

CLINICAL RESEARCH ARTICLE



# Body composition in term neonates of mothers with hypertensive disorders of pregnancy

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**BACKGROUND:** Neonates of gravidas with hypertensive disorders of pregnancy (HDP) are at increased lifelong risk of cardiometabolic complications. Neonatal adiposity measured by body composition (BC) is a better surrogate of nutritional status than birth weight. Data comparing BC in term neonates of hypertensive and normotensive pregnant patients is lacking. Our objective was to compare body composition in both groups of neonates.

**METHODS:** This was a retrospective cohort study from March 2018 to June 2019 at our tertiary institution where term neonatal BC are routinely measured. Neonates of patients with HDP and matched controls were included. Skin fold thickness (SFT) and percent body fat (PBF) were calculated using a validated anthropometric formula and compared using Mann–Whitney *U* and chi-square tests.

**RESULTS:** One hundred and forty-two neonates of patients with HDP were compared to 150 controls. Demographic characteristics were similar except for higher pre-pregnancy BMI ( $29.7 \pm 8.4$  vs  $26.75 \pm 7.1$ ,  $p < 0.01$ ) in the HDP group. SFT was not significantly different ( $4.6$  vs  $4.4$  mm,  $p = 0.09$ ) but PBF was higher in the hypertensive group ( $13.15$  vs  $11.72$ ,  $p = 0.01$ ).

**CONCLUSIONS:** PBF is higher in neonates of mothers with HDP, which may contribute to an increased risk of cardiometabolic complications later in life.

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## IMPACT:

- Birth weight percentiles do not explain the predisposition to cardiovascular complications in offspring of hypertensive mothers.
- Body composition estimation may provide an explanation for this increased risk.
- Percent body fat is higher in term neonates of mothers with hypertensive disorders of pregnancy than neonates of normotensive mothers.
- Body composition is different in term neonates of mothers with hypertensive disorders of pregnancy.

## INTRODUCTION

Hypertensive disorders of pregnancy complicate about 1 in 10 pregnancies, with preeclampsia complicating 2–8% of pregnancies and chronic hypertension complicating 1.5% of pregnancies.<sup>1,2</sup> Chronic hypertension is defined as elevated blood pressure (BP)  $\geq 140/90$  mmHg predating pregnancy or diagnosed before 20 weeks of gestation or that persists after 12 weeks postpartum.<sup>2</sup> Preeclampsia is a disorder of pregnancy associated with new-onset hypertension, with or without proteinuria that occurs after 20 weeks of gestation and frequently near term.<sup>3</sup> Women with pregnancies complicated by preeclampsia and other hypertensive disorders of pregnancy are at increased risks of cardiovascular complications later in life.<sup>4,5</sup> Recent studies have shown that their offspring are also at increased risks of complications such as obesity, stroke and cardiovascular disease.<sup>6,7</sup> The reason for this is unclear.

One of the hypotheses of the pathogenesis of preeclampsia is the ischemic model, which theorizes that decreased uteroplacental perfusion leads to intrauterine growth restriction and low birth weight.<sup>8</sup> Studies have been carried out comparing birth weight, Body Mass Index (BMI) and Ponderal index of preterm babies born to mothers with preeclampsia with that of infants of normotensive mothers. These studies found no weight differences between term infants of mothers with preeclampsia when compared with normotensive pregnancies but that preterm infants of mothers with preeclampsia were of lower birth weights when compared with normotensive pregnancies.<sup>9,10</sup> However, data comparing body composition in term neonates of hypertensive mothers with their normotensive counterparts is lacking.

Birth weights provide limited information on the nutritional status of the infant and it is now widely accepted that body composition studies provide a better indicator of the human

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biological response to genetic and environmental influences than measures of body size and height.<sup>11</sup> Body composition in its simplest model divides the body into two components—lean body mass (fat free mass) and fat mass—thereby providing an estimate of adiposity (percent body fat).<sup>12</sup> Studies that have assessed lean body mass (LBM) and fat body mass have tended to find that birth weight is positively associated with LBM and negatively associated with relative adiposity. This suggests that the association between birth weight and BMI does not necessarily reflect increased adiposity at higher birth weights.<sup>13</sup>

The aim of our study was to compare the body composition of term neonates of mothers with hypertensive disorders of pregnancy with neonates of normotensive mothers using a validated anthropometric formula at birth. Prematurity is a known risk factor for future cardiovascular disease and may be a confounder, therefore we limited our analysis to only term neonates.<sup>14</sup> Our hypothesis was that neonates of mothers with hypertensive disorders of pregnancy will have increased adiposity at birth.

## MATERIALS AND METHODS

This was a retrospective cohort study of term infants (born at or beyond 37 weeks 0 days gestational age) at MetroHealth Medical Center from March 2018 till June 2019. Body composition assessment is routinely performed on all term neonates at our institution on admission to the newborn nursery. This is achieved with a validated anthropometric formula using birth weight, birth length, obtained by using a hard-surface length board, (Dynamic Machine, Elyria, OH) and suprailiac skin fold thickness. The suprailiac skin fold thickness is measured immediately above the iliac crest at the mid-axillary line using the Harpenden (Baty International, Sussex, UK) skinfold calipers on the left side of the body. This skinfold measurement is obtained by lifting the skin with the thumb and index finger, with care taken not to include any underlying tissue. Skin fold measurements are recorded to the nearest 0.1 mm. At least two measurements are taken and rounded to the nearest 0.1 mm. A third measurement is taken if both measurements are not within 0.5 mm of each other and the two closest measurements are averaged. We utilized the Catalano formula<sup>15</sup> which was validated against total body electric conductivity (TOBEC) and calculates Neonatal Fat Mass (FM) using the equation.

Neonatal (FM) =  $[0.54657 + 0.39055 \times \text{Birth weight (g)} + 0.0453 \times \text{Flank Skinfold (mm)} - 0.03237 \times \text{Length (cm)}]$ .

Neonatal percent Body Fat (PBF) is then calculated as  $\text{PBF} = \text{FM (kg)}/\text{wgt (kg)} \times 100$ .

The Catalano formula was validated against TOBEC in 84% of neonates in the first 24 h, 95% after 48 h and the remaining 5% at 72 h after delivery. In this validation study, there was no significant difference in male: female ratio (52 vs 48%,  $p = 0.8$ )

This formula was built into our electronic medical record. Skin fold thickness data at our institution is prospectively collected and entered into a research database and the electronic medical record. Our clinical postpartum nurses have undergone body composition training using the Maternal-Fetal Medicine Units (MFMU) network training and quality assurance protocol. Our group validated this training confirming that neonatal skin fold thickness measurements can be accurately obtained and introduced into routine clinical practice.<sup>16</sup>

The skin fold thickness used in our study were collected by various postpartum nurses who have undergone the MFMU network training described above and are subject to rigorous ongoing quality assurance protocol. All skin fold thickness in the study were measured within 24 h of delivery.

Our study cohort was identified from our hospital delivery records. Each study subject was individually matched to a control by gestational age, infant sex, and date of delivery. Mothers with hypertensive disorders of pregnancy from March 2018 till June 2019 who delivered at term were identified from our perinatal database, which is an IRB-approved research database containing all delivery records of mothers and their newborn. Some of the data contained in the database include gestational age at delivery, mode of delivery, delivery complications, maternal BMI, medical complications and other demographic information. Neonatal data include infant sex, birth weight, birth length and Neonatal Intensive Care Unit admission status. Patients were included in the study if they were 18 years

old and older, had a diagnosis of preeclampsia, gestational hypertension or chronic hypertension, and delivered at or beyond 37 weeks and 0 days of gestation. Only mothers whose infants had both their skin fold thickness and percent body fat calculated and who met inclusion criteria were included in the final analysis. Infants with congenital anomalies and patients with incomplete data such as those whose infants did not have both the skin fold thickness recorded and percent body fat calculated were excluded from the study.

The diagnosis of hypertensive disorders of pregnancy was based on standard ACOG criteria.<sup>1</sup> The study cohort were matched to normotensive mothers by gestational age, infant sex, and delivery date using the perinatal database. Race as described in this study refers to patient self-identified race which was abstracted from the electronic medical records. Once eligible patients were identified from hospital delivery records, all relevant demographic, clinical, neonatal and delivery outcomes were abstracted from the electronic medical records.

Median skin fold thickness, percent body fat, demographic and obstetric characteristics were compared and a Mann–Whitney *U* and chi-square tests were performed as appropriate with a two-sided alpha set at 0.05 for significance. Data analysis was performed using the R statistical software. The study was approved by the MetroHealth Institutional Review Board (IRB Study 19-00515).

## RESULTS

One hundred and fifty term neonates were identified during the study period and compared to 150 controls. Eight infants in the study group lacked complete data and were therefore excluded from final analysis. In total, we analyzed data for 142 infants in the hypertensive group and 150 in the control group. The study cohort was composed of 13% with a diagnosis of chronic hypertension, 55% with gestational hypertension, 22% with preeclampsia without severe features and 10% preeclampsia with severe features. Due to the small sample size, superimposed preeclampsia was not separately characterized and patients with chronic hypertension with superimposed preeclampsia were classified as preeclampsia for data analysis purposes.

Demographic characteristics were similar in the hypertensive and normotensive groups respectively. The gestational age at delivery was not significantly different between groups 37.9 vs 37.8 weeks,  $p = 0.29$  with similar distribution of males and females neonates in both groups (54 v 51%,  $p = 0.62$ ). Our cohort was racially and ethnically diverse. Pre-pregnancy BMI was significantly higher in the hypertensive cohort  $29.7 \pm 8.4$  vs  $26.8 \pm 7.1$ ,  $p < 0.01$  (Table 1). Patients in the hypertensive group were more likely to be primiparous (40 vs 23%,  $p = 0.03$ ) and undergo induction of labor (73 vs 35%,  $p < 0.01$ ). Pregnancy and medical complication such as gestational diabetes and pre-gestational diabetes were similarly distributed between both groups.

The frequency of NICU admission (8.5 vs 5.3%,  $p = 0.28$ ) and low birth weight (4 vs 7%,  $p = 0.25$ ) were not significantly different between both groups. However, the median birth weight was significantly higher in the hypertensive group ( $3170 \pm 441$  vs  $3010 \pm 447$  g,  $p < 0.01$ ). In addition, median percent body fat was significantly higher in the hypertensive group compared to the normotensive group (13.2 vs 11.7%,  $p = 0.01$ ; Fig. 1). Median skin fold thickness was similar between groups (4.6 vs 4.4 mm,  $p = 0.09$ ; Fig. 2). Controlling for BMI as a confounder, did not alter our study finding. Using an analysis of covariance to control for BMI resulted in an increase in *p* value from 0.01 to 0.026, which was still statistically significant. In addition when chronic hypertension was excluded from the analysis, the anthropometric findings were unchanged.

## DISCUSSION

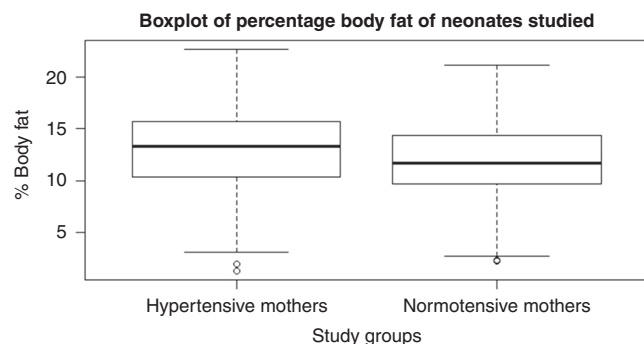
Our study comparing body composition in offspring of mothers with hypertensive disorders of pregnancies with those of normotensive mothers shows that neonates of mothers with hypertensive disorders of pregnancy have increased body weight

**Table 1.** Comparing characteristics of mothers with hypertensive disorders of pregnancy with normotensive mothers.

	Hypertensive cohort (N = 142) N (%) or N ± SD	Normotensive cohort (N = 150) N (%) or N ± SD	p value
Primiparous	57 (40)	35 (23)	0.03 <sup>a</sup>
Age (years)	28 ± 5.7	28 ± 6.3	0.19
Pre-pregnancy BMI	29.7 ± 8.4	26.8 ± 7.1	<0.01 <sup>a</sup>
EGA at delivery (weeks)	37.8 ± 1	37.9 ± 1	0.29
Race			0.19
White	59 (42)	62 (41.3)	
Black	67 (47)	57 (38)	
Asian	3 (2)	9 (6)	
Smoker	18 (13)	30 (20)	0.15
Medical complications			0.22
Gestational diabetes	12 (8.4)	11 (7)	
Pre-gestational diabetes	6 (4.2)	3 (2)	
Induction of labor	103 (73)	52 (35)	<0.01 <sup>a</sup>
Vaginal delivery	105 (74)	119 (79.3)	0.56
Male infant sex	77 (54)	77 (51)	0.62
NICU admission	12 (8.5)	8 (5.3)	0.28
Low birth weight	6 (4)	11 (7%)	0.25
Infant weight (g)	3170 ± 441	3010 ± 447	0.01 <sup>a</sup>
Infant length (cm)	49 ± 2	48.5 ± 2	0.05

BMI Body Mass Index, NICU Neonatal Intensive care Unit, EGA estimated gestational age.

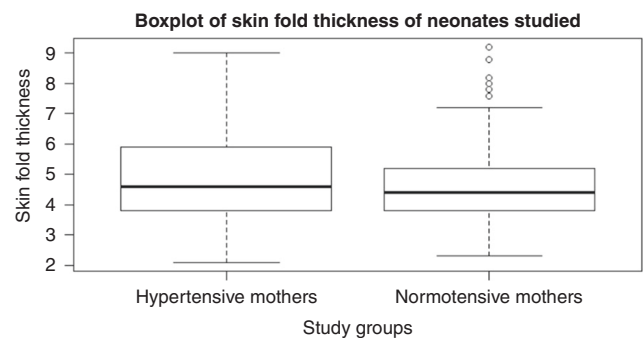
<sup>a</sup>Statistically significant  $p < 0.05$ .



**Fig. 1** Boxplot of percent body fat of neonates of mothers with hypertensive disorders of pregnancy compared with neonates of normotensive mothers. Median 13.15 ± 3.7 vs 11.72 ± 3.7. \*\* $p = 0.01$ . \*\*Statistically significant.

and percent body fat. Excluding patients diagnosed with chronic hypertension did not alter these findings. Not all anthropometric measurements were different, as skin fold thickness was not different between both groups, Fig. 1. However our study may not have been powered to detect this difference. It is possible that both low-birth-weight infants and infants of mothers with hypertensive disorders of pregnancy have a common pathway of impaired placentation resulting in an intrauterine environment in which they are prone to “energy conservation” leading to this increased adiposity at birth. The increased rate of inductions in the hypertensive group is most likely due to the American College of Obstetricians and Gynecologists recommendation for induction at term in these groups of patients.<sup>17</sup>

Multiple studies have been conducted comparing birth percentiles in neonates of hypertensive mothers with their normotensive counterparts.<sup>10,18</sup> These studies, however, do not



**Fig. 2** Boxplot of skin fold thickness of neonates of mothers with hypertensive disorders of pregnancy compared with neonates of normotensive mothers. Median 4.6 vs 4.4,  $p = 0.09$ .

directly compare body composition at birth, which is a better surrogate of nutritional status. The studies were restricted to mothers with preeclampsia, excluding patients with other hypertensive disorders such as gestational hypertension or chronic hypertension. To our knowledge, no prior studies have been conducted using a validated anthropometric formula to compare body composition at birth in term infants of mothers with hypertensive disorders of pregnancy with their normotensive counterparts.

Obed et al. compared birth weight, BMI, and Ponderal index in infants of mothers with preeclampsia with infants of normotensive mothers concluding that birth weights were similar in term pregnancies in both groups but preterm infants of mothers with preeclampsia weighed less.<sup>10</sup> Some have compared adiposity in preterm offspring of mothers with preeclampsia with that of preterm offspring born to normotensive mothers using dual-energy X-ray absorptiometry (DEXA) at adolescence concluding that male children of mothers with preeclampsia have greater

adiposity.<sup>19</sup> Others have compared anthropometric measurements in early puberty of children born to mothers with preeclampsia with normotensive mothers concluding that female offspring of mothers with preeclampsia have a higher BMI and larger waist circumference especially if their mothers were obese.<sup>20</sup> In another study of pregnant women without a diagnosis of hypertension, mid-to-late pregnancy increases in blood pressure was associated with lower percent fat mass at birth using air displacement plethysmography.<sup>21</sup>

As seen in Table 1, the majority of our study and control patients were Non-Hispanic White and Non-Hispanic Black patients (89 and 79%, respectively) which may appear to limit its applicability to all racial groupings. However, the Catalano formula that we utilized was derived in 64% of Non-Hispanic White/Caucasian infants and has now been validated by other studies in other ethnic groups thereby validating its use in our multi-ethnic cohort.<sup>22,23</sup>

Newborn adiposity is considered a nutritional measure of the fetal intrauterine environment and representative of future health.<sup>23</sup> Body weight for length measures which are commonly used to identify individuals at risk of obesity do not differentiate between fat mass and fat free mass and are poor indicators of nutritional status.<sup>22,24</sup> Birth weight measures such as Ponderal Index also do not distinguish between different body compositions which may be present in different ethnic groups whereas body composition eliminates these assumptions and directly measures adiposity.<sup>25</sup> Other methods such as air displacement plethysmography, bioelectrical impedance, magnetic resonance imaging, and DEXA are impractical for everyday use. In the initial study from which the Catalano formula was derived using backward stepwise linear regressions, it was determined that birth weight, skin fold thickness, and infant length were the variables that correlated the most with neonatal fat when validated against TOBEC. Neonatal sex did not have a similar effect and was therefore not included in the equation.<sup>15</sup>

The Catalano formula was recently validated against air displacement plethysmography, which is considered the optimal method of measuring body composition by researchers and also validated in a multi-ethnic cohort of infants.<sup>22,26</sup> We chose this validated anthropometric formula as our method of estimating body composition as it is practical, can be easily replicated, and adopted into daily clinical practice to assess an important marker of neonatal adiposity, which may have implications for future health and chronic disease risk.

Our finding of increased body fat percent will be helpful in counseling parents of these infants and designing primary prevention strategies even from an early age in an effort to prevent morbidity and mortality in later life. BMI in infancy is said to track moderately well into adulthood with greater than a 50% chance of adult obesity in children with a BMI >95% for their expected age.<sup>27,28</sup> A systemic review and met-analysis published in 2014 concluded that BMI had a high specificity but low sensitivity in detecting excess adiposity in children and failed to identify about 25% of children with excess percent body fat.<sup>29</sup> Therefore targeting interventions using body composition which better reflects adiposity and is a more sensitive marker may be more successful in identifying at risk groups. Singhal and Lucas were of the opinion that fast infant growth is the primary cause of the increased cardiovascular risk in preterm or small for gestational age infants who also have increased adiposity at birth.<sup>14</sup> Dietary and other behavioral interventions targeted at this group of infants as they grow may be helpful in reducing their later life risk of cardiovascular and other complications.

Our study findings showing an increased percent body fat in offspring of patients with hypertensive disorders of pregnancy is unique and further large scale prospective studies will be needed to confirm our findings especially in a multi-ethnic cohort before generalizing our findings to all ethnic groups. Larger cohorts

studies sufficiently powered to assess differences in anthropometrics are needed. Ideally ongoing prospective cohort studies establishing clinical (and biological) risk to chronic disease, prospective assessment of primary prevention and assessment of whether severity of hypertension has an impact on neonatal anthropometrics are needed. Longitudinal studies to track body composition into adulthood to determine if this finding of increased adiposity holds true are also needed.

A strength of our study is the fact that we have a validated database of newborn anthropometric measurements that is prospectively collected by trained nurses. We also used a body composition formula which has been extensively validated. The anthropometric equation, the Catalano equation, has been validated from prior studies and in this age group.<sup>15</sup> This equation has also been utilized in large multinational epidemiologic trials.<sup>30,31</sup> The use of a single skin fold measurement makes this equation easy to use and also minimizes error. Limitations of our study include its retrospective nature and our findings are limited to term infants which cannot be generalized to preterm infants who are at risk not only of complications associated with prematurity but also later life cardiovascular complications of hypertensive pregnancies. Importantly, the gestational age at diagnosis of preeclampsia or hypertension was not accounted for in this study. We were limited by the small sample size in that we could not make comparisons within the groups to see if our findings were true in all the subgroups studied or if the findings were skewed by a particular sub-group of hypertensive mothers. Although our study addressed baseline differences and we utilized matching as a means of reducing selection bias, there may have been other neonatal or maternal characteristics that cannot be measured due to the retrospective nature of our study that may have accounted for the difference noted in body composition between groups. Specifically, the hypertensive cohort had a higher pre-pregnancy BMI than the normotensive cohort. Although hypertensive disorders and maternal obesity often go hand in hand, maternal obesity is a biologically plausible alternate explanation for this study's findings of increased percent body fat in offspring of hypertensive mothers.

In conclusion, percent body fat is higher in neonates of mothers with hypertensive disorders of pregnancy when compared to neonates of normotensive mothers. Alterations in adiposity might contribute to an increased risk of cardiovascular and other complications in later life.

#### DATA AVAILABILITY

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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## AUTHOR CONTRIBUTIONS

All authors have met the authorship requirement. O.A.A. and K.S.G. made substantial contributions to study conception and acquisition of data O.A.A., K.S.G., and J.R.L. all contributed to study design, analysis and interpretation of data, and drafting, revising, and approval of the version to be published.

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## COMPETING INTERESTS

The authors declare no competing interests.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Patient consent was not required for this study.

## ADDITIONAL INFORMATION

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