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Blood Pressure in Pregnancy – A Stress Test for Hypertension? Five-Year, Prospective, Follow-Up of the ROLO Study.

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Pregnancy– A Stress Test for Hypertension?

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Keywords:

Hypertension, pregnancy, maternal hypertension, cardiovascular disease, metabolic syndrome.

Disclosures

No conflicts of interest identified.

Author Contribution

1. Designed research: RC, EOB, FMcA
2. Conducted research: MB, EOB, RC, AC, AA, MT, PT, MKcK, FMcA
3. Analyzed data: MB, EOB, RC, AC, AA, MT, PT, MKcK, FMcA
4. Wrote the paper: MB, EOB, RC, AC, AA, MT, PT, MKcK, FMcA
5. Primary responsibility for final paper: FMcA
7. Other: All of the authors reviewed and revised the final version of the manuscript

Ethics Statement

The ROLO study was ethically approved by the NMH ethics committee in December 2006. This has no reference number. For the 5 year follow-up study ethical approval was obtained from the ethics committee Our Ladies Children's Hospital, Crumlin, Dublin, Ireland in October 2012, reference number: GEN/279/12.

Sources of Funding

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Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Main Text

Abstract

Objective: To investigate if maternal blood pressure (BP) below the diagnostic criteria of hypertensive disorders of pregnancy (HDP) is associated with maternal BP 5 years later.

Design: Prospective, observational study

Setting: Dublin, Ireland (2007-2011)

Sample: 329 women from the ROLO study (Randomised cOntrol trial of LOw glycaemic index diet to prevent the recurrence of macrosomia)

Methods: Maternal BP measurements were taken during pregnancy (13, 28, and 34 weeks gestation and day 1 post-partum) and at the 5 year follow-up. Systolic BP (SBP) and diastolic BP (DBP) were categorised as normal (SBP <120 and DBP <80 mmHg), elevated (SBP 120-129 and DBP <80 mmHg), HTN stage 1 (SBP 130-139 or DBP 80-89 mmHg), or HTN stage 2 (SBP ≥140 or DBP ≥90 mmHg) at each timepoint.

Main Outcome Measures: Maternal blood pressure at the 5 year follow-up

Results: Women with elevated BP at 28 and 34 weeks' gestation had 2.68 (95% CI:1.36-5.26) and 2.45-fold (95% CI:1.22-4.95) increased odds of HTN stage 1 respectively, at the 5 year follow-up, compared to those with normal BP in pregnancy.

Conclusion: Elevated BP at 28 and 34 weeks gestation was associated with an increased risk of HTN stage 1 5 years later. Thus, raised BP, below the diagnostic criteria of HDP, could be flagged for follow-up post-partum.

Funding: Health Research Board, Health Research centre for Health and Diet Research, Ireland, The National Maternity Hospital Medical Fund and the European Union's Seventh Framework Programme.

Keywords: Maternal blood pressure, hypertension, cardiovascular disease

Introduction

Pregnancy is often considered a stress test for life as it may uncover conditions which reappear in later life. Many examples exist such as preeclampsia and the development of hypertension (HTN) post-partum (1) as well as antenatal insulin resistance and the development of type 2 diabetes mellitus post-partum (2, 3).

Much research exists on the relationship between maternal blood glucose levels below that diagnostic for gestational diabetes mellitus (GDM) and adverse pregnancy outcomes. In

2018, O'Brien et al. demonstrated that each 1 mmol/L increase in fasting blood glucose in early pregnancy lead to a 1.70 mmol/mol increase in HbA1c at 5 years post-partum (4). Given this relationship, and the metabolic dysregulation which occurs in pregnancy, it is surprising that there is limited research on blood pressure (BP) below the diagnostic threshold of hypertensive disorders of pregnancy (HDP) and future health outcomes.

HDP are identified as systolic BP (SBP) ≥ 140 mmHg or diastolic BP (DBP) ≥ 90 mmHg (5). HDP rank as one of the most common causes of premature maternal death (6). HDP, such as preeclampsia and gestational HTN, increase one's risk of HTN post-partum (7-10). However, little is known about the relationship between BP below the diagnostic threshold for HDP and the risk of HTN post-partum.

A revision of the 7th Joint National Committee (JNC) guideline (11) advises that BP in non-pregnant populations be categorised as normal BP (SBP <120 and DBP <80 mmHg), elevated BP (SBP 120-129 and DBP <80 mmHg), HTN stage 1 (SBP 130-139 or DBP 80-89 mmHg) and HTN stage 2 (SBP ≥ 140 or DBP ≥ 90 mmHg) (12). This was suggested following a number of meta-analyses which demonstrated that those with elevated BP or HTN stage 1 had an increased risk of future cardiovascular disease (CVD) (13). With CVD being a leading cause of death in women, and HTN a known risk factor, HTN is of importance to overall lifetime health in females (6, 14).

In 2017, Dunietz et al. investigated BP below the diagnostic criteria of HDP and future HTN risk (15). It concluded that, those with moderately elevated BP in pregnancy had increased odds of HTN at the 7-15 year follow-up, odds ratio (OR)=2.6 (95% CI:1.2-5.5). Although these findings do suggest increased risk of HTN following moderately elevated BP, more research is needed to confirm these findings.

The ROLO study (Randomised cOntrol trial of LOw glycaemic index diet for the prevention of recurrence of macrosomia) presents a well-characterised, healthy pregnant cohort, with longitudinal follow-up (16). Using the ROLO data we aimed to investigate the association between maternal BP below the diagnostic criteria of HDP and maternal BP at the 5 year follow-up, investigate if other maternal characteristics, in pregnancy and at the 5 year follow-up, were associated with BP at the 5 year follow-up and investigate differences in mean SBP,

DBP and mean arterial pressure (MAP) for the control and intervention group of the ROLO study in pregnancy, 1-day post-partum and at the 5 year follow-up.

Methods

Study design

This is a prospective, observational study of 329 women from the ROLO study. The ROLO study was conducted in the National Maternity Hospital (NMH), Dublin, Ireland (2007-2011) (16). Ethical approval was obtained from the NMH ethics committee. This randomised control trial randomised 800 secundigravid females who had previously delivered an infant that was macrosomic ($>4000\text{g}$ birth weight). Participants were excluded if they had a history of gestational diabetes, conditions requiring medication or were pregnant with twins/triplets. The intervention arm attended a low glycaemic index (GI) diet education session. A low GI diet was further reinforced at 28 and 34 weeks gestation. The control group received standard antenatal care with no dietary intervention. The primary and secondary outcomes were birthweight and gestational weight gain (GWG), respectively. The dietary intervention did not reduce the rate of macrosomia, however, it did have positive effects on GWG and glucose intolerance (16).

Longitudinal data was collected at multiple timepoints (3-months, 6-months, 2-years and 5 years after the birth of their second child). The 5 year follow-up (ROLO Kids) is the focus of this present research and was carried out at Our Ladies Children's Hospital, Crumlin, Dublin, Ireland and NMH, Dublin, Ireland. Ethical approval for this was obtained from Our Ladies Children's Hospital Crumlin, Dublin, Ireland ethics committee.

403 of the 759 mother-child dyads from the ROLO study participated in the ROLO Kids follow-up. Of this, 329 mothers with BP measurements at the 5 year follow-up and at least 1 BP measurement in pregnancy, were included in this present analysis (Figure 1).

A wall-mounted stadiometer was used to measure height, without shoes and to the nearest 0.1cm. Weight was measured in light clothing using an electronic Seca weighing scales (Seca GmbH and Co. KG, Germany) to the nearest 0.1kg. BMI (kg/m^2) was calculated and participants were classified as underweight, normal weight, overweight or obese using WHO BMI categories (17). The above was carried out in early pregnancy and 5 years post-partum. Weight was measured throughout pregnancy and total GWG calculated. GWG was categorised as inadequate, adequate or excessive according to Institute of Medicine 2009 criteria (18).

Auscultatory BP was measured by a blinded clinician at 13, 28 and 34 weeks gestation and 1-day post-partum. This was done using a calibrated mobile Trimline aneroid sphygmomanometer (Trimline Medical Products Corp, USA), recommended for use in pregnancy (19). Participants were seated at a 45 degree angle with their arm relaxed and supported at heart level. An appropriately sized cuff was used (19). BP in pregnancy was a clinical measurement carried out by a Doctor at 13, 28 and 34 weeks gestation and 1-day post-partum. If this measurement was deemed raised it was repeated three times and an average of these readings taken. This is standard antenatal practice at NMH.

At the 5 year follow-up, BP was measured using an automatic BP device. This was measured by a trained researcher with the participant seated quietly, their feet on the floor and arm supported at heart level (11). For the first half of the 5 year follow-up (2011-2013), BP was not measured in participants with a mid-upper arm circumference (MUAC) $>33\text{cm}$, as an appropriate size cuff was not available. The device used was the Omron Automatic Blood Pressure Monitor Model M6 HEM 7211 (Omron Healthcare, Lake Forest, IL, USA), validated for use in non-pregnant populations (20). BP was measured once at the 5 year follow-up, unless deemed hypertensive ($\text{SBP} \geq 140 \text{ mmHg}$ and/or $\text{DBP} \geq 90 \text{ mmHg}$) in which case the participants were informed and the second BP measurement was taken later during the appointment and an average of both readings noted. MAP was estimated at each timepoint (21). MAP was estimated at each timepoint using the formula $\text{DBP} + (1/3 \times (\text{SBP} - \text{DBP}))$.

As this was a clinically orientated pragmatic study, it was deemed appropriate to use different BP measurement devices in pregnancy and at the 5 year follow-up. Higher sensitivity and

specificity of aneroid measurements has been suggested (22) and therefore were used by trained clinicians at each timepoint in pregnancy. BP was measured at the 5 year follow-up by researchers, not trained clinicians, and so an electronic device was deemed most appropriate.

BP was categorised at 13, 28, and 34 weeks gestation, 1-day post-partum and at the 5 year follow-up as normal BP (SBP <120 and DBP <80 mmHg), elevated BP (SBP 120-129 and DBP <80 mmHg), HTN stage 1 (SBP 130-139 or DBP 80-89 mmHg) and HTN stage 2 (SBP $\geq$ 140 or DBP $\geq$ 90 mmHg). (12) Participants were also identified as having HTN stage 2 at the 5 year follow-up if they self-reported via questionnaire, being on HTN medication or diagnosis of HTN.

Statistical analysis

Variables were assessed for normality using the Kolmogorov-Smirnov test and visual inspection of the histograms. Maternal characteristics were assessed using descriptive statistics. Independent-samples t-tests were carried out to identify differences in mean BP between the control and intervention group at each timepoint. Pearson's and Spearman's Rank correlation coefficients were used to investigate bivariate associations between continuous variables and BP at the 5 year follow-up. A one-way ANOVA was performed to investigate associations between maternal characteristics and BP category at the 5 year follow-up. Chi-square tests were used to investigate relationships between BP category at the 5 year follow-up and other categorical variables.

For chi-square and regression analysis participants with HTN stage 1 and 2 in pregnancy were combined due to insufficient numbers in each category. All variables with p -values <0.1 were entered into multinomial logistic regression. Unadjusted multinomial logistic regression was carried out, followed by adjustment for age at the 5 year follow-up (years), BMI at early pregnancy (kg/m^2) and grouping (control vs intervention). All confounders selected were based on *a priori* approach. Statistical significance was inferred when p -values <0.05. Data analysis was conducted using IBM SPSS Statistics 24.0 statistical software for Mac (IBM, Armonk, NY).

Results

The maternal characteristics of this sample were analysed (Table 1). This showed that the sample was highly educated, with 62.6% having a third level education. They were mainly Caucasian (99.1%) with low smoking rates (14%) (Table 1). The mean SBP, DBP, and MAP at each timepoint during pregnancy did not vary greatly, however, standard deviation (SD) demonstrated variance around the mean. Interestingly, SBP, DBP, and MAP differed significantly from each timepoint in pregnancy to the 5 year follow-up (Table S1.1). For example, the mean difference in MAP from the booking visit, 28 weeks' gestation, 34 weeks' gestation and day-1 post-partum to the 5 year follow-up was 4.39, 4.63, 3.77 and 3.63, respectively. No significant differences were seen between mean SBP, DBP, and MAP between the control and intervention group (Table S1.2). At the 5 year follow-up percentage frequencies of those with normal BP, elevated BP, HTN stage 1, and HTN stage 2 were 58.7%, 14.6%, 18.2% and 8.5% respectively.

Significant positive associations were seen between SBP, DBP, and MAP in pregnancy and SBP, DBP, and MAP at the 5 year follow-up (Table S 2). No significant associations were seen for parity and SBP, DBP or MAP BP measurements (Table S 2). Significant differences were seen between those with normal BP and HTN stage 2 at the 5 year follow-up depending on SBP and MAP at 34 weeks gestation (Table S 3) and (Figure 2). Chi-square analysis on BP category at 13, 28, and 34 weeks gestation was significantly associated with BP category at the 5 year follow-up (Table S 4)

On multinomial logistic regression, in the adjusted model, compared to those with normal BP at booking, those with elevated BP had 3.0 fold increased odds of HTN stage 2 at follow-up (95% CI: 1.05-8.52), $P=0.04$. Furthermore, at 28 and 34 weeks gestation, elevated BP led to 2.68 and 2.45-fold increased odds of HTN stage 1 at the 5 year follow-up (95% CI:1.36-5.27), $P=0.004$ and (95% CI: 1.22-4.95), $P=0.012$, respectively. Each 1 mmHg increase in SBP and DBP at 34 weeks' gestation lead to 1.04 and 1.05 increased odds of HTN stage 1 and 2 respectively, 5 years later. Similarly, each mmHg increase in MAP at 34 weeks gestation lead to a 1.05 and 1.08 increased odds of HTN stage 1 and 2 respectively, at the 5 year follow-up (Table 2).

Significant differences were observed for weight and BMI, in early pregnancy and 5 years post-partum, between those with normal BP and HTN stage 2 at the 5 year follow-up (Table S 3). On carrying out adjusted multinomial logistic regression (Table 2), it was observed that,

at the 5 year follow-up, each 1 kg increase in maternal weight was significantly associated with a 1.05 increased odds of HTN stage 1 at the 5 year follow-up. Also, each 1 kg/m² increase in BMI in early pregnancy conferred a 1.16 increased odds of HTN stage 2 at the 5 year follow-up. Similarly, each 1 mmol/L increase in fasting blood glucose in early pregnancy conferred a 3.95-fold increased odds of HTN stage 2 at the 5 year follow-up, (95% CI: 1.07-14.59), $P=0.039$.

Discussion

Main Findings:

The primary finding from this study were that at 28 and 34 weeks gestation, elevated BP was associated with a 2.68 and 2.45-fold increased odds of HTN stage 1 at 5 years later, respectively. At 34 weeks gestation each 1 mmHg increase in SBP, DBP and MAP led to small but significantly increased odds of HTN stage 1 and 2 5 years later. Each 1 kg increase in maternal weight led to a 1.05-fold increased odds of HTN stage 1 at the 5 year follow-up. Also each 1 kg/m² increase in BMI and each 1 mmol/L increase in fasting blood glucose in early pregnancy conferred a 1.16 and 3.95-fold increased odds of HTN stage 2, respectively, 5 years later.

Findings suggest that 28 and 34 weeks' gestation act as key timepoints to assess BP, with the view of evaluating future HTN risk. This concurs with evidence from Dunietz et al. (15). Findings from our study demonstrated that elevated BP at 28 and 34 weeks' gestation also increases one's odds of HTN stage 1 5 years later. This suggests that pregnancy is unmasking a subclinical condition which may arise in later life. Associations between BP at booking visit (13 weeks gestation) and day-1 post-partum (when metabolic profile is expected to return to pre-pregnancy values) with 5 year follow-up BP may indicate that those with elevated BP, HTN stage 1 or 2 at these timepoints have a degree of metabolic dysregulation prior to pregnancy.

Strengths and Limitations:

Studies of this nature come with limitations, interobserver variability and rounding of terminal digits in BP measurement may have been present in this study. Participants self-reported their diagnosis of HTN and medications, which may have led to misreporting. At the 5 year follow-up 57 participants with a mid-upper arm circumference > 33cm were not

included, potentially skewing the results towards those with a healthy BMI. Although a different BP measurement device was used during pregnancy and at the 5 year follow-up, all BP measurements were carried out using the same device at each respective timepoint. Therefore, the trends and results observed are unlikely to be altered by the differences in the devices used. Despite these limitations, it is believed that the findings from this research significantly add to the paucity of research in this area. Since all women measured on same device at respective timepoints, the trends observed are unlikely to be altered by device differences.

Interpretation:

The identification of non-pregnant BP thresholds that increase the risk of HTN post-partum when applied to pregnant populations may be used to revise clinical guidelines for BP in pregnancy, as no guidance outside HDP exists. The finding that elevated BP in pregnancy confers future HTN risk contradicts evidence in non-pregnant populations, which suggests that SBP 130-139 mmHg or DBP 80-89 mmHg confers an increased risk of impaired future cardiovascular health compared to lower thresholds. (13) However, it is conceivable that as BP generally drops in pregnancy, (23) these slight elevations in BP (namely, SBP 120-129 mmHg) may confer increased risk. These small increases may appear insignificant in current antenatal practice, however it is clear from the evidence presented that these indicate increased risk of HTN post-partum.

It is surprising to note, that those with HTN stage 1 or HTN stage 2 at 28 and 34 weeks gestation had increased odds of HTN stage 1 and 2 at follow-up, yet these were not statistically significant. This non-significant finding could be explained by these women already being identified as high risk for future HTN and thus managed with pharmacological treatment. Also, this present analysis may have been underpowered to detect this association.

Increases in SBP, DBP and MAP at 34 weeks gestation increased the risk of HTN stage 1 and 2 5 years later. Although SBP and DBP are routinely measured in pregnancy, MAP is rarely calculated in clinical practice. (24) MAP is suggested as an indicator of future cardiovascular disease risk in non-pregnant populations. (25) Thus, MAP may act as a useful assessment tool in pregnancy to identify future HTN risk. Given the newly introduced electronic records into many Maternity Hospitals, calculation of MAP may be an easy and practical addition to patient records.

No significant differences were observed between the control and intervention group for SBP, DBP, or MAP. Similar findings were described for other maternal characteristics within the ROLO cohort, investigated elsewhere.(4) This finding also suggests that although the ROLO study had positive effects of GWG this did not have a lasting impact on BP, as suggested in previous research. (26)

BMI at early pregnancy and weight at the 5 year follow-up were associated with HTN stage 1 at the 5 year follow-up. This concurs with evidence which suggests pre-pregnancy BMI influences HTN risk post-partum. (10) Increases in fasting blood glucose at 13 weeks gestation increased the risk of HTN stage 2 at follow-up. This may be explained by increases in fasting blood glucose early in pregnancy indicating a degree of metabolic syndrome prior to pregnancy or arising *de Novo* in pregnancy. Thus, fasting blood glucose early in pregnancy may identify those at risk of HTN and metabolic syndrome post-partum. Although in current clinical practice oral glucose tolerance tests are used for women with gestational diabetes mellitus to assess future diabetes mellitus risk, the findings suggest this may also be useful to assess future HTN risk post-partum.

This research suggests the application of BP thresholds used in non-pregnant populations, (12) to pregnant populations to identify those at risk of future HTN. Annual BP checks within primary care, following elevated BP at 28 and 34 weeks gestation, may help manage such risk. The evidence presented also suggests that MAP should routinely be used to evaluate BP in pregnancy. As a clinically orientated, pragmatic study, there are numerous strengths such as the direct application of findings to clinical practice. Other strengths include, that this is the first analysis of BP below HDP in a healthy, pregnancy cohort. It is also, to the best of our knowledge, the first study of its kind to assess MAP in pregnancy and the risk of future HTN.

Conclusion

In conclusion, this study has identified key timepoints, measurements and thresholds at which women face increased risks of HTN post-partum. These novel findings suggest that raised BP below the diagnostic criteria of HDP should be flagged for follow-up post-partum. This may

lead to more timely non-pharmacological interventions thus having an economic benefit but more importantly benefitting overall lifetime health in females.

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Tables

Table 1. Maternal Characteristics

Demographics	N
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Gestation at booking visit ^a	328	12.7	2.25
Age at delivery ^a	329	33.2	3.98
Age at 5 year follow up ^a	329	38.4	3.99
Parity at 5 year follow-up ^a	329	2.5	0.63
Ethnicity, Caucasian ^b	329	326	99.1
Education, completed 3 rd level education ^b	286	179	62.6
Grouping, intervention ^b	329	166	50.5
Smoking			
Yes, at booking ^b	329	9	2.7
Ever, at 5 year follow-up ^b	329	46	14
Yes, at 5 year follow-up ^b	291	26	8.9
Anthropometry			
Height (cm) early pregnancy ^a	327	165.9	6.4
Weight (kg)			
Early pregnancy ^a	327	70.4	11.27
5 year follow-up ^a	327	70.0	11.44
BMI (kg/m ²)			
At booking visit ^a	327	25.6	3.96
5 year follow up ^a	325	25.5	3.94
Booking- underweight ^b	327	2	0.6
Booking- normal weight ^b	327	155	47.4
Booking- overweight ^b	327	130	39.8
Booking- obese ^b	327	40	12.2
5 year follow up- underweight ^b	325	2	0.6
5 year follow up- normal weight ^b	325	138	42.5
5 year follow up – overweight ^b	325	141	42.9
5 year follow up- obese ^b	325	44	13.5
Blood pressure			
Systolic blood pressure (mm Hg)			
at booking visit ^a	301	112.4	11.81
at 28 weeks gestation ^a	319	112.2	11.1
at 34 weeks gestation ^a	320	112.4	9.87
at day 1 post-partum ^a	307	112.9	10.28

at 5 year follow-up ^a	329	117.3	12.4
Diastolic blood pressure (mm Hg)			
at booking visit ^a	301	67.1	7.03
at 28 weeks gestation ^a	319	66.7	7.18
at 34 weeks gestation ^a	320	68.1	7.64
at day 1 post-partum ^a	307	68.0	7.76
at 5 year follow-up ^a	329	71.3	9.32
Mean Arterial Pressure (mm Hg)			
at baseline visit ^a	301	82.5	7.5
at 28 weeks gestation ^a	319	81.8	7.56
at 34 weeks gestation ^a	320	82.9	7.16
at day 1 post-partum ^a	307	83.0	7.61
at 5 year follow-up ^a	329	86.6	9.5
Gestational weight gain			
Total (kg) ^a	271	13	4.15
Inadequate, IOM guideline ^b	271	51	18.8
Adequate, IOM guideline ^b	271	98	36.2
Excessive, IOM guideline ^b	271	122	45
Blood glucose measures			
Fasting glucose early pregnancy (mmol/L) ^a	316	4.5	0.35
Fasting glucose 28 weeks gestation (mmol/L) ^a	308	4.5	0.46
Glucose intolerance in pregnancy , yes ^b	325	77	23.7
5 year HbA1c mmol/mol ^a	141	31.4	2.73

a, mean (standard deviation); b, n (%); c, median (interquartile range); mmHg, millimeters of mercury; HbA1c, glycated hemoglobin; mmol/mol, millimole per mole; m, meter; cm, centimeter; kcal, kilocalorie; kg, kilogram, mg, milligrams; ml, milliliter; METs, metabolic equivalent tasks; MAP, mean arterial pressure; BP, blood pressure; HTN, hypertension; SBP, systolic BP; DBP, diastolic BP; Normal BP, SBP <120 mmHg and DBP < 80 mmHg; Elevated BP, SBP 120-129 mmHg and DBP <80 mmHg; HTN stage 1, SBP 130-139 mmHg or DBP 80-89 mmHg; HTN stage 2, SBP ≥140 mmHg or DBP ≥ 90 mmHg. Those at 5 year follow-up are identified as HTN stage 2 if they have diagnosis of HTN, on medications for HTN or SBP ≥140 mmHg or DBP ≥ 90 mmHg. Institute of Medicine (IOM) total gestational weight gain (GWG) guidelines: underweight, 12-18kg; normal weight, 11.5-16kg;

overweight, 7-11.5kg; obese (all cases), 5-9kg; BMI, body mass index; BMI WHO categories: underweight <18.5kg/m²; normal weight, 18.5-24.9 kg/m²; overweight, 25.0-29.9 kg/m²; obese all classes $\geq$ 30kg/m².

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Table 2. Multinomial Logistic Regression between Maternal Characteristics and Blood Pressure Category at the 5 Year Follow-Up

	Elevated BP		HTN stage 1		HTN stage 2		
	Model 1 OR (95% CI)	P	Model 1 OR (95% CI)	P	Model 1 OR (95% CI)	P	Model P
Anthropometry							
Weight, early pregnancy (kg)	1.01(0.95-1.07)	0.821	1.05(0.99-1.11)	0.091	1.01(0.94-1.08)	0.844	0.045
Weight, at 5 year follow-up (kg)	1.03(0.99-1.07)	0.200	1.05(1.01-1.09)	0.008*	1.02(0.97-1.07)	0.565	0.012
BMI, early pregnancy (kg/m ²)	1.08(0.99-1.17)	0.072	1.05(0.97-1.13)	0.224	1.16(1.06-1.27)	0.001*	0.030
BMI category early pregnancy							0.167
Overweight	1.47(0.52-4.13)	0.467	1.24(0.49-3.17)	0.655	1.65(0.48-5.70)	0.425	
Obese	3.82(0.45-32.32)	0.218	1.37(0.17-11.05)	0.769	3.66(0.32-41.84)	0.300	
BMI, at 5 year follow-up	0.88(0.31-2.51)	0.808	1.44(0.57-3.60)	0.441	0.88(0.22-3.47)	0.856	0.086
Fasting blood glucose measures (mmol/L)							
Fasting glucose early pregnancy	0.66(0.25-1.79)	0.415	1.18(0.48-2.94)	0.720	3.95(1.07-14.59)	0.039	0.040
Fasting glucose 28 weeks gestation	0.85(0.38-1.89)	0.693	1.12(0.55-2.29)	0.753	2.04(0.83-5.02)	0.119	0.070
Continuous BP (mmHg)							

SBP at booking	0.99(0.97-1.03)	0.861	1.01(0.98-1.03)	0.636	1.03(0.99-1.07)	0.106	0.019
SBP at 28 weeks gestation	1.01(0.98-1.04)	0.756	1.02(0.99-1.04)	0.290	1.03(0.99-1.07)	0.137	0.020
SBP at 34 weeks gestation	1.03(0.99-1.07)	0.067	1.04(1.01-1.07)	0.015*	1.05(1.01-1.07)	0.015*	0.009
SBP at 1 day post-partum	1.01(0.98-1.05)	0.548	1.04(1.00-1.07)	0.034*	1.04(0.99-1.08)	0.087	0.017
DBP at 28 weeks gestation	1.02(0.98-1.07)	0.350	1.02(0.98-1.06)	0.431	1.06(0.99-1.12)	0.078	0.016
DBP at 34 weeks gestation	1.03(0.99-1.06)	0.067	1.04(1.01-1.07)	0.015*	1.05(1.01-1.10)	0.018*	0.009
DBP day-1 post-partum	1.01(0.96-1.05)	0.827	1.03(0.99-1.07)	0.112	1.04(0.98-1.10)	0.185	0.039
MAP at booking	0.99(0.94-1.03)	0.569	1.10(0.97-1.05)	0.666	1.06(1.00-1.13)	0.052	0.011
MAP at 28 weeks gestation	1.02(0.97-1.06)	0.466	1.02(0.98-1.06)	0.307	1.06(0.99-1.12)	0.063	0.014
MAP 34 weeks gestation	1.03(0.99-1.08)	0.175	1.05(1.00-1.09)	0.042*	1.08(1.01-1.14)	0.019*	0.017
Map day-1 post-partum	1.01(0.97-1.06)	0.675	1.04(1.00-1.09)	0.042*	1.05(0.99-1.11)	0.093	0.019
Categories of BP							
Booking category							
Normal BP	Referent		Referent		Referent		0.002
Elevated BP	0.56(0.18-1.75)	0.317	2.02(0.98-4.17)	0.058	3.00(1.07-8.54)	0.036*	
HTN stage 1/stage 2 combined	1.40(0.64-3.10)	0.404	0.76(0.32-1.82)	0.532	2.69(0.95-7.63)	0.087	
28 weeks gestation							
Normal BP	Referent		Referent		Referent		0.000
Elevated BP	1.19(0.50-2.83)	0.690	2.68(1.36-5.26)	0.004*	2.05(0.66-6.32)	0.214	
HTN stage 1/ stage 2 combined	1.43(0.64-3.18)	0.386	0.42(0.14-1.28)	0.127	2.33(0.84-6.46)	0.104	
34 weeks gestation category							

Normal BP	Referent		Referent		Referent		0.017
Elevated BP	0.68(0.22-1.76)	0.376	2.45(1.22-4.95)	0.012*	2.51(0.90-7.03)	0.079	
HTN stage 1/ stage 2 combined	1.63(0.74-3.59)	0.224	1.42(0.63-3.21)	0.394	1.67(0.54-5.20)	0.374	
Day-1 post-partum category							
Normal BP	Referent		Referent		Referent		0.050
Elevated BP	0.63(0.22-1.75)	0.372	2.45(0.96-4.33)	0.012*	2.54(0.91-7.12)	0.074	
HTN stage 1/ stage 2 combined	1.58(0.72-3.46)	0.251	1.38(0.62-3.09)	0.435	2.22(0.78-6.30)	0.134	

Table 2 Model 1: adjusted for age at 5 year follow-up, BMI at early pregnancy and grouping (control vs. intervention). Normal BP is referent value. ROLO study (n=759), Randomised cOntrol trial of Low glycaemic index diet to prevent recurrence of fetal macrosomia; ROLO Kids (n=403), 5 year follow-up of the ROLO study CI, confidence interval; BP, blood pressure; BMI, body mass index; HTN, hypertension; SBP, systolic BP; DBP, diastolic BP; Normal BP, SBP <120 mmHg and DBP < 80 mmHg; Elevated BP, SBP 120-129 mmHg and DBP <80 mmHg; HTN stage 1, SBP 130-139 mmHg or DBP 80-89 mmHg; HTN stage 2, SBP ≥140 mmHg or DBP ≥ 90 mmHg. Those at year-5 follow-up are identified as HTN stage 2 if they have diagnosis of HTN, on medications for HTN or SBP ≥140 mmHg or DBP ≥ 90 mmHg

Figures

Figure 1. Flow Chart of Participants from the ROLO Kids Study included in this Analysis

ROLO study, Randomised cOntrol trial of Low glycaemic index diet to prevent recurrence of fetal macrosomia; ROLO Kids, 5 year follow-up of the ROLO study; MUAC, mid-upper arm circumference; BP, blood pressure.

Figure 2. Boxplot of SBP and MAP at 34 weeks' gestation and 5 year follow-up blood pressure category generated by SPSS one-way ANOVA analysis. Significant differences were seen between those with normal BP and those with HTN stage 2 at the 5 year follow-up according to SBP and MAP at 34 weeks' gestation.

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