MOLECULAR AND EXPERIMENTAL BIOLOGY IN MEDICINE

ORIGINAL ARTICLE

THE ASSOCIATION BETWEEN MATERNAL ANTHROPOMETRY AND BLOOD PRESSURE IN PREGNANCY – RESULTS FROM THE CROATIAN ISLANDS' BIRTH COHORT STUDY (CRIBS)

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Abstract: Elevated blood pressure (BP) in pregnancy, especially gestational hypertension and preeclampsia, can lead to serious pregnancy complications and adverse birth outcomes. A large body of literature already reported the effect of baseline body mass index (BMI) on changes in blood pressure during pregnancy. The aim of this study was therefore to define trajectory of systolic (SBP) and diastolic (DBP) blood pressure in 308 pregnant participants from the CRIBS study (146 from the mainland and 162 from the islands of Brač and Hvar) and to analyze the association of blood pressure with maternal BMI prior to pregnancy and maternal anthropometry during pregnancy. Pregnant women included in the CRIBS study had no history of chronic diseases. The BP of CRIBS participants was measured at least once in each trimester, and maternal pre-pregnancy weight was self-reported. All analyses were performed using SPSS 10.0. Results showed that pre-pregnancy BMI was the strongest predictor of pregnancy blood pressure. This association was evident for pre-pregnancy BMI independently ($p<0.001$), and it also persisted after adjusting for maternal age, education, income, parity, smoking and physical activity ($p<0.05$). The association between maternal anthropometry during pregnancy and blood pressure was not as strong and was therefore less informative. The study reinforces the role of BMI on SBP and DBP and highlights its importance during prenatal care monitoring. Significant association also emerged between blood pressure in pregnancy and place of residence (mainland vs. island). Women on Dalmatian islands have lower educational level, higher pre-pregnancy BMI and different levels of blood pressure than women from the mainland (namely, higher SBP and lower DBP). Such comparisons between mainland and island populations are valuable, because they can, in the long term, lead to better maternal health care on the islands.

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INTRODUCTION

According to the World Health Organization, both pregnancy and childbirth have become much safer in the developed world, with maternal mortality being 10 per 100,000 live births in comparison with 900 per 100,000 in Sub-Saharan Africa.[1] However, there are still many risk factors for maternal and child health, one of which is maternal obesity, which increased in prevalence by 20% in recent years.[2, 3] Besides high pre-pregnancy BMI and obesity, gestational diabetes and malnutrition during pregnancy are also among significant risk factors for both the mother's health during pregnancy, and for adverse birth outcomes.[4-6] They can also influence fetal programming and can have a long-term adverse effect on the child's health later in life.[7]

Furthermore, it has been suggested that obesity is a risk factor for elevated blood pressure, preeclampsia and gestational hypertension.[8] Elevated blood pressure in pregnancy, especially gestational hypertension and preeclampsia, can lead to serious pregnancy complications and adverse birth outcomes, such as decreased blood flow to the placenta, placental abruption, intrauterine growth restriction, premature delivery, future cardiovascular disease and organ damage.[9, 10] Therefore, it is important to gain detailed insight into the associations of pre-pregnancy BMI and maternal anthropometry with blood pressure during pregnancy in order to be able to facilitate interventional and educational strategies to minimize maternal and child health risks.

Birth cohort studies, together with long-term follow-up studies, provide a unique opportunity to monitor early-life factors associated with maternal and child health. The Croatian Islands Birth Cohort Study (CRIBS) is the first prospective birth cohort study to be conducted in South-eastern Europe. It was designed to follow a sample of 500 pregnant women and their children from birth to two years of age in the populations from the Croatian Dalmatian islands of Hvar and Brač, and the mainland population in and around the city of Split. Preliminary results from the CRIBS already reported on the association of pre-pregnancy BMI with higher blood glucose levels and increased birth weight, birth length and head circumference of newborns,[11] on the adherence of participants to the Mediterranean diet[12] and on the positive association between light occupational activity of the mother and fetal growth rate in normal pregnancies.[13] The most recent study published by Perinić Lewis and collaborators (2019) presented the sociodemographic profile of the participants in the CRIBS study.[14] They state that in comparison with women from the mainland, islander women more often gave birth to more than one child, finished only secondary school, more often lived in extended families and had a lower average household income.

The aim of this study was to define the trajectory of systolic (SBP) and diastolic (DBP) blood pressure during pregnancy in 308 participants from the CRIBS study, to analyze the association of blood pressure in pregnancy with maternal BMI prior to pregnancy and maternal anthropometry during pregnancy, as well as to test possible differences between island and mainland subpopulations. Such studies that report the effect of anthropometry and baseline BMI on the change in blood pressure during pregnancy are still lacking in Croatia and we therefore see this study as a valuable contribution.

MATERIAL AND METHODS

All CRIBS participants signed an informed consent prior to their inclusion in the study, and they all gave birth at the University Hospital Centre Split. The study protocol was approved by the Ethics Committee of the Institute for Anthropological Research in Zagreb. Criteria for the inclusion in the study were: no history of chronic diseases, natural conception and singleton pregnancies (Figure 1). The present study was conducted on 308 CRIBS participants – 146 from the Split area and 162 from the Dalmatian islands of Brač (n=120) and Hvar (n=42). The SBP and DBP measurements were performed during each antenatal visit to the gynecology practices, in a seated position using a mercury sphygmomanometer. Elevated blood pressure in pregnancy was defined when systolic pressure was ≥120 mmHg and diastolic <80 mmHg.[15, 16] The measurements ranged from one to seven per

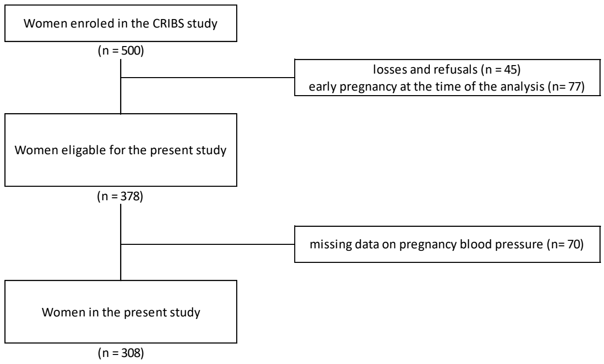


Figure 1. The study flow chart

trimester and, for the purpose of this study, average systolic and diastolic blood pressure in each trimester were calculated for each participant. Pre-pregnancy BMI was calculated from pregnant women's self-reported height and weight. The classification of the pre-pregnancy BMI of CRIBS participants according to WHO was as follows: underweight (BMI <18.5 kg/m2); normal weight (BMI 18.5-24.9 kg/m2); overweight (BMI 25-29.9 kg/m2); and obese (BMI ≥30 kg/m2). Other maternal anthropometric measurements were taken once in each trimester, during three visits to the gynecology practices (between the 12th and 14th week of gestation, between the 18th and 28th week of gestation and between the 30th and 32nd week of gestation), and they included measurements of middle upper arm and abdomen circumference, and skinfold thicknesses of upper-arm triceps and biceps. All measurements were performed by the nurses, trained by project associates to take research-standard measures in anthropometry. They were carried out following the standard International Biological Program protocol (1981). Longitudinal measures and circumferences were recorded to the nearest 0.1 centimeter (cm), skinfolds to the nearest 0.1 millimeter (mm), and weight to the nearest 0.1 kilogram (kg) with instruments used routinely in clinical practice by the midwives and medical doctors.

Questionnaire data used in the present study included sociodemographic and socioeconomic characteristics (age, place of residence, education, average household income per month), parity (primipara, multipara), information on smoking and physical activity during pregnancy. Categories of educational level of the CRIBS mothers were as follows: lower or middle level of education (elementary school, vocational school, secondary schools) and higher education (university degree - BSc/BA, MSc/MA and PhD levels). Participants were asked to report their monthly household income and we pooled their answers into two categories: <1 000 EUR per month and >1 000 EUR per month. Lifestyle habits were assessed through smoking and activity patterns. Participants were asked whether they smoked in pregnancy and if not, if they have stopped smoking because of the pregnancy.

The differences between different groups were tested using the Chi-square test, Student`s t-test and One-way ANOVA. Multivariable logistic regression analysis was used to assess how predictor (explanatory) variables (pre-pregnancy BMI, maternal age, parity, education, monthly income, smoking, physical activity) relate to blood pressure in pregnancy. All the analyses were performed using the SPSS Statistics 11.0 statistical package for Windows (SPSS Inc., Chicago, IL, USA), with statistical significance set at $p<0.05$.

RESULTS

Baseline characteristics of CRIBS participants with regards to their location (mainland; city of Split vs. islands of Brač and Hvar) are presented in Table 1. The participants were evenly distributed between the two location categories (47.5% from the mainland and 52.5% from the islands). The mean age of participants was 30.33 ± 4.46 years, ranging between 19 and 45 years of age. More than half of the participants (55%) were >30 years old, which suggests that Dalmatian women follow the global trend of later childbearing.[14] There was statistically significant difference ($p<0.05$) between women from the mainland and from the islands in parity (43.9% of primipara on mainland vs. 30.8% on the islands), educational level (34.6% of women with lower education on the mainland vs. 64.5% on the islands) and average monthly household income (30.6% with a low household income on the mainland vs. 48.1% on the islands). Our findings that more women were primiparous, attained higher education and had a higher income on the mainland compared to the islands are in line with a previous study published on a similar CRIBS sample.[14] There was no significant difference in smoking and activity status between the two locations. The majority of participants had pre-pregnancy BMI values within the normal range; however, there were significantly ($p<0.05$) more underweight women on the islands than on the mainland. Significantly more ($p<0.05$) overweight and obese women were found on the islands as well. Significant differences between participants from the mainland and from the islands were also evident for blood pressure, especially SBP ($p\leq0.001$) - women from the islands had higher mean values and a steeper increase over the course of pregnancy (Table 2). Differences between the two island subsamples (island of Brač vs. island of Hvar) were not tested because of unequal sample sizes (120 participants from Brač and 42 from Hvar).

Table 1. Baseline characteristics of cribs women by place of residence*

CHARACTERISTICS	LOCATION, N (%)		p-value
	mainland	island	
maternal age			
18 - 25 years	15 (11.8)	13 (11.4)	0.129
25 - 30 years	35 (27.6)	45 (39.5)	
30 - 35 years	60 (47.2)	38 (33.3)	
> 35 years	17 (13.4)	18 (15.8)	
total	127 (100)	114 (100)	
education			
lower	44 (34.6)	71 (64.5)	**0.000**
university	83 (65.4)	39 (35.5)	
total	127 (100)	110 (100)	
income			
<1000€	38 (30.6)	51 (48.1)	**0.007**
>1000€	86 (69.4)	55 (51.9)	
total	124 (100)	106 (100)	
parity			
primipara	50 (43.9)	32 (30.8)	**0.046**
multipara	64 (56.1)	72 (69.2)	
total	114 (100)	104 (100)	
smoking			
smoking in pregnancy	19 (17.1)	23 (25.0)	0.460
stopped smoking	42 (37.8)	31 (33.7)	
never smoked	50 (45.1)	38 (41.3)	
total	111 (100)	92 (100)	
activity			
low	16 (15.0)	8 (9.1)	0.353
moderate	74 (69.2)	60 (68.2)	
high	17 (15.8)	20 (22.7)	
total	107 (100)	88 (100)	
pre-pregnancy BMI			
underweight	3 (2.4)	11 (9.7)	**0.021**
normal weight	99 (80.5)	76 (67.3)	
overweight and obese	21 (17.1)	26 (23.0)	
total	123 (100)	113 (100)	

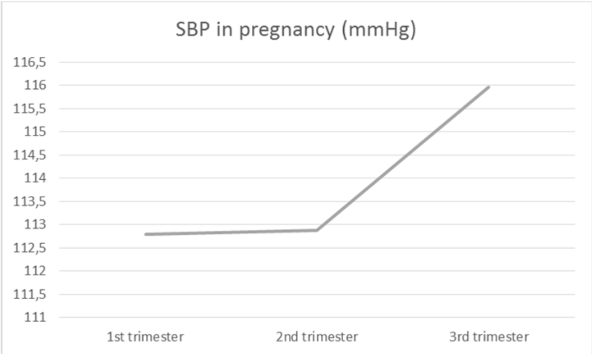
Legend: * Chi-square test; significant values ($p<0.05$) are bolded; BMI – body mass index

Table 2. Systolic (SBP) and diastolic (DBP) blood pressure values by place of residence of the CRIBS mothers*

		mainland	island	p-value
SBP	1st trimester	112.48 ± 10.4	112.38 ± 13.9	**0.001**
	2nd trimester	112.94 ± 8.3	113.99 ± 13.4	**0.000**
	3rd trimester	115.60 ± 9.4	116.78 ± 13.8	**0.000**
DBP	1st trimester	66.71 ± 7.7	65.04 ± 9.1	0.195
	2nd trimester	67.16 ± 6.5	64.93 ± 8.7	**0.005**
	3rd trimester	69.81 ± 6.9	68.02 ± 9.8	**0.015**

Legend: * Student's t-test; significant values ($p<0.05$) are bolded

With regards to blood pressure in pregnancy, less than 2% of women had pregnancy-induced hypertension (SBP >140 mmHg and/or DBP >90 mmHg). However, mean BP changed throughout pregnancy trimesters (Figure 2). Mean SBP of 112.8 mmHg in the 1^{st} and in the 2^{nd} trimester rose to almost 116 mmHg in the 3^{rd} trimester ($p<0.001$). Mean DBP in the 3rd trimester (68.7 mmHg) was also higher than in the first two trimesters (65.5 mmHg). When divided into two categories according to cut-off values for elevated blood pressure in pregnancy (≥120/<80 mmHg), there were



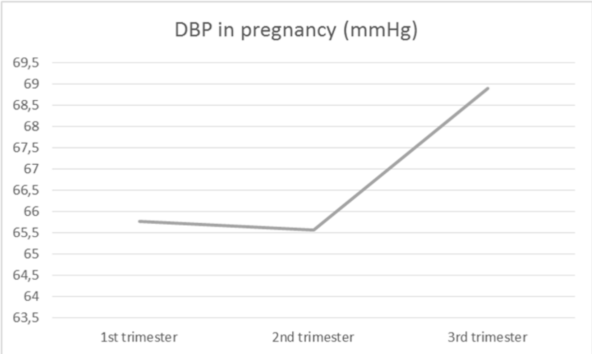


Figure 2. The change in average systolic and diastolic blood pressure throughout pregnancy, per trimester
Legend: SBP – systolic blood pressure; DBP – diastolic blood pressure

32% of women with elevated blood pressure in the first trimester, 26% in the second trimester and again 31% in the third trimester (Figure 3). Women with elevated blood pressure (≥120/<80 mmHg) also had wider ranges of all anthropometric measures (body mass, upper arm and abdominal circumference, biceps and triceps skinfolds) compared to those with normal blood pressure (Table 3). There was a significant difference in body mass between women with normal SBP and DBP

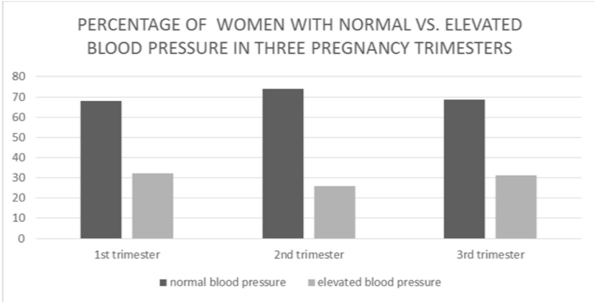


Figure 3. Number of sampled women with normal and elevated (≥120/<80 mmHg) average blood pressure per each trimester

and women with elevated SBP and DBP in the first trimester. Also, a significant difference in body mass and abdominal circumference was established between women with normal SBP and women with elevated SBP in the second trimester. A significant difference in upper arm circumference was detected between women with normal SBP and DBP and women with elevated SBP and DBP in the second trimester. In the third trimester, the only significant difference was noted in body mass and only between women with normal SBP and women with elevated SBP. There was no statistically significant difference in DBP in the third trimester.

Furthermore, there was a significant rise in average SBP and DBP per trimester against different BMI categories (Figure 4). Mean SBP and DBP of pre-pregnancy obese women (BMI>30 kg/m2) in all three trimesters were significantly higher than in pre-pregnancy underweight, normal weight or overweight women (p<0.05). Our results indicated that pre-pregnancy BMI was the strongest predictor of pregnancy blood pressure. This association was evident for pre-pregnancy BMI independently (p<0.001), and it also persisted after adjusting for maternal age, education, income, parity, smoking and physical activity in a multivariable binary logistic regression model (p<0.05) (Table 4). The

Table 3. Changes in anthropometric measures of the CRIBS mothers during pregnancy according to blood pressure*

	SBP			DBP		
	<120 mmHg range	≥120 mmHg range	p-value	<80 mmHg range	≥80 mmHg range	p-value
FIRST TRIMESTER VARIABLES						
body mass (kg)	**44-99**	**48-123**	**0.005**	**44-99**	**59-123**	**0.004**
upper arm circumference (mm)	210-395	225-400	0.266	210-395	230-400	0.088
abdominal circumference (mm)	72-121	66-131	0.069	66-121	84-131	0.234
biceps skinfold (mm)	4-40	8-43	0.970	4-43	10-34	0.458
triceps skinfold (mm)	8-45	10-44	0.759	8-45	10-38	0.335
SECOND TRIMESTER VARIABLES						
body mass (kg)	**49-93.5**	**55.5-124.5**	**0.000**	49-117	70-124.5	0.062
upper arm circumference (mm)	**210-365**	**250-410**	**0.005**	**210-400**	**265-410**	**0.011**
abdominal circumference (mm)	**69-123**	**82-134**	**0.001**	69-129	92-134	0.083
biceps skinfold (mm)	4-43	8-44	0.438	4-44	12-34	0.898
triceps skinfold (mm)	8-45	12-44	0.070	8-45	20-40	0.410
THIRD TRIMESTER VARIABLES						
body mass (kg)	**55-120**	**55-131**	**0.046**	55-123	69-131	0.202
upper arm circumference (mm)	220-380	240-410	0.099	220-400	270-410	0.228
abdominal circumference (mm)	83-140	94-140	0.388	83-140	102-140	0.195
biceps skinfold (mm)	4-42	10-43	0.057	4-43	10-34	0.170
triceps skinfold (mm)	8-45	16-46	0.626	8-46	16-40	0.388

Legend: * Student's t-test; significant values (p<0.05) are bolded; SBP – systolic blood pressure; DBP – diastolic blood pressure

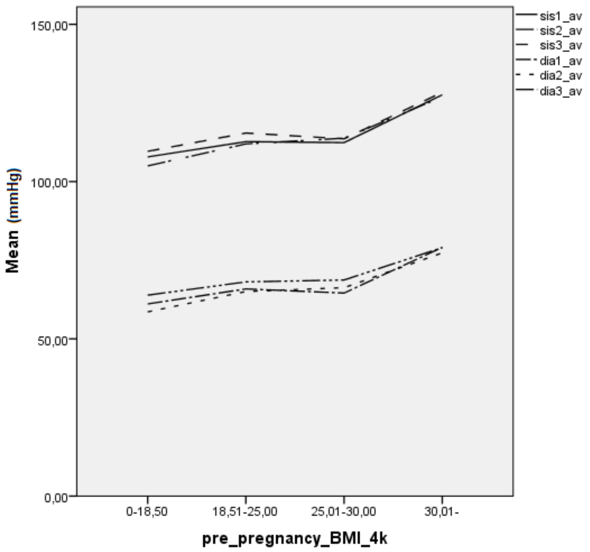


Figure 4. Average systolic and average diastolic blood pressures per trimester against four pre-pregnancy BMI categories (One-way ANOVA; p<0.001)
Legend: pre-pregnancy_BMI_4k – pre-pregnancy body mass index in four categories (<18.5 kg/m2 underweight, 18.5-25 kg/m2 normal weight, 25-30 kg/m2 overweight and ≥30 kg/m2 obese)
sis1_av, sis2_av, sis3_av – average systolic blood pressure in the first, second and third trimester, respectively
dia1_av, dia2_av, dia3_av - average diastolic blood pressure in the first, second and third trimester, respectively

logistic regression analysis did not find such a statistically significant correlation between other anthropometric measures and blood pressure.

DISCUSSION

The observed difference in sociodemographic profile between women from the Dalmatian islands of Brač and Hvar and the mainland population from the city of Split is in line with the previously reported results for the similar CRIBS sample.[14] CRIBS pregnant women live in accordance with contemporary demographic trends (later childbearing), but differences between a more urban mainland population (higher education, higher income, more primipara) and a traditional island setting (lower education and income, more children per family) is still recognizable. Differences between the two groups were also detected with regards to pre-pregnancy BMI and blood pressure (p<0.05) There is a substantial body of literature suggesting an association of socioeconomic disparities with pre-pregnancy BMI and confirming that women with a higher education are more likely to have a lower pre-pregnancy BMI because they are aware of the adverse influence increased body weight has on maternal and child health during pregnancy.[17, 18] Since baseline BMI also has an influence on blood pressure

Table 4. Multivariable regression analyses of the association between socioeconomic variables, lifestyle and blood pressure for each trimester separately

		OR	95% CI	β	p-value
1st TRIMESTER BP IN PREGNANCY (referent: normal blood pressure)	age (yrs)	1.005	0.910-1.110	0.005	**0.013** (Cox&Snell R Square 12.7%, Nagelkerke R Square 17.3%)
	education (yrs)	0.865	0.401-1.867	-0.145	
	smoking in pregnancy (ref. not smoking)	1.076	0.444-2.607	0.074	
	pre-pregnancy BMI (kg/m^2)	**1.230**	**1.098-1.378**	**0.207**	
	income (ref. >1000€)	0.856	0.395-1.855	-0.156	
	parity (ref. multipara)	1.766	0.752-4.145	0.569	
	activity in pregnancy (ref. high)				
	low	0.566	0.443-3.032	-0.570	
	moderate	1.159	0.138-2.336	0.148	
	location (ref. island)	0.827	0.392-1.746	-0.190	
2nd TRIMESTER BP IN PREGNANCY (referent: normal blood pressure)	age (yrs)	1.038	0.934-1.153	0.037	**0.005** (Cox&Snell R Square 12.9%, Nagelkerke R Square 19.0%)
	education (yrs)	1.043	0.448-2.426	0.042	
	smoking in pregnancy (ref. not smoking)	0.729	0.273-1.948	-0.316	
	pre-pregnancy BMI (kg/m^2)	**1.219**	**1.098-1.354**	**0.198**	
	income (ref. >1000€)	1.106	0.485-2.523	0.101	
	parity (ref. multipara)	1.859	0.747-4.625	0.620	
	activity in pregnancy (ref. high)				
	low	0.587	0.124-2.781	-0.533	
	moderate	1.221	0.455-3.275	0.200	
	location (ref. island)	0.594	0.270-1.309	-0.520	
3rd TRIMESTER BP IN PREGNANCY (referent: normal blood pressure)	age (yrs)	0.990	0.901-1.087	-0.010	0.057 (Cox&Snell R Square 10.6%, Nagelkerke R Square 14.2%)
	education (yrs)	0.712	0.321-1.582	-0.339	
	smoking in pregnancy (ref. not smoking)	1.032	0.403-2.642	0.032	
	pre-pregnancy BMI (kg/m^2)	1.136	1.026-1.258	0.128	
	income (ref. >1000€)	0.492	0.221-1.097	-0.709	
	parity (ref. multipara)	2.187	0.969-4.939	0.783	
	activity in pregnancy (ref. high)				
	low	0.705	0.179-2.777	-0.350	
	moderate	0.730	0.291-1.829	-0.315	
	location (ref. island)	0.645	0.310-1.343	-0.438	

Legend: * statistically significant values are bolded (p<0.05); BMI – body mass index; BP – blood pressure values, it is not surprising that differences in mean blood pressure were also detected between island and mainland populations.

The general trajectory of SBP and DBP in our sample corresponded to the normal changes in blood pressure during pregnancy. Both SBP and DBP were rather stable in the first two trimesters (although a slight second-trimester drop in average DBP has been detected), followed by a significant increase in the third trimester. This corresponds to other similar studies, where studied women had the same blood pressure in the first two trimesters or a slight decrease from early to mid-pregnancy, followed by an increase in the last trimester.[8, 19]

Furthermore, our results indicated a strong association between pre-pregnancy BMI and both SBP and DBP. Although the prevalence of overweight and obesity in our sample was lower than in other western European countries (<20%),[2] women who entered their pregnancy with a BMI in the overweight or obese category presented higher values of both SBP and DBP. This effect was present consistently over the course of pregnancy, in accordance with the reports from previous studies.[8, 20, 21] Elevated pregnancy blood pressure associated with maternal pre-pregnancy BMI is also in accordance with a large body of literature that documents increased pre-eclampsia risk among overweight and obese women.[19, 22, 23]

As a change in body composition and an accretion of water occurs differently in women during pregnancy, body weight gain might not be the best and only measure reflecting changes in fat storage. One of the methods for estimating body composition and the amount of body fat, besides weight and BMI, are additional anthropometric measurements - body circumferences and skinfold thickness measures.[24] This study reported significant differences in anthropometric measures during pregnancy between women with normal BP and women with elevated BP; however, more anthropometric measures were associated with SBP than with DBP. However, when compared to the association between pre-pregnancy BMI and blood pressure, the results obtained for body mass, circumferences and skinfolds were less informative.

We can conclude that, in general, maternal anthropometry was predictive for elevated blood pressure in pregnancy. Women with higher pre-pregnancy BMI and higher anthropometric values during pregnancy also had higher blood pressure values in pregnancy, especially SBP. However, pre-pregnancy BMI has to be highlighted as the strongest predictor for elevated BP, both independently and after adjusting for other maternal socioeconomic and lifestyle characteristics. This study reinforces the role of BMI on SBP and DBP and once again highlights its importance during prenatal care monitoring, and in studies assessing BP in pregnancy. An interesting association has also emerged between blood pressure in pregnancy and place of residence (mainland vs. island). Women on islands have a lower educational level, higher pre-pregnancy BMI, and higher SBP and lower DBP than women from the mainland. Such comparisons between mainland and island populations pinpoint serious health issues present among women on the islands and can, in the long-term, lead to appropriate interventions or changes in health policies in Dalmatia. This, together with better education of Croatian islanders on risk factors for maternal and child health, would lead to better maternal health care on the islands.

The key strengths of this study are that it presents the results from the first birth cohort study in Croatia and Southeastern Europe, and that the participants were recruited from a healthy Dalmatian population, both the urban (mainland) and rural (island) area. Also, it highlights the need for better maternal health care on the islands and for the development of population-specific strategies for healthy pregnancies and healthy lifestyle attitudes in Croatia. The major limitation of the study is the relatively small sample size. The next step would be to have a nation-wide coverage and to include more island populations in order to obtain significant results.

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