisbane, Australia. American journal of epidemiology. 2012;175(2):99-107.
11. Bonell A, Hirst J, Vicedo-Cabrera AM, Haines A, Prentice AM, Maxwell NS. A protocol for an observational cohort study of heat strain and its effect on fetal wellbeing in pregnant farmers in The Gambia. Wellcome Open Res. 2020;5:32.
12. Ebi KL, Capon A, Berry P, Broderick C, de Dear R, Havenith G, et al. Hot weather and heat extremes: health risks. Lancet. 2021;398(10301):698-708.
13. Bell AW, Hales JR, Fawcett AA, King RB. Effects of exercise and heat stress on regional blood flow in pregnant sheep. J Appl Physiol. 1986;60(5):1759-64.
14. Morgan TK. Role of the Placenta in Preterm Birth: A Review. Am J Perinatol. 2016;33(3):258-66.
15. Rigano S, Ferrazzi E, Boito S, Pennati G, Padoan A, Galan H. Blood flow volume of uterine arteries in human pregnancies determined using 3D and bi-dimensional imaging, angio-Doppler, and fluid-dynamic modeling. Placenta. 2010;31(1):37-43.
16. Hlongwane T, Cronje T, Nkosi B, Pattinson RC. The prevalence of abnormal Doppler's of the umbilical artery in a low-risk pregnant population in South Africa. EClinicalMedicine. 2021;34:100792.
17. Theron GB, Theron AM, Odendaal HJ, Bunn AE. Comparison between a newly developed PC-based Doppler umbilical artery waveform analyser and a commercial unit. S Afr Med J. 2005;95(1):62-4.
18. Lancaster GA, Thabane L. Guidelines for reporting non-randomised pilot and feasibility studies. Pilot and Feasibility Studies. 2019;5(1):114.
19. Bonell A, Sonko B, Badjie J, Samateh T, Saidy T, Sosseh F, et al. Assessing the Effect of Environmental Heat Stress on Maternal Physiology and Fetal Blood Flow in Pregnant Subsistence Farmers in West Africa. PREPRINT. 2021.
20. Havenith G, Fiala D. Thermal indices and thermophysiological modeling for heat stress. Comprehensive Physiology. 2016;6(1):255-302.
21. Di Napoli C, Pappenberger F, Cloke HL. Assessing heat-related health risk in Europe via the Universal Thermal Climate Index (UTCI). Int J Biometeorol. 2018;62(7):1155-65.
22. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Medicine and science in sports and exercise. 2007;39(8):1423-34.

23. Vaha-Eskeli K, Pirhonen J, Seppanen A, Erkkola R. Doppler flow measurement of uterine and umbilical arteries in heat stress during late pregnancy. Am J Perinatol. 1991;8(6):385-9.
24. Ravanelli N, Casasola W, English T, Edwards KM, Jay O. Heat stress and fetal risk . Environmental limits for exercise and passive heat stress during pregnancy : a systematic review with best evidence synthesis. 2018(October 2016):1-8.
25. Smallcombe JW, Puhenthirar A, Casasola W, Inoue DS, Chaseling GK, Ravanelli N, et al. Thermoregulation During Pregnancy: a Controlled Trial Investigating the Risk of Maternal Hyperthermia During Exercise in the Heat. Sports Medicine. 2021.
26. ACOG Committee Opinion No. 650: Physical Activity and Exercise During Pregnancy and the Postpartum Period. Obstet Gynecol. 2015;126(6):e135-e42.
27. Salvesen K, Hem E, Sundgot-Borgen J. Fetal wellbeing may be compromised during strenuous exercise among pregnant elite athletes. Br J Sports Med. 2012;46(4):279-83.

Figure 1: Association between FHR and UTCI (A), and FHR and WBGT (B). Linear model with 95% CI as shading.

Figure 2: Association between change in umbilical artery RI and UTCI (A) and WBGT (B). Multilevel model output with 95% CI as shading.

**Table 1: Demographic, social, obstetric and anthropometric characteristics of those with adverse pregnancy outcomes and those without.**

| | Adverse pregnancy outcome<br>n = 17 | No adverse outcome<br>n = 23 |
|---|---|---|
| Age (years) | 32.3 ± 7.6 | 31.6 ± 7.3 |
| Occupation – farmers/other | 16/1 | 16/7 |
| Marital status: Married | 17 | 21 |
| Single | 0 | 1 |
| Widowed | 0 | 1 |
| | Median (IQR) or Mean ± SD | |
| Gravida | 5 (5.0) | 5 (3.5) |
| Parity | 3 (4.0) | 4 (3.0) |
| GA at study visit | 31.1 ± 3.1 | 30.5 ± 2.9 |

| | | |
|---|---|---|
| Height (cm) | 161.2 ± 5.4 | 162.6 ± 6.3 |
| Weight (kg) | 62.3 ± 7.7 | 64.8 ± 12.1 |
| BMI (kg/m$^2$) | 24.0 ± 2.9 | 24.5 ± 3.9 |
| Blood Pressure | 108/72 | 115/72 |
| Hb (g/dL) | 11.3 ± 1.1 | 11.0 ± 1.6 |
| Infection during pregnancy (%) | 7/17 (41%) | 13/23 (57%) |
| Pre-eclampsia/eclampsia (%) | 1/17 (6%) | 5/18 (28%) |
| Gestational age at birth (weeks) | 38.4 ± 3.3 | 40.1 ± 1.7 |
| Birth Weight (kg) | 2.8 ± 0.5 | 3.4 ± 0.4 |
| Adverse outcomes: | | |
| Stillbirths | 3/40 (7.5%) | |
| Preterm births | 7/40 (17.5%) | |
| Low birth weight | 6/40 (15%) | |
| Small for gestational age | 8/40 (20%) | |

**Table 2: details of participants who had stillbirths**

| | Case A | Case B | Case C |
|---|---|---|---|
| Maternal age | 40-45 years | 40-45 years | 25-30 years |
| Gravida/Parity | 12/7 | 10/9 | 2/1 |
| Previous stillbirth | Yes | No | No |
| Previous miscarriage | Yes | No | No |
| Previous neonatal death | No | Yes | No |

| | | | |
|---|---|---|---|
| GA at visit | 31+6 | 34+5 | 32+1 |
| UA RI – baseline RC | High risk | Low risk | Low risk |
| UA RI – during work RC | High risk | High risk | Low risk |
| UA RI – after work RC | High risk | High risk | Low risk |
| Action | Referred for urgent care | Referred for urgent care | Normal care |
| GA at delivery | 37+1 | 40+1 | 42+2 |
| Outcome | Stillbirth | Stillbirth | Likely intrapartum death |

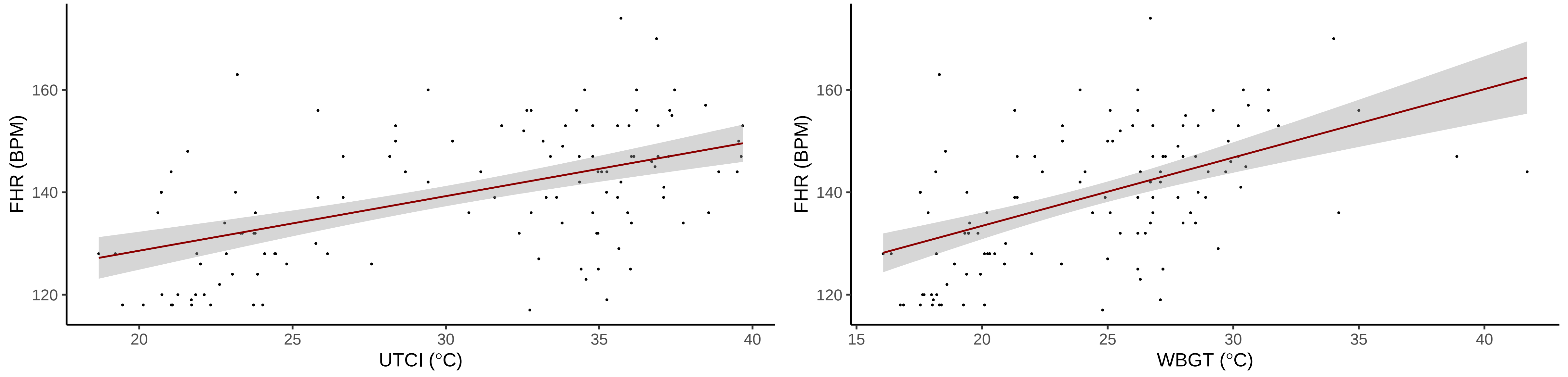
LBW = low birth weight; UA RI = umbilical artery resistance index; RC = risk category (low risk, intermediate risk, high risk based on z-score); GA = gestational age

**Table 3: Mean +/- SD of environmental conditions, maternal tympanic temperature, fetal heart rate and umbilical artery resistance index**

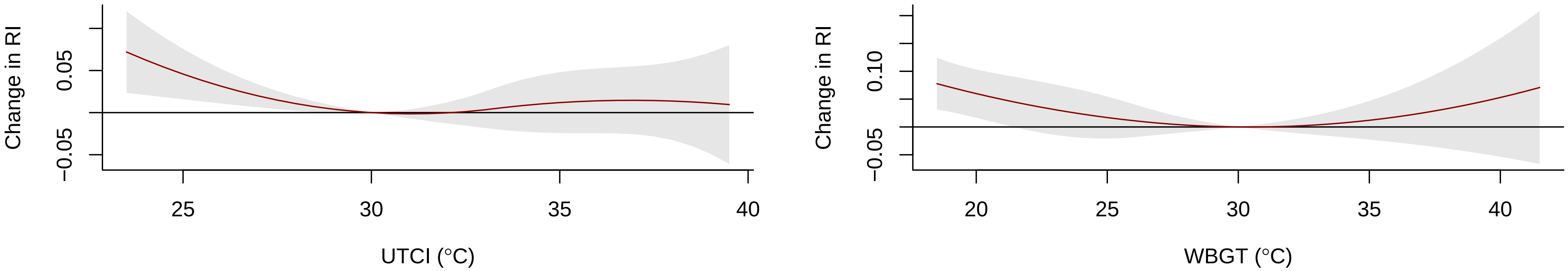
| | Baseline | | Mid-way | | End of shift | |
|---|---|---|---|---|---|---|
| | APO | No APO | APO | No APO | APO | No APO |
| UTCI (°C) | 23.1 ± 1.3 | 22.1 ± 2.2 | 34.2 ± 4.0 | 33.6 ± 4.2 | 34.1 ±3.2 | 34.5 ± 2.7 |
| WBGT (°C) | 19.3 ± 1.0 | 18.6 ± 1.8 | 27.3 ± 4.1 | 27.2 ± 4.5 | 27.3 ± 3.6 | 27.7 ± 2.7 |
| Air temp (°C) | 24.0 ± 1.5 | 22.9 ± 2.0 | 34.2 ± 3.6 | 33.9 ± 4.1 | 34.4 ±3.2 | 34.8 ± 3.0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| $T_{tym}$ (°C) | 36.9 ±0.2 | 36.9 ± 0.2 | 37.2 ± 0.4 | 37.1 ± 0.3 | 37.1 ± 0.3 | 37.3 ± 0.3 |
| PAEE (kcal/kg/hr) | - | - | - | - | 3.1 ± 0.9 | 3.1 ± 0.7 |
| FHR (b.min$^{-1}$) | 128.4 ± 8.4 | 126.4 ± 7.8 | 142.2 ± 14.4 | 147.3 ± 7.1 | 143.7 ± 11.8 | 144.9 ± 11.5 |
| RI | 0.68 ± 0.10 | 0.65 ± 0.08 | 0.69 ± 0.10 | 0.67 ± 0.05 | 0.66 ±0.05 | 0.65 ± 0.07 |
| z-score | 0.74 ± 1.59 | 0.43 ± 1.23 | 0.964 ± 1.58 | 0.52 ± 0.74 | 0.51 ± 0.89 | 0.23 ± 1.13 |

UTCI = universal climate thermal index; WBGT = wet bulb globe temperature; $T_{tym}$ = tympanic temperature; PAEE = physical activity energy expenditure; FHR = fetal heart rate; RI = umbilical artery resistance index.



FHR (BPM)
160
140
120
20
25
30
35
40
UTCI (°C)
FHR (BPM)
160
140
120
15
20
25
30
35
40
WBGT (°C)



Change in RI
0.05
−0.05
25
30
35
40
UTCI (°C)
Change in RI
0.10
0.05
−0.05
20
25
30
35
40
WBGT (°C)