**Online Supplemental Data**

**Elevated blood pressure in pregnant women with gestational diabetes according to the World Health Organization criteria: Importance of overweight**

Anna Birukov, PhD1,2,3, Dorte Glintborg, PhD4,5, Matthias B. Schulze, DrPH1,2,3,6, Tina K. Jensen, PhD7,8,9, Louise B. Andersen, PhD5,10, Kristin Kräker, PhD3,11,12,13, Elli Polemiti, MSc1,2, Boye L. Jensen, PhD14, Jan S. Jørgensen, PhD5,9,10, Ralf Dechend, MD3,10,11,12,15, Marianne S. Andersen, PhD4,5

1Department of Molecular Epidemiology, German Institute of Human Nutrition Potsdam-Rehbrücke, Nuthetal, Germany

2German Center for Diabetes Research (DZD), München-Neuherberg, Germany

3DZHK (German Centre for Cardiovascular Research), partner site Berlin, Berlin, Germany

4Department of Endocrinology, Odense University Hospital, Odense, Denmark

5Institute of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

6Institute of Nutritional Science, University of Potsdam, Nuthetal, Germany

7Department of Environmental Medicine, Odense University Hospital, Odense, Denmark

8OPEN Patient data Explorative Network, Odense University Hospital, Odense, Denmark 9Odense Child Cohort, Hans Christian Andersen Children’s Hospital, Odense University Hospital, Odense, Denmark

10Department of Obstetrics and Gynecology, Odense University Hospital, Odense, Denmark

11Experimental and Clinical Research Center, a joint cooperation between Max-Delbrück-Center for Molecular Medicine and Charité - Universitätsmedizin Berlin, Berlin, Germany

12Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany

13Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany

14Institute for Molecular Medicine, University of Southern Denmark, Odense, Denmark

15HELIOS-Klinikum, Berlin, Department of Cardiology and Nephrology, Germany

**Short Title:** Blood pressure in GDM-WHO

**Key words:** gestational diabetes mellitus, GDM, blood pressure, WHO, overweight, insulin resistance, pregnancy

**Correspondence to**

Anna Birukov, Department of Molecular Epidemiology, German Institute of Human Nutrition Potsdam-Rehbrücke, Arthur-Scheunert-Allee 114-116, Nuthetal, Germany, telephone: +49 33200882431, E-mail: [anna.birukov@dife.de](mailto:anna.birukov@dife.de)

and Marianne S. Andersen, Department of Endocrinology, Odense University Hospital, Kløvervænget 6, 3rd floor, DK-5000 Odense C, Denmark, E-mail: [Marianne.Andersen1@rsyd.dk](mailto:Marianne.Andersen1@rsyd.dk)

**Supplementary Methods**

The Danish obstetric guideline recommends that blood pressure is assessed by a general practitioner at GW 6-10, GW 25, and GW 32 and by a midwife at GW 29, GW 35 (primipara), GW 37 (primipara), GW 39, and if the due date has passed, at GW 41. HDP was defined as gestational hypertension or preeclampsia according to the Danish Society of Obstetrics and Gynecology diagnostic criteria of hypertension and preeclampsia 2007–2012 as follows: Gestational hypertension was characterized as de novo BP >140/90 mmHg after 20 weeks of gestation on two or more episodes with at least 4 h in between or significant aggravation of pre-existing hypertension, preeclampsia as gestational hypertension with proteinuria (>0.3 g/24 h or ≥1+ on sterile urine dipstick)1.

**References**

1. Luef BM, Andersen LB, Renault KM, Nohr EA, Jorgensen JS, Christesen HT. Validation of hospital discharge diagnoses for hypertensive disorders of pregnancy. Acta Obstet Gynecol Scand 2016;95:1288-94.

**Supplementary Figures**

**Supplementary Figure S1**. Flowchart of inclusion.

Included in the OCC: n=2,874

No blood or FPG at GA 28-30 weeks available: n=1,293

No blood pressure records available: n=95

Available for analyses: n=1230

GDM-WHO: n=498

Rest of the cohort: n=732

Exclusions: n=256

Twin pregnancies: n=0

PCOS: n=145

IVF: n=97

HDP before GA 28: n=4

Early GDM: n=10

Blood pressure and FPG available: n=1,486

GDM-WHO was defined as FPG ≥5.1 mmol/l. OCC=Odense Child Cohort, FPG=fasting plasma glucose, GA=gestational age, PCOS=polycystic ovary syndrome, IVF=in-vitro fertilization, HDP=hypertensive disorders of pregnancy, GDM-WHO=gestational diabetes mellitus according to the World Health Organization 2013 thresholds.

**Supplementary Tables**

**Supplementary Table S1**. Available blood pressure records per 4 gestational weeks interval in women with FPG, n=1230.

|  |  |  |
| --- | --- | --- |
|  | **SBP records, n (%)** | **DBP records, n (%)** |
| **Gestational age, weeks** |  |  |
| ≤12.0 | 1163 (94.6) | 1162 (94.5) |
| 12.1 to 16.0 | 529 (43.0) | 529 (43.0) |
| 16.1 to 20.0 | 189 (15.4) | 189 (15.4) |
| 20.1 to 24.0 | 536 (43.6) | 535 (43.5) |
| 24.1 to 28.0 | 796 (64.7) | 796 (64.7) |
| 28.1 to 32.0 | 980 (79.7) | 979 (79.6) |
| 32.1 to 36.0 | 967 (78.6) | 967 (78.6) |
| 36.1 to 40.0 | 1062 (86.3) | 1062 (86.3) |
| >40.0 | 279 (22.7) | 279 (22.7) |
| **Number of blood pressure records per woman** |  |  |
| 1 | 70 (5.7) | 70 (5.7) |
| 2 | 9 (0.7) | 10 (0.8) |
| 3 | 36 (2.9) | 37 (3.0) |
| 4 | 161 (13.1) | 159 (12.9) |
| 5 | 326 (26.5) | 326 (26.5) |
| 6 | 401 (32.6) | 401 (32.6) |
| 7 | 194 (15.8) | 194 (15.8) |
| 8 | 30 (2.4) | 30 (2.4) |
| 9 | 3 (0.2) | 3 (0.2) |

FPG=fasting plasma glucose, SBP=systolic blood pressure, DBP=diastolic blood pressure.

**Supplementary Table S2.** Blood pressure trajectories in women with5.6>FPG ≥5.1 and FPG ≥5.6 as compared to women with FPG<5.1 (reference) and stratified by overweight status.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Overweight, n=438** | |  | **Lean, n=792** | |  | **Complete cohort, n=1230** | |
|  | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** |  | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** |  | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** |
| FPG<5.1 | ref | ref |  | ref | ref |  | ref | ref |
| 5.6>FPG ≥5.1 | 1.98 (0.32; 3.65) | 1.50 (0.25; 2.76) |  | -0.15 (-1.44; 1.14) | 0.41 (-0.57; 1.40) |  | 0.71 (-0.31; 1.74) | 0.81 (0.04; 1.58) |
| FPG ≥5.6 | 4.03 (1.89; 6.17) | 2.04 (0.42; 3.65) |  | 1.00 (-1.25; 3.26) | 0.31 (-1.42; 2.03) |  | 2.36 (0.82; 3.91) | 1.13 (-0.03; 2.30) |

**Supplementary Table S3.** Associations between glycemic status at GW 28-30 and blood pressure trajectory throughout pregnancy, stratified by pre-pregnancy BMI.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **BMI≥30, n=141** | |  | **30>BMI≥25, n=297** | |  | **BMI<25, n=792** | |
|  | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** |  | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** |  | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** | |
| GDM-WHO | 3.72 (0.84; 6.60) | 2.92 (0.80; 5.04) |  | 2.28 (0.48; 4.08) | 1.18 (-0.21; 2.57) |  | 0.08 (-1.12; 1.28) | 0.39 (-0.52; 1.31) | |
| FPG ≥5.6 mmol/l | 3.93 (1.13; 6.73) | 1.15 (-0.96; 3.26) |  | 2.38 (-0.40; 5.15) | 1.60 (-0.53; 3.72) |  | 1.05 (-1.17; 3.27) | 0.18 (-1.52; 1.88) | |
| FPG (log2) | 11.4 (1.82; 21.0) | 6.62 (-0.52; 13.8) |  | 9.96 (1.65; 18.3) | 6.49 (0.11; 12.9) |  | 1.43 (-3.54; 6.40) | 0.87 (-2.92; 4.67) | |

GDM was defined according to the WHO 2013 threshold of FPG ≥5.1 mmol/l. Overweight status was defined as BMI ≥25 kg/m2. FPG=fasting plasma glucose, SBP=systolic blood pressure, DBP=diastolic blood pressure, HR=hazard ratio, CI=confidence interval, HDP=hypertensive disorders of pregnancy, including preeclampsia, HR=hazard ratio, CI=confidence interval. Associations were assessed with linear mixed models and adjusted for age, pre-pregnancy BMI, smoking, parity.

**Supplementary Table S4.** Adjusted analyses between glycemic status, blood pressure trajectory following blood sampling (28 to 40+ GW), in the complete cohort and stratified by overweight status.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Overweight, n=406** | |  | **Lean, n=748** | |  | **Complete cohort, n=1,154** | |
|  | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** |  | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** |  | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** |
| GDM-WHO | 2.15 (0.40; 3.91) | 1.63 (0.33; 2.93) |  | 0.47 (-0.88; 1.83) | 0.44 (-0.59; 1.47) |  | 1.19 (0.11; 2.26) | 0.91 (0.10; 1.71) |
| FPG ≥5.6 mmol/l | 2.18 (-0.07; 4.43) | 1.07 (-0.61; 2.74) |  | 1.52 (-0.97; 4.01) | 0.09 (-1.81; 1.99) |  | 1.83 (0.16; 3.50) | 0.64 (-0.62; 1.89) |
| FPG (log2) | 8.38 (1.18; 15.6) | 6.76 (1.41; 12.1) |  | 2.76 (-2.83; 8.35) | 1.02 (-3.23; 5.27) |  | 5.16 (0.74; 9.58) | 3.31 (-0.02; 6.63) |

**Supplementary Table S5.** Adjusted associations between insulin resistance assessed by HOMA-IR and gestational blood pressure trajectory.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Overweight, n=438** | | |  | | **Lean, n=792** | | | **Complete cohort, n=1230** | | | |
| **HOMA-IR quartiles, median (IQR)** |  | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** |  | | **Beta coefficients (95% CI) for SBP trajectory** | | **Beta coefficients (95% CI) for DBP trajectory** |  | | **Beta coefficients (95% CI) for SBP trajectory** | **Beta coefficients (95% CI) for DBP trajectory** |
| 1st: 1.22 (0.99-1.35) |  | ref | ref |  | | ref | | ref |  | | ref | ref |
| 2nd: 1.83 (1.66-1.98) |  | 2.58 (-0.55; 5.70) | 1.66 (-0.67; 3.98) |  | | 1.34 (-0.06; 2.74) | | 1.15 (0.08; 2.21) |  | | 1.51 (0.24; 2.77) | 1.02 (0.06; 1.97) |
| 3rd: 2.61 (2.34-2.89) |  | 4.10 (1.18; 7.02) | 3.53 (1.36; 5.71) |  | | 1.34 (-0.18; 2.85) | | 1.41 (0.25; 2.56) |  | | 2.07 (0.78; 3.36) | 1.74 (0.77; 2.72) |
| 4th: 4.17 (3.69-5.41) |  | 5.20 (2.30; 8.09) | 4.25 (2.09; 6.40) |  | | 0.91 (-0.95; 2.77) | | 1.50 (0.09; 2.92) |  | | 2.46 (1.01; 3.92) | 2.34 (1.24; 3.43) |
| HOMA-IR (log2) |  | 2.01 (0.92; 3.09) | 1.67 (0.87; 2.48) |  | | 0.45 (-0.31; 1.21) | | 0.65 (0.07; 1.23) |  | | 1.00 (0.38; 1.63) | 0.98 (0.51; 1.45) |

GDM was defined according to the WHO 2013 threshold of FPG ≥5.1 mmol/l. Overweight status was defined as BMI ≥25 kg/m2. Associations were assessed with linear mixed models. Models were adjusted for age, pre-pregnancy BMI, smoking, parity. GW=gestational weeks, FPG=fasting plasma glucose, SBP=systolic blood pressure, DBP=diastolic blood pressure, BMI=body mass index, HOMA-IR=homeostatic model assessment for insulin resistance, IQR=interquartile range.

**Supplementary Table S6.** Risk of HDP in women with5.6>FPG ≥5.1 and FPG ≥5.6 as compared to women with FPG<5.1 (reference) and stratified by overweight status.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Overweight, n=438** | | | **Lean, n=792** | | **Complete cohort, n=1230** | |
|  | **HR (95% CI) for HDP** | | | **HR (95% CI) for HDP** | | **HR (95% CI) for HDP** | |
| FPG<5.1 | | ref | ref | | ref | |
| 5.6>FPG ≥5.1 | | 1.05 (0.62; 1.81) | 1.47 (0.81, 2.66) | | 1.23 (0.82 to 1.83) | |
| FPG ≥5.6 | | 1.20 (0.60; 2.40) | 2.24 (0.91; 5.47) | | 1.56 (0.91 to 2.67) | |

**Supplementary Table S7.** Associations between glycemic status at GW 28-30 and risk of HDP, stratified by pre-pregnancy BMI.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **BMI≥30, n=141** |  | **30>BMI≥25, n=297** |  | **BMI<25, n=792** |
|  | **HR (95% CI) for HDP** |  | **HR (95% CI) for HDP** |  | **HR (95% CI) for HDP** |
| GDM-WHO | 1.02 (0.42; 2.48) |  | 1.20 (0.64; 2.22) |  | 1.60 (0.92; 2.77) |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| FPG ≥5.6 mmol/l | 0.79 (0.32; 1.95) |  | 2.45 (1.14; 5.26) |  | 1.94 (0.82; 4.58) |
| FPG (log2) | 2.05 (0.08; 51.8) |  | 6.22 (0.37; 105.9) |  | 10.1 (0.97; 104.5) |

Overweight status was defined as BMI ≥25 kg/m2. GW=gestational weeks, FPG=fasting plasma glucose, HR=hazard ratio, CI=confidence interval, HDP=hypertensive disorders of pregnancy, including preeclampsia. Associations were assessed with Cox proportional hazards models and adjusted for 1st trimester blood pressure, age, pre-pregnancy BMI, smoking and parity.

**Supplementary Table S8.** Adjusted associations between insulin resistance assessed by HOMA-IR and risk of HDP.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Overweight, n=438** | **Lean, n=792** | **Complete cohort, n=1230** |
| **HOMA-IR quartiles, median (IQR)** | **HR (95% CI) for HDP** | **HR (95% CI) for HDP** | **HR (95% CI) for HDP** |
| 1st: 1.22 (0.99-1.35) | ref | ref | ref |
| 2nd: 1.83 (1.66-1.98) | 3.09 (0.37; 25.7) | 1.32 (0.62; 2.80) | 1.29 (0.66 to 2.56) |
| 3rd: 2.61 (2.34-2.89) | 6.61 (0.89; 48.9) | 1.68 (0.76; 3.68) | 2.11 (1.11 to 4.01) |
| 4th: 4.17 (3.69-5.41) | 6.21 (0.84; 46.0) | 2.12 (0.89; 5.04) | 2.21 (1.13 to 4.33) |
| HOMA-IR (log2) | 1.47 (1.04; 2.08) | 1.50 (1.08; 2.08) | 1.47 (1.16 to 1.88) |

Overweight status was defined as BMI ≥25 kg/m2, HOMA-IR=homeostasis model assessment for insulin resistance, IQR=interquartile range, HR=hazard ratio, CI=confidence interval, HDP=hypertensive disorders of pregnancy, including preeclampsia. Associations were assessed with Cox proportional hazards models and adjusted for 1st trimester blood pressure, age, pre-pregnancy BMI, smoking and parity.