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## Ultrasound Measurement of the Fetal Adrenal Gland as a Predictor of Spontaneous Preterm Birth

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### Abstract

**Objective**—To estimate whether ultrasound measurement of the fetal adrenal gland remote from delivery in asymptomatic women can accurately predict spontaneous preterm birth.

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\*For a list of institutions and researchers that compose the Nulliparous Pregnancy Outcomes Study, see Appendix 1 online at <http://links.lww.com/xxx>.

Financial Disclosure

The authors did not report any potential conflicts of interest.

Presented in at the 33<sup>rd</sup> Annual Clinical Meeting of the Society of Maternal Fetal Medicine, February 2-7, 2015, San Diego, California.

**Methods**—We conducted a prospective multicenter observational nested cohort study of asymptomatic nulliparous women with a singleton pregnancy to study adverse pregnancy outcomes. Between 22 0/7 and 30 6/7 weeks of gestation, credentialed ultrasonographers measured the width (w), length (l), and when able, depth (d) of the “fetal zone” of the fetal adrenal gland as well as the width (W), length (L) and depth (D) of the total gland. We used the ratios of each measurement (w/W, l/L and d/D) to control for variation in adrenal size by gestational age. The accuracy of each ratio measurement in predicting spontaneous preterm birth <37 0/7 weeks (“SPTB37”) and spontaneous preterm birth <34 0/7 weeks (“SPTB34”) was assessed by receiver operating characteristic (ROC) curves, using area under the curve (AUC).

**Results**—Pregnancy outcomes were available for 1,697 women with one or more fetal adrenal gland measurements. SPTB37 and SPTB34 occurred in 82 (4.8%) and 6 women (0.4%), respectively. None of the fetal adrenal gland measurements distinguished spontaneous preterm birth from term birth. The AUCs (95% CIs) for SPTB37 were 0.51 (0.45, 0.58), 0.50 (0.44, 0.56), and 0.52 (0.41, 0.63) for w/W, l/L and d/D ratios, respectively. The AUCs for SPTB34 were 0.52 (0.25, 0.79) and 0.55 (0.31, 0.79) for w/W and l/L ratios. Additionally, none of the means of the gland measurements were statistically different between those delivering at term and spontaneous at preterm ( $p>0.05$ ).

**Conclusion**—Fetal adrenal size, as measured by ultrasound between 22 0/7 and 30 6/7 weeks, is not predictive of spontaneous preterm birth in asymptomatic nulliparous women.

## Introduction

Preterm birth remains the most pressing public health problem in obstetrics, affecting 11.54% of US newborns in 2012 with direct costs of at least \$65,600 per neonate<sup>1,2</sup>. Recently interventions such as progesterone and cervical cerclage have been shown to decrease the rate of preterm birth among at risk women<sup>3-5</sup>. Nonetheless, the impact of these efforts has been limited by a lack of accurate predictors of preterm birth<sup>6-8</sup>.

It has long been known that the fetal adrenal gland plays an integral role in both term and preterm parturition<sup>9</sup>. For example, necropsy studies of preterm fetuses demonstrated that the gross weight of the fetal adrenal gland is significantly greater among those fetuses that undergo spontaneous preterm birth compared to those delivered for maternal reasons<sup>10</sup>. Likewise, it has been noted that the “fetal zone” of the adrenal gland is greatest in size immediately before spontaneous birth and quickly involutes following delivery<sup>11</sup>.

These findings led a group of investigators to examine the role of ultrasound measurement of the fetal adrenal gland in the acute prediction of spontaneous preterm birth. In a cohort of 126 women with and without symptoms of preterm labor, Turan and colleagues measured the volume of the fetal adrenal gland to determine if it differentiated women who went on to deliver in the next 5 days. They found that women who delivered in the next 5 days had larger adrenal volumes compared to those who did not<sup>12</sup>. In a subsequent publication, Turan et al examined the fetal adrenal gland in 74 women with preterm labor symptoms using a simplified ultrasound technique examining the ratio of the depth of the fetal adrenal zone (d) to the depth of the total gland (D). Similar to their prior experience, they found that this

measurement discriminated women who went on to deliver within 7 days and those who did not<sup>13</sup>.

Recognizing that the process of parturition occurs over weeks to months prior to delivery<sup>14</sup> and that this extended timeline may provide an opportunity to clinically intervene, we sought to examine whether ultrasound measurement of the fetal adrenal gland can accurately identify asymptomatic nulliparous women who will undergo spontaneous preterm birth. Our primary hypothesis was that the measurement of the ratio of the fetal zone to the overall adrenal gland will discriminate fetuses destined to deliver prematurely from those who will deliver at term.

## Materials and Methods

The Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be (nuMoM2b) Network was formed with the goal of predicting adverse pregnancy outcomes, including spontaneous preterm birth, among nulliparous women. Eight institutions, recruited 10,038 nulliparous women with singleton pregnancies into a prospective observational study that involved serial evaluation at 3 separate time periods during pregnancy. Prior to the initiation of the study, institutional review board approval was obtained from each clinical site and the data coordinating center. Further description of the methods of the study can be found in the publication by Haas, et al<sup>15</sup>.

Prior to the initiation of the adrenal ultrasound portion of the study, study ultrasonographers were required to demonstrate competency in both identifying and measuring the adrenal gland in a transverse plane; and when possible in the coronal or in the sagittal plane. These skills were taught through mandatory attendance of a webinar and, where required, hands on training with a credentialed ultrasonographer. Due to technical difficulty of consistently obtaining high quality sagittal adrenal gland measurements as described in the prior publication by Turan<sup>16</sup>, a decision was made to simplify the technique and primarily examine the fetal adrenal gland in the transverse plane. Ultrasonographers were encouraged, but not required, to become credentialed in measuring the depth of the gland in either the coronal or sagittal plane as well.

A modification of the previously described technique of measuring the ratio of the fetal zone/total gland measurement in the sagittal plane, measurement of the fetal zone/total gland measurement in the transverse plane (length and width) had been systematically measured by Dr. Turan in a prior study. He found that these measurements have similar, albeit slightly lower, sensitivity and specificity compared to the sagittal measurement (personal communication). Ultrasonographers were instructed on how to correctly identify the closest adrenal gland in the transverse plane. They were then to measure the length (L) and width (W) of the total gland as well as the length (l) and width (w) of the fetal zone. Calipers were to be placed directly over the intersection of the gland with the surrounding soft tissues and the intersection of the fetal zone and surrounding gland. Both the length and width of the zone and total gland were measured along the same meridian. This allowed the ratio of the fetal zone to that of the total gland length and width (l/L & w/W) to be accurately determined (See Figure 1). By examining the ratio of the fetal zone to the total gland we are

able to mitigate differences in measurement that may be the result of fetal size or gestational age<sup>16</sup>.

Ultrasonographers were instructed to take 3 measurements of the glands' width and length; with the mean values (zone, total, and ratio) used for the analysis. Credentialed ultrasonographers universally completed an online didactic session followed by successful submission of 5 serial examinations that were blindly reviewed centrally. A total of 29 ultrasonographers were successfully credentialed across the 8 clinical sites.

To ensure ongoing quality, every 10<sup>th</sup> examination was centrally reviewed and if an inadequate examination occurred, feedback was provided to the ultrasonographer and a progressive system of central review was provided. Ultrasonographers were permitted to spend up to 20 minutes completing the examination per patient and if unable to obtain adequate images, they were instructed to designate the study as incomplete. No specifications were placed on the type of ultrasound unit to be utilized.

The sample size goal for the study was 1,500 to 2,000 women with measurements, based on precision estimates for the area under a receiver operating characteristic curve (AUC). It was assumed that 9% of women would experience a spontaneous preterm birth, and standard errors (SE) for AUCs of 0.80 and 0.65 were computed. An AUC of 0.65 was considered conservative and a sample size of 1,500 provided an SE of 0.027 and 2,000 provided an SE of 0.023. Nulliparous women with a singleton fetus enrolled in the parent study undergoing ultrasound between 22 and 0/7 and 30 6/7 weeks gestation were recruited into this study. This time frame was the last pre-specified visit in the parent study and was chosen as it was most proximal to the time of preterm birth. All participants had a certain due date corroborated or established by an ultrasound prior to 14 0/7 weeks<sup>15</sup>. Women with uterine anomalies, hydramnios (AFI  $\geq$  25.0 cm), history of 3 or more prior spontaneous losses  $<$ 20 weeks, presumptively lethal fetal malformations or known or suspected aneuploidy (e.g. malformations strongly linked with aneuploidy such as congenital diaphragmatic hernia) were excluded. Women who had undergone multi-fetal reduction, received a cerclage at any point or received progesterone after 15 weeks were also excluded. Those women deemed non-compliant with prior study procedures were similarly not enrolled in this portion of the study.

Our primary outcome was spontaneous preterm birth, which was defined as delivery occurring before 37 0/7 weeks following spontaneous onset of preterm labor or preterm premature rupture of the membranes (PPROM) or fetal membrane prolapse (membranes beyond the cervical os) regardless of subsequent labor augmentation or cesarean delivery. Other pre-specified outcomes included spontaneous preterm birth before 34 0/7 weeks and delivery within 2 weeks of the fetal adrenal measurement.

Analysis consisted of descriptive statistics, including sensitivity and specificity for predicting spontaneous preterm birth over the range of possible cutoffs of the ratio measures and computation of the area under each receiver operating characteristic (ROC) curve. Wilcoxon rank sum tests were used to test for differences in location of the data (e.g., differences in medians). A p-value  $<$ 0.05 (2-sided) was viewed as statistically significant.

Intraclass correlation coefficients were computed from the 3 repeated measurements the ultrasonographers were instructed to obtain. All analyses were conducted using SAS 9.3/9.4 software (SAS Institute Inc., Cary, NC, USA).

## Results

A total of 2,108 women underwent an attempt at assessment of the fetal adrenal gland with 1,723 (81.7%) having a successful measurement (Figure 2). As part of the ongoing central review, 95 studies were excluded and 290 exceeded the 20 minutes allowed to obtain an adequate image. Thus satisfactory studies were obtained in 81.7% of attempts.. Women in whom measurements could not be obtained tended to have a higher BMI (33.2%) with BMI greater than or equal to 30.0 m<sup>2</sup>/kg among those without a measurement versus 19.9% among those with a measurement ( $p<0.001$ ). Nonetheless, adequate measurements were obtained in the majority of obese women (78.0%). Normative values of measurement by gestational age are available in Table 1.

Pregnancy outcomes were available for 1697 (98.5%) women with one or more fetal adrenal gland measurements. Spontaneous preterm birth before 37 weeks was experienced by 82 women (4.8%) and before 34 weeks by 6 women (0.4%). There were 1,566 term births. The remaining births were 49 indicated preterm births, including one stillbirth which was censored for the primary analysis.

Baseline characteristics are presented in Table 2 for the 1723 women with fetal adrenal gland measurements. The median age was 27 years (interquartile range: 22-31). The race-ethnicity distribution was 55.7% non-Hispanic white, 12.4% non-Hispanic black, 22.9% Hispanic, 5.4% Asian, and 3.6% other. This was a first pregnancy for 73.9% of the women.

Table 3 provides descriptive statistics for the fetal adrenal gland measurements and a context on the timing with respect to the pregnancy for women with spontaneous preterm birth ( $n=82$ ) and term birth ( $n=1,562$ ). Ultrasound assessment of the fetal adrenal gland occurred at a mean of 27.4 weeks ( $+/-SD1.5$ ). No women delivered within 2 weeks of the time of ultrasound assessment of the fetal adrenal gland. The mean time elapsed between ultrasound measurements of the adrenal gland and preterm delivery was 55.3 ( $+/-SD 13.9$ ) days (range 18-93 days). Medians (intraquartile ranges, IQRs) for length, width, and depth of the total gland, fetal zone, and ratio are displayed in Table 3. None of the measurements differed significantly between women who delivered prematurely and those who delivered at term. Receiver operating characteristic curves and areas under the curves (AUCs) are shown in Figure 3 for the ratio measures as predictors of spontaneous preterm birth. Panel 1 contrasts spontaneous preterm birth  $<37$  0/7 weeks (“SPTB37”) versus term birth and to reflect a pure predictive framework, Panel 2 contrasts SPTB37 versus all other births. None of the AUCs were statistically different from 0.50, suggesting that measurements of the ratio of the fetal adrenal zone to the overall gland does not discriminate women who are destined to spontaneously deliver prematurely from those who do not. The AUCs (95% CIs) for SPTB37 were 0.51 (0.45, 0.58), 0.50 (0.44, 0.56), and 0.52 (0.41, 0.63) for w/W, l/L and d/D ratios, respectively, and for spontaneous preterm birth  $<34$  0/7 weeks (“SPTB34”) were 0.52 (0.25, 0.79) and 0.55 (0.31, 0.79) for w/W and l/L ratios. There was only one

spontaneous preterm birth < 34 0/7 weeks with a d/D ratio measure. Intraclass correlation coefficients of the ratios for the measurements repeated three times by the ultrasonographer were 0.70, 0.74, and 0.77 for w/W, l/L and d/D, respectively. The median (interquartile range) on the difference between these ratio measurements (absolute value of the maximum difference between the three measurements) were 9.6% (9.4%), 7.9% (8.0%), and 8.6% (8.5%) for w/W, l/L and d/D, respectively.

## Discussion

In contrast to the two prior studies by Turan in symptomatic women, the size of the fetal adrenal gland was not predictive of preterm birth in asymptomatic women<sup>12,16</sup>. This finding is consistent with an investigation performed by Salari, who likewise examined the fetal adrenal gland in a cohort of asymptomatic women<sup>17</sup>. Several explanations may be offered as to the reason for these discrepant findings.

Foremost is the fact that we examined asymptomatic women who averaged 55 days from the time of their ultrasound to their preterm birth. It is conceivable that the changes of the adrenal gland occur over a shorter duration and the value of the adrenal gland measurement is only as an acute (within 5-7 days) marker of spontaneous preterm birth rather than an early marker, such as cervical length<sup>7</sup>.

This finding is surprising since maternal estriol levels, which are primarily derived from the fetal adrenal gland, have been noted to rise approximately 4 weeks prior to the onset of preterm birth<sup>18,19</sup>. Moreover, other investigators found that maternal cortico-releasing hormone levels (a surrogate marker of the size of the fetal adrenal) begin to rise at 16 to 20 weeks in women who go on to have preterm birth<sup>20</sup>.

Also, it is well known that preterm birth is a common outcome of 4 antecedent pathways: inflammation, myometrial stretch, activation of the maternal-fetal Hypothalamic Pituitary-Adrenal (HPA) axis and decidual hemorrhage<sup>21</sup>. It is conceivable that changes in the fetal zone may not occur if the pathway to preterm parturition is not through activation of the maternal-fetal HPA. Meaningful attribution to these four different pathways has yet to be parsed out. Moreover, the fact that preterm birth has these 4 antecedent pathways dramatically adds to the complexity of screening in low risk populations. In addition each of these pathways may have different biomarkers that are expressed at different gestational epochs; making the discrimination of women who deliver at term from those who deliver preterm very challenging.

Strengths of our study include the very large sample size and multicenter approach. Furthermore ongoing assessment of ultrasound quality was closely followed throughout the duration of the study. Limitations of our study include the fact that the rate of spontaneous preterm birth was smaller than anticipated and that no woman delivered within 2 weeks of the time that she had the ultrasound measurement. The parent study prospectively recruited women seeking care in the first trimester. This resulted in a cohort of parturients of a higher socio-economic status and lower risk for preterm birth than that found in the general population<sup>23</sup>. Our outcome of interest was spontaneous preterm birth, which excludes



women with iatrogenic prematurity. Iatrogenic prematurity typically represents a third of preterm birth<sup>22</sup>. Spontaneous preterm birth occurred at a rate of 5% in our study population. It is noteworthy that the precision of the AUC measurements that were planned with an assumption of 9% spontaneous preterm births are still adequate using a 5% spontaneous preterm birth rate. The standard error for an AUC of 0.65 would be 0.035 (at 5%) instead of 0.027 (at 9%) for N=1,500 and 0.030 instead of 0.023 for N=2,000. Future studies of the fetal adrenal gland may yield different results for high risk groups and a shorter time frames between measurement and the preterm birth. Nonetheless, as a single early marker, measurement of the fetal adrenal gland does not appear to predict preterm birth in asymptomatic women.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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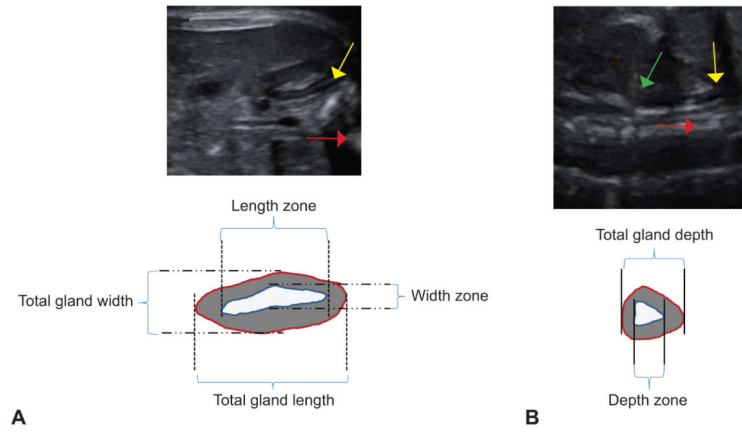
Supported by the following grants from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) to examine adverse outcomes in a cohort of 10,000 nulliparous patients: U10 HD063036, RTI International; U10 HD063072, Case Western Reserve University; U10 HD063047, Columbia University; U10 HD063037, Indiana University; U10 HD063041, University of Pittsburgh; U10 HD063020, Northwestern University; U10 HD063046, University of California Irvine; U10 HD063048, University of Pennsylvania; and U10 HD063053, University of Utah. R21 HD068809-01A1 The Fetal Adrenal Gland as a Predictor of Spontaneous Preterm Birth, Columbia University.

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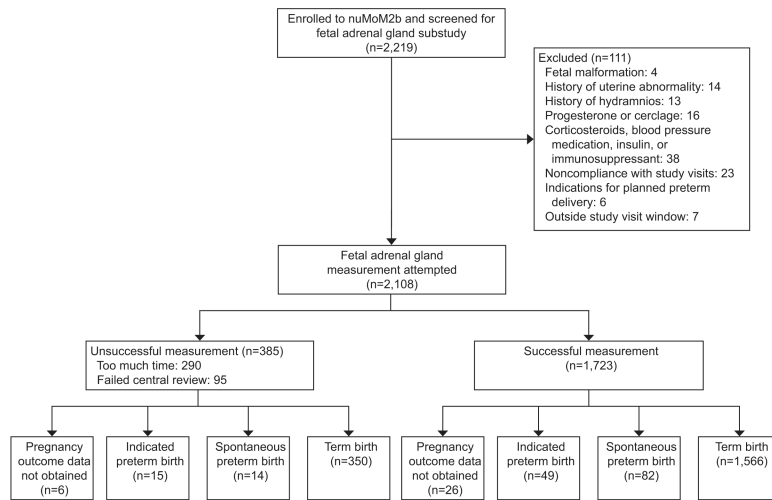
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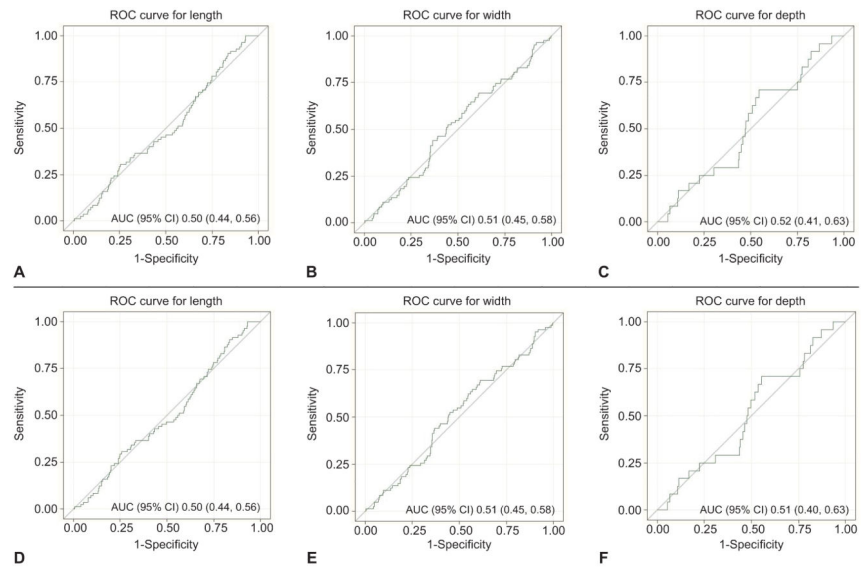
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**Figure 1.** Technique for measuring the fetal adrenal gland. **A.** Transverse measurements. *Yellow arrow*, adrenal gland; *red arrow*, spine. **B.** Sagittal measurements. *Yellow arrow*, adrenal gland; *red arrow*, spine; *green arrow*, kidney.



**Figure 2.** Success with fetal adrenal gland measurement and pregnancy outcome groups. nuMoM2b, Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be.



**Figure 3.** Receiver operator characteristic (ROC) curve for fetal adrenal gland ratio measures for prediction of spontaneous preterm birth. **A–C.** Term births used for controls. **D–F.** Indicated preterm births used for controls. AUC, area under the curve; CI, confidence interval.

**Table 1**

Percentiles for Fetal Adrenal Gland Measurements by Gestational Age

Gestational Age (weeks)	Direction Measured (mm)	Entity Measured	N	Percentiles				
				10th	25th	50th	75th	90th
22	Length	Gland (L)	12		11.2	13.4	15.8	
		Zone (l)	12		6.1	8.3	10.0	
	Width	Gland (W)	12		3.9	4.8	6.8	
		Zone (w)	12		1.5	2.5	3.6	
		Ratio (w/W)	12		39.8%	44.4%	59.9%	
	Depth	Gland (D)	5		8.5	9.5	11.1	
		Zone (d)	5		5.4	6.2	6.7	
	23	Length	Gland (L)	18		14.5	15.4	16.1
Zone (l)			18		8.5	9.9	11.6	
Width		Gland (W)	18		3.3	7.1	9.0	
		Zone (w)	18		1.8	4.5	5.5	
		Ratio (w/W)	18		50.7%	59.5%	67.9%	
Depth		Gland (D)	6		6.6	8.8	12.5	
		Zone (d)	6		3.2	5.0	7.9	
24		Length	Gland (L)	36	11.8	13.9	16.0	17.7
	Zone (l)		36	6.9	8.4	9.5	11.6	13.2
	Width	Gland (W)	36	2.7	4.1	6.8	8.7	10.5
		Zone (w)	36	1.1	1.6	3.5	4.8	6.0
		Ratio (w/W)	36	36.9%	40.0%	47.9%	57.3%	66.3%
	Depth	Gland (D)	12		7.6	9.8	11.3	
		Zone (d)	12		4.2	6.2	6.9	
	25	Length	Gland (L)	85	12.0	14.9	17.3	19.3
Zone (l)			85	7.4	9.1	10.7	12.2	13.9
Width		Gland (W)	85	3.2	4.3	8.0	9.7	11.7
		Zone (w)	85	1.4	2.0	4.5	5.6	6.5
		Ratio (w/W)	85	37.4%	43.7%	52.9%	60.3%	67.5%
Depth		Gland (D)	24	7.1	7.8	9.6	11.7	12.7
		Zone (d)	24	3.6	4.6	5.6	6.5	8.3
26		Length	Gland (L)	190	13.6	15.9	18.0	19.6
	Zone (l)		190	8.2	9.4	10.9	12.4	14.8
	Width	Gland (W)	190	4.0	7.0	8.6	9.8	11.6
		Zone (w)	190	1.6	3.0	4.3	5.5	6.5

Gestational Age (weeks)	Direction Measured (mm)	Entity Measured	N	Percentiles				
				10th	25th	50th	75th	90th
		Ratio (w/W)	190	35.6%	41.4%	49.4%	58.5%	66.8%
	Depth	Gland (D)	46	7.8	9.5	11.3	13.1	15.3
		Zone (d)	46	4.2	4.9	6.7	7.9	9.4
27	Length	Gland (L)	447	14.7	16.8	18.9	20.6	22.4
		Zone (l)	447	8.2	9.7	11.3	13.5	14.9
	Width	Gland (W)	446	3.8	7.3	9.1	10.8	12.6
		Zone (w)	446	1.5	3.1	4.5	5.9	7.2
		Ratio (w/W)	446	34.3%	40.6%	50.4%	58.6%	66.8%
	Depth	Gland (D)	118	8.1	10.0	11.2	13.3	15.2
		Zone (d)	118	3.6	4.6	6.5	8.0	9.5
	28	Length	Gland (L)	521	14.6	16.8	19.3	21.3
Zone (l)			521	8.5	10.3	12.1	13.7	15.4
Width		Gland (W)	520	4.1	7.2	9.1	10.9	12.5
		Zone (w)	520	1.6	3.1	4.8	6.0	7.2
		Ratio (w/W)	520	34.5%	41.5%	51.9%	60.4%	66.5%
Depth		Gland (D)	179	7.9	9.7	11.5	13.6	15.7
		Zone (d)	179	3.9	5.1	6.5	7.9	9.5
29		Length	Gland (L)	373	15.0	16.7	19.3	21.1
	Zone (l)		373	8.5	10.2	11.6	13.2	15.3
	Width	Gland (W)	372	4.1	6.8	9.1	10.9	13.0
		Zone (w)	372	1.5	2.8	4.6	5.7	7.3
		Ratio (w/W)	372	33.0%	39.9%	48.3%	58.1%	65.2%
	Depth	Gland (D)	121	8.1	9.5	10.9	13.2	15.0
		Zone (d)	121	3.9	4.9	6.0	7.7	9.5
	30	Length	Gland (L)	35	14.5	17.2	20.0	21.6
Zone (l)			35	7.6	9.6	11.6	13.2	13.5
Width		Gland (W)	35	4.5	7.5	8.9	10.2	12.0
		Zone (w)	35	1.9	3.3	4.1	5.3	6.6
		Ratio (w/W)	35	35.4%	39.2%	47.2%	54.7%	65.2%
Depth		Gland (D)	8		8.5	11.2	13.2	
		Zone (d)	8		3.2	4.8	6.7	

**Table 2**

## Baseline Characteristics of Women Included in Analysis

Characteristic	Statistic
Maternal age, in years	
Mean (standard deviation)	26.7 (5.6)
Median (interquartile range)	27.0 (22.0, 31.0)
N	1723
Gravidity: n (%)	
1	1274/1723 (73.9)
2	337/1723 (19.6)
3+	112/1723 (6.5)
Body mass index (BMI), in kg/m <sup>2</sup> : n (%) <sup>*</sup>	
Underweight / Normal (<25)	951/1714 (55.5)
Overweight (25 to <30)	422/1714 (24.6)
Obese / Morbidly Obese (30+)	341/1714 (19.9)
Maternal race/ethnicity: n (%)	
Non-Hispanic White	959/1723 (55.7)
Non-Hispanic Black	214/1723 (12.4)
Hispanic	395/1723 (22.9)
Asian	93/1723 (5.4)
Other	62/1723 (3.6)
Education status attained: n (%)	
less than high school	166/1723 (9.6)
completed high school or GED	225/1723 (13.1)
some college	334/1723 (19.4)
associate or technical degree	175/1723 (10.2)
completed college	447/1723 (25.9)
degree work beyond college	376/1723 (21.8)
Insurance: n/N (%) <sup>*</sup>	
government insurance	576/1708 (33.7)
military insurance	12/1708 (0.7)
commercial health insurance	1097/1708 (64.2)
personal household income	238/1708 (13.9)
other	28/1708 (1.6)
Income and size of household relative to Federal poverty level: n (%) <sup>*</sup>	
>200%	930/1353 (68.7)
100-200%	194/1353 (14.3)
<100%	229/1353 (16.9)



Characteristic	Statistic
Smoked during 3 months prior to pregnancy: n/N (%)	193/1723 (17.0)
Smoked in month prior to study ultrasound: n/N (%) *	71/1720 (4.1)
Chronic hypertension: n/N (%) *	59/1707 (3.5)
Diabetes: n/N (%) *	29/1710 (1.7)

\* This characteristic was not available on the total number of women included in the analysis. This is most notable for income. Percentages add to more than 100% for insurance, as participants were allowed to select multiple methods of payment.

**Table 3**

Fetal Adrenal Gland Measurements and Timing in Context with the Pregnancy for Spontaneous Preterm Births Versus Term Births\*

Variable	Spontaneous Preterm Birth			Term Birth		
	N	Median (IQR)	Range	N	Median (IQR)	Range
<b>Length (mm)</b>						
Gland (L)	82	18.9 (4.4)	10.4 – 24.3	156 2	18.8 (4.5)	7.6 – 35.6
Zone (l)	82	11.3 (3.6)	7.0 – 18.7	156 2	11.6 (3.5)	1.1 – 21.2
Ratio (l/L)	82	60.1% (16.4%)	46.9% – 86.1%	156 2	62.1% (16.0%)	7.0% – 88.8%
<b>Width (mm)</b>						
Gland (W)	82	9.2 (2.8)	1.8 – 17.0	156 0	8.9 (3.8)	1.9 – 18.8
Zone (w)	82	4.3 (2.3)	0.8 – 10.5	156 0	4.6 (2.9)	0.6 – 13.1
Ratio (w/W)	82	48.5% (15.9%)	19.9% – 79.5%	156 0	50.5% (18.3%)	14.5% – 85.8%
<b>Depth (mm)</b>						
Gland (D)	24	10.2 (3.0)	6.2 – 17.7	474	11.2 (3.8)	3.2 – 21.6
Zone (d)	24	6.0 (2.6)	3.3 – 12.4	474	6.4 (3.0)	1.7 – 12.7
Ratio (d/D)	24	58.1% (17.5%)	34.3% – 72.7%	474	59.3% (17.7%)	17.0% – 84.8%
<b>Gestational age (weeks)</b>						
Ultrasound	82	28.0 (2.0)	22 – 29	156 6	28.0 (1.0)	22 – 30
Delivery	82	36.0 (1.0)	30 – 36	156 6	39.0 (1.0)	37 – 42
<b>Ultrasound to Delivery (days)</b>	82	54.5 (15.0)	18 – 93	156 6	82.0 (15.0)	48 – 126

IQR=interquartile range.

\* No significant differences were noted on fetal adrenal gland measurements (at  $p < 0.05$ ) based on the Wilcoxon rank-sum test.