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Article

Maternal BMI and Diagnostic Accuracy of Estimated Fetal Growth to Predict Abnormal Birthweight: Results from the NICHD Fetal Growth Studies

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Abstract: Background/Objectives: To assess the diagnostic accuracy of sonographic estimated fetal weight (EFW) in predicting small (SGA) or large (LGA) for gestational age birthweight and examine its association with maternal body mass index (BMI). **Methods:** NICHD Fetal Growth Studies participants with complete data on maternal BMI (10–13.9 weeks), EFW within 14 days of delivery (18–41.3 weeks), and birthweight were included. Participants were categorized as normal (BMI 18.5–24.9 kg/m²) or overweight/obese (BMI >24.9 to 44.9 kg/m²). EFW accuracy was evaluated using area under the Receiver Operating Characteristics curves (AUC) for SGA and LGA classification, and EFW error was analyzed across BMI groups. **Results:** Among 1289 women, 714 (55.4%) were in the normal BMI group. AUCs for LGA prediction were similar between BMI groups (.77±.03 for normal vs. .79±.02 for overweight/obese, $p = .593$). However, for SGA, AUCs were higher in the overweight/obese group (.91±.01 vs. .84±.02, $p = .004$), indicating improved accuracy. EFW absolute and percent errors were comparable across BMI groups in the full, AGA, and LGA birth cohort separately, but were lower marginally ($p = .058$ and $.080$ for absolute and percent errors, respectively) in the overweight/obese group in the SGA birth cohort. **Conclusions:** EFW has acceptable accuracy for predicting LGA, unaffected by BMI. However, for SGA, EFW accuracy is significantly higher in the overweight/obese group, suggesting BMI influences diagnostic performance in SGA but not LGA classification.

Keywords: biomarkers; abnormal birthweight outcomes; BMI; Diagnosis; ROC curve

1. Introduction

In obstetrics, abnormal birth weight is an important predictor of complications among both newborns and mothers and an important indicator of neonatal morbidity. Macrosomia or large-for-gestational-age (LGA), defined as birthweight > 10th percentile for gestational age (GA) and small-for-gestational-age (SGA), defined as birthweight < 10th percentile for GA, are some well-studied birthweight categories used as a proxy for abnormal growth [1,2]. LGA is associated with a range of neonatal complications, including shoulder dystocia, brachial plexus injury, and birth asphyxia [3–5], while SGA as a proxy for intrauterine growth restriction is associated with an increased risk of hypoxia, perinatal asphyxia, and long-term developmental delays [6,7]. Delivery of LGA neonates also poses risks for mothers including genital tract injury, prolonged labor, and postpartum bleeding [8–12]. Early prediction of SGA and LGA is clinically important as it improves the management of delivery and postnatal care and reduces neonatal and maternal risks. Estimated fetal weight (EFW) using ultrasound fetal biometry has been studied extensively as such a predictor [13–17].

The accuracy of sonographic EFW in predicting birthweight could potentially be influenced by maternal body mass index (BMI), as ultrasound waves might be attenuated by excessive adipose

tissues and abdominal fat resulting in reduced image quality, difficulty in visualization of fetal structures and therefore more inaccurate measurements [18]. The associations of maternal BMI and the accuracy of EFW in predicting birthweight in the literature are mixed. Primarily using difference between EFW and actual birth weight as a measure of error, studies showed that maternal BMI does not impact the predictive power of EFW [19–24]. Others [25,26] found that the accuracy of EFW is lower (i.e., the error is higher) for women with higher BMI. Another study also found that high maternal BMI limits visualization of fetal anatomy during a standard ultrasound examination at 18 to 24 weeks [27].

These studies all assumed that the effect of maternal BMI on EFW accuracy is uniform for the entire distribution of birthweight. It is possible that any potential BMI effect may vary at different parts of the birthweight distribution. The tail regions of birthweight distribution are of special clinical importance, as the lower and upper deciles correspond to SGA and LGA, respectively. Neel et al. [28] evaluated the ability of the third trimester EFW to discriminate SGA and LGA but did not investigate the impact of BMI (they restricted to women with BMI > 35 kg/m²). They found limited ability of EFW in identifying SGA and LGA. In comparison, Dude et al. [29] found higher sensitivity of EFW in discriminating SGA and LGA than the Neel study, but the overall diagnostic accuracy measures were not significantly different between women with BMI 35–39 kg/m² and those with BMI ≥ 40 kg/m². This null finding could have been a result of low statistical power, as the sample size was small. [29] Both studies were in a single hospital setting, and included only participants with obese BMI, which may limit the generalizability of findings. Without a normal BMI group for comparison, it's hard to determine how BMI affects sensitivity, especially since factors like sonographer skill can also influence accuracy.

In this paper, we used data from a large pregnancy cohort to estimate diagnostic accuracies of late third trimester sonographic EFW in predicting SGA and LGA and to examine whether these diagnostic accuracy measures were associated with maternal BMI. We also investigated the accuracy of EFW in different parts of the birthweight distribution.

2. Materials and Methods

The NICHD Fetal Growth Studies-Singletons [30–32] included women who were obese (pre-pregnancy BMI: 30–44.9 kg/m²) and non-obese (pre-pregnancy BMI: 19–29.9 kg/m²). All participants were aged 18–40 years, had a viable singleton pregnancy, and intended to deliver at one of the participating hospitals. Recruitment took place at 12 clinical sites across the U.S. between July 2009 and January 2013, with follow-up through delivery. Human subjects' approval was obtained from all participating sites, the NICHD, and data-coordinating center, and all women gave written informed consent prior to any data collection (ClinicalTrials.gov Identifier: NCT00912132).

Following a standardized sonogram at 10w0d–13w6d, each woman was randomized to 1 of 4 follow-up visit schedules with 5 additional study sonograms (targeted ranges: 16–22, 24–29, 30–33, 34–37, and 38–41 gestational weeks). Study visits could occur ±1 week from the targeted GA. Study sonographers underwent training and credentialing prior to enrollment and followed a standardized protocol. Ultrasound measurements were performed using standard operating procedures and identical equipment. Fetal biometry included head circumference (HC) and abdominal circumference (AC) using the ellipse function, and femur length (FL) using the linear function measured at all study visits including 10w0d–13w6d. Voluson ultrasound machines were configured so that the sonographers were blinded to the measurements. EFW was computed from HC, AC, and FL using a formula of Hadlock et al. [33]. Measurements and images were captured in ViewPoint (GE Healthcare) and electronically transferred to the study's imaging data-coordination center. Quality assurance was performed on 5% of the scans and demonstrated correlations between the site sonographers and experts > 0.99 for all biometric parameters and coefficients of variation ≤ 3%. In-person interviews were conducted at each research visit to ascertain information on lifestyle, and reproductive and medical history. Demographic data; antenatal history; and labor, delivery, and

neonatal course and outcomes were abstracted from the prenatal record, labor and delivery summary, and hospital and neonatal records by trained research personnel.

Birthweight distribution was divided into three parts: SGA where birthweight is below 10th percentile for GA, LGA where birthweight is above 90th percentile for GA, and AGA between 10th-90th percentile of birthweight [34]. Absolute error was defined as the absolute value of estimated fetal weight minus birth weight, and absolute percent error was defined as absolute error divided by birth weight multiplied by 100. EFW of each woman at sonographic visit within 14 days of delivery date were used. If a woman had multiple ultrasound visits within 14 days of delivery date, only the last EFW was used.

We compared demographic and obstetric characteristics of women characterized by maternal BMI group using *t*-test for continuous variables, and chi-square test for categorical variables. Lehman family of ROC model [35] were used to estimate the AUC and associated standard errors and 95% confidence intervals. Comparisons were considered statistically significant at the *p* < 0.05 level for two-sided hypotheses. Analyses were performed using R (version 4.0.2, <http://www.R-project.org>).

Sensitivity analyses were performed across various subsets of the data to examine the robustness of the primary findings. One such analysis relaxed the 14-day threshold of a sonographic visit to within 7, 21, and 28 days of delivery. Additional sensitivity analyses were performed by restricting the delivery time to different GA windows: 34-36, 36-38, and 38-40 weeks, as compared to an unrestricted window in the primary analysis. Further sensitivity analyses were done on data with only term pregnancies, and on data with only nulliparous women. All the sensitivity analysis results were tabulated in the supplement.

3. Results

Of the enrolled women in the NICHD Fetal Growth Studies-Singletons, 1289 were used in the analysis; see the flow chart in Supp. Figure 1 for the various data attritions. Of those 1289 subjects, 99 (7.7%), 1060 (82.2%) and 130 (10.1%) were classified as SGA, AGA and LGA respectively. The BMI measured at enrollment was used to classify women into normal (BMI: 18.5-24.9) and overweight/obese (BMI: ≥ 25 to 45.0) groups. Respectively, 714 (55.4%) and 575 (44.6%) were in the normal and overweight/obese categories. Table 1 presents baseline characteristics of the cohort stratified by maternal BMI group. While maternal age, GA at ultrasound visit, and GA at delivery were not found to be associated with BMI (*p* = 0.293, 0.726 and 0.978 respectively), race and parity were associated (*p* < 0.001 for both). Overall, average birthweight was significantly higher for the overweight/obese compared to normal BMI group (*p* < 0.001). For the SGA births, the differences were not found to be statistically significant (*p* = 0.827). In contrast, for LGA births, average birthweight was higher in the overweight/obese group than in the normal BMI group (*p* = 0.038). Although the proportion of LGA was higher in the overweight/obese BMI group than in the normal group (*p* = 0.001), the proportions of SGA were not different between the two (*p* = 0.161). Overall, the amniotic fluid did not vary between the BMI groups (*p* = 0.306) or SGA/AGA/LGA groups (*p* = 0.825, 0.415, and 0.305 respectively).

Table 1. Characteristics of study participants by BMI group, 14 days threshold (* denotes significant difference between BMI groups).

Characteristics	BMI group		<i>p</i>
	Normal (n=714)	Overweight/Obese (n=575)	
Age (years)	28.6±5.4	28.3±5.5	0.293
Race			<0.001*
White	221 (31%)	154 (26.8%)	
African American	155 (21.7%)	189 (32.9%)	

Hispanic	172 (24.1%)	190 (33%)	
Asian & Pacific Islander	166 (23.2%)	42 (7.3%)	
BMI (kg/m ²) at enrollment	21.9±1.7	30.0±4.6	<0.001*
Parity			<0.001*
Parity: Nulliparous	359 (50.3%)	212 (36.9%)	
Parity = 1	252 (35.3%)	210 (36.5%)	
Parity > 1	103 (14.4%)	153 (26.6%)	
Amniotic fluid index	14.1±4.7±	14.4±4.8	0.306
Amniotic fluid index in SGA	11.9±4	11.8±3.9	0.825
Amniotic fluid index in AGA	14.1±4.7	14.3±4.7	0.415
Amniotic fluid index in LGA	17.0±4.8	16.0±5.2	0.305
GA at US visit (weeks)	38.2±1.5	38.2±1.6	0.978
GA at delivery (weeks)	39.3±1.4	39.3±1.6	0.726
Time to delivery (days)	7.8±4.1	7.6±4.0	0.409
Birthweight (g)	3312.6±461.1	3434.4±496	<0.001*
Birthweight in SGA (g)	2648.1±267.2	2659.8±241.4	0.827
Birthweight in AGA (g)	3317±380.8	3376±384.3	0.013*
Birthweight in LGA (g)	4040.7±310.7	4156.7±309.1	0.038*
EFW (g)	3182.1±504.4	3309.7±547.3	<0.001*
EFW within 10% of birth weight	506 (70.9%)	408 (71.0%)	1.000
EFW within 20% of birth weight	689 (96.5%)	557 (96.9%)	0.994
Absolute error (g)	251.4±181.5	258.6±209.1	0.506
Absolute percent error	7.6±5.4	7.6±5.9	0.881
SGA	62 (8.7%)	37 (6.4%)	0.161
LGA	53 (7.4%)	77 (13.4%)	0.001*

The discriminatory capacity of EFW to differentiate LGA and non-LGA birthweight was not different ($p = 0.562$) between the two BMI groups (AUC 0.769 and 0.788 respectively for normal and overweight/obese group, Table 2). For differentiating SGA from non-SGA, the discriminating capacity differed between BMI groups ($p = 0.002$) with AUC estimates of 0.839 and 0.911 for normal and overweight/obese groups, respectively. For both BMI groups, the AUC estimates for discriminating SGA from non-SGA were found to be higher than that for discriminating LGA from non-LGA.

Table 2. AUC estimates of EFW for discriminating LGA and SGA by BMI group, 14 days threshold (* denotes significantly difference between BMI groups).

BMI group	SGA			LGA		
	Est	SE	<i>p</i>	Est	SE	<i>p</i>
Normal	0.839	0.019	0.002*	0.769	0.027	0.562
Overweight/Obese	0.911	0.015		0.788	0.022	

Absolute (percent) errors of EFW for the entire cohort ranged from 251.4±181.5 g (7.6±5.4) to 258.6±209.1 g (7.6±5.9) for normal and overweight/obese BMI groups, respectively, although the differences were not statistically significant ($p = 0.506$ for absolute error and $p = 0.881$ for absolute percent error). Similar nonsignificant associations between BMI and absolute and percent errors were

found separately for AGA and LGA cohorts. For the AGA cohort, the absolute (percent) errors of EFW ranged from 249.2±178.4 g (7.6±5.4) to 253.0±191.6 g (7.6±5.8) with $p = 0.744$ and 0.937 respectively for absolute error and absolute percent error (Table 3). For the LGA cohort, the absolute (percent) errors of EFW were 346.4±223.4 g (8.7±5.7) and 348.6±297.8 g (8.4±7.1) with $p = 0.963$ and 0.831 (Table 3). Although the overweight/obese BMI group had slightly higher absolute error for LGA and AGA, the opposite was observed for SGA. Among the SGA cohort, the absolute (percent) errors of EFW were 191.0±137.5 g (7.2±5.1) and 141.9±92.9 g (5.5±3.8) for normal and overweight/obese BMI groups respectively, with $p = 0.058$ and 0.080 . Although only marginally significant, these results confirm the AUC findings that EFW has a higher accuracy in predicting birthweight among women in the overweight/obese BMI group than those in the normal BMI group for discriminating SGA.

Table 3. Distribution of important covariates by BMI group, for different diseased categories, 14 days threshold (* denotes significant difference between BMI groups).

Birthweight category	Characteristics	BMI group		p
		Normal	Overweight/Obese	
SGA	n	62	37	
	EFW within 10% of birth weight	71.0	86.5	0.128
	EFW within 20% of birth weight	100.0	100.0	-
	GA at US visit (weeks)	38.0±1.2	38.1±1.4	0.922
	GA at delivery (weeks)	39.2±1.3	39.1±1.4	0.740
	Time to delivery (days)	8.3±4.3	7.5±3.6	0.336
	EFW (g)	2617.2±394.4	2604±295.8	0.861
	Absolute error (g)	191.0±137.5	141.9±92.9	0.058
	Absolute percent error	7.2±5.1	5.5±3.8	0.080
AGA	n	599	461	
	EFW within 10% of birth weight	71.3	70.7	0.893
	EFW within 20% of birth weight	96.2	96.7	0.732
	GA at US visit (weeks)	38.2±1.5	38.2±1.7	0.833
	GA at delivery (weeks)	39.3±1.4	39.3±1.6	0.615
	Time to delivery (days)	7.8±4.0	7.6±4.0	0.452
	EFW (g)	3188.3±452.8	3262.4±470.4	0.010*
	Absolute error (g)	249.2±178.4	253.0±191.6	0.744
	Absolute percent error	7.6±5.4	7.6±5.8	0.937
LGA	n	53	77	
	EFW within 10% of birth weight	66.0	64.9	1.000
	EFW within 20% of birth weight	96.2	96.1	1.000
	GA at US visit (weeks)	38.1±1.3	38.2±1.2	0.560
	GA at delivery (weeks)	39.2±1.2	39.3±1.1	0.450
	Time to delivery (days)	7.8±3.9	8±4.2	0.789
	EFW (g)	3772.5±460.7	3931.4±483.6	0.063
	Absolute error (g)	346.4±223.4	348.6±297.8	0.963
	Absolute percent error	8.7±5.7	8.4±7.1	0.831

For the combined cohort, the proportion of ultrasound EFW within ±10% and within ±20% of the birth weight were similar between the BMI groups. Overall, percentages of EFW within ±10%

($\pm 20\%$) were 70.9% (96.5%) and 71.0% (96.9%) for normal and overweight/obese BMI groups respectively ($p = 1.000$ and 0.832 respectively). The same pattern of similar percentages classified within $\pm 10\%$ and $\pm 20\%$ was true for both the AGA and LGA cohorts. For AGA cohort, percentages of EFW within $\pm 10\%$ ($\pm 20\%$) were 71.3% (96.2%) and 70.7% (96.7%) for normal and overweight/obese BMI groups respectively ($p = 0.893$ and 0.732). For LGA cohort, percentages of EFW within $\pm 10\%$ ($\pm 20\%$) were 66.0% (96.2%) and 64.9% (96.1%) for normal and overweight/obese BMI groups respectively ($p = 1.000$ for both BMI groups). In contrast for the SGA cohort, percentages of EFW within $\pm 10\%$ ($\pm 20\%$) were 71.0% (100%) and 86.5% (100%) for normal and overweight/obese BMI groups respectively ($p = 0.128$ for within $\pm 10\%$ and not available for within $\pm 20\%$) denoting higher accuracy for the overweight/obese group, despite lack of statistical significance. These findings were also consistent with those that evaluated AUC and absolute (percent) errors.

The sensitivity results using different lengths of time between the last EFW and birthweight (7, 21, 28 days) were generally consistent with the primary findings (Supp. Tables 1–3). Specifically, there were no differences in diagnostic accuracy for LGA between BMI groups, but for discriminating SGA, the diagnostic accuracy estimates of overweight/obese group were all higher than the normal group.

The analyses using EFW from different GA windows (Supp. Tables 4–5) yielded AUC estimates (Supp. Table 4) that were directionally consistent with the primary findings. For the AGA and LGA cohorts, errors remained stable or showed non-significant increases with higher BMI. However, for the SGA cohort, error metrics were lower in the overweight/obese group within the 38–40 weeks GA window ($p = 0.019$ and 0.028 for absolute error and absolute percent error, respectively; Supp. Table 5).

Similarly, analyses restricted to term pregnancies and nulliparous women (Supp. Tables 6, 8) showed comparable patterns to the primary results. While the error trends for term pregnancies (Supp. Table 7) aligned with the main findings, results for nulliparous women (Supp. Table 9) diverged. Specifically, for overall, SGA, and LGA cohorts, errors tended to decrease—though not significantly—with increasing BMI.

4. Discussion

The novel findings in this paper contribute to our understanding of the diagnostic capacities of EFW in differentiating between SGA and non-SGA, as well as LGA and non-LGA fetuses. Specifically, we found that when distinguishing between SGA and non-SGA, the diagnostic capacity of EFW was notably higher in the overweight/obese group compared to the normal BMI group. This finding suggests that maternal BMI may play a role in the accuracy of EFW in predicting SGA in these populations. However, when attempting to discriminate between LGA and non-LGA, the results were less clear-cut. The direction of the estimates for LGA discrimination was mixed, and none of the estimates reached statistical significance. The combination of SGA/higher BMI that improves the predictive power of EFW is notable. SGA fetuses include those with intrauterine growth restriction (IUGR), which is often caused by placental insufficiency or other pathological conditions, such as maternal pregestational diabetes and hypertensive disorders of pregnancy [36]. In women with higher BMI, these factors may be more pronounced, leading to a more apparent discrepancy between the expected and actual fetal growth.

Interestingly, the diagnostic capacity to discriminate SGA from non-SGA was generally higher than that of discriminating LGA from non-LGA. This higher discriminant ability was corroborated by the finding that the absolute (percent) errors of EFW were generally higher for LGA and lower for SGA, which is consistent with what others have found [37]; measurements may be more accurate in a smaller fetus. In the case of LGA, there are often difficulties in accurately measuring fetal dimensions due to the larger size of the fetus. This can introduce measurement errors that are more significant in LGA fetuses compared to SGA fetuses, especially in cases of maternal factors that affect the clarity of ultrasound imaging.

The unexpected finding of higher discriminant ability for SGA in women with overweight or obesity compared to women with normal BMI warrants further investigation. Although the AUC for

predicting SGA was relatively high for both BMI groups, the lower variability in EFW for women with overweight/obese BMI may have contributed to the higher AUC in this group. There may also be unknown factors that influence both maternal BMI and SGA prediction.

There are a few limitations in this study that should be considered when interpreting the results. Firstly, the study cohort predominantly consisted of women with lower-risk pregnancies, which may limit the generalizability of the findings to higher-risk populations. Women with complex medical conditions or those who are at a higher risk for adverse pregnancy outcomes may exhibit different diagnostic patterns, and the findings from this cohort may not fully apply to these groups.

Another limitation lies in the BMI categorization. The study groups—normal BMI and overweight/obese—were based on the maternal BMI measured at the beginning of the pregnancy rather than on the BMI closer to delivery. Maternal weight and BMI can change significantly throughout pregnancy, and these changes may influence fetal growth and the diagnostic accuracy of EFW. By relying solely on baseline BMI, the study may not fully account for these changes, potentially affecting the accuracy of its findings.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org. In the supplementary material, we have mainly provided sensitivity analyses to validate our main findings. The sensitivity analysis is done for different subsets of the data categorized by different thresholds (Supp. Tables 1–3), different GA windows (Supp. Tables 4–5), only term pregnancy at 14 days threshold (Supp. Tables 6–7), and only nulliparous cohort at 14 days threshold (Supp. Tables 8–9).

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data generated by this project will be available upon reasonable request from the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

The following abbreviations are used in this manuscript:

SGA	Small for gestational age
LGA	Large for gestational age
AGA	Appropriate for gestational age

GA	Gestational age
BMI	Body mass index
EFW	Estimated fetal weight
NICHD	Eunice Kennedy Shriver National Institute of Child Health & Human Development
ROC	Receiver Operating Characteristics
AUC	Area under ROC curve
HC	Head circumference
FL	Femur length
AC	Abdominal circumference

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