

Analysis of factors influencing accuracy of ultrasound-based fetal weight estimation

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Abstract

Context: The primary objective of this study was to examine the impact of maternal age, parity, gestational age, fetal gender, gestational diabetes mellitus, and pregnancy-induced hypertension on the accuracy of ultrasonography-based fetal weight estimation. The secondary objective was to find the impact of a formula selection on the accuracy of fetal weight estimation. **Subjects and Methods:** The inclusion criteria were a live-birth singleton pregnancy and the last ultrasound scan to delivery interval ≤ 7 days. Fetal weight was estimated using the Hadlock-4 formula. To study the concurrent impact of all the factors on the accuracy, cases were divided into two subcategories based on percentage error, with $\pm 10\%$ as a threshold. The accuracy of Hadlock-4 formula was compared with the two Indian population-based formulas, Hiwale-1 and Hiwale-2. **Results:** In total, 184 cases were included in the study. It was observed that the systematic error in weight estimation was significantly less in the male fetuses ($8.45 \pm 9.34\%$) in comparison to the female fetuses ($11.71 \pm 10.34\%$). The combined impact of all the factors on the accuracy was found to be nonsignificant by the multivariate analysis. The Hiwale-1 ($-0.59 \pm 8.75\%$) and Hiwale-2 ($-0.65 \pm 8.7\%$) formulas had statistically significant less errors compared to the Hadlock-4 formula ($11.67 \pm 7.95\%$). **Conclusion:** All the studied clinical factors were found to have a limited impact on the overall accuracy of fetal weight estimation. However, the formula selection was found to have a significant impact on the accuracy, with the native population-based formulas being significantly more accurate.

Key words: Factors affecting accuracy; fetal ultrasonography; fetal weight; India; multivariate analysis

Introduction

A number of maternal, fetal, and acquisition related factors have been investigated to find out their possible impact on the accuracy of ultrasound-based fetal weight estimation.^[1-5] Among these factors, formula/model accuracy, amniotic fluid index (AFI), maternal body mass index (BMI), fetal weight, presentation, and fetal gender are the most studied factors.^[6,7] Other factors, such as the time gap between ultrasound scan and delivery, measurement

error, and examiner's skill and experience, have been also investigated to find out their potential impact on the accuracy of fetal weight estimation.^[8-11] However, the exact impact of these factors is still not fully understood. Conflicting results from the different studies have made it even more complicated.^[6] Variations in study design and statistical analysis, nonconsistent categorization of the

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influencing factors, and use of different formulas for fetal weight estimation make it even more difficult to draw a valid inference from these studies.

Given the importance of fetal weight estimation in clinical decision making, it is imperative for a practitioner to have detailed information on the possible sources of inaccuracy and their extent. Having such information could help a practitioner to account for such factors for informed decision making. Unfortunately, not much work has been published from India on this particular topic.^[12,13] Moreover, difference in genetic, anthropometric, nutritional, and fetal growth patterns between Indian and other populations^[14] makes it impractical to use accuracy information published on other populations for the Indian population.^[15] On the contrary, use of information from other population-based studies may lead to propagation of error, making the estimation more inaccurate and may lead to bad clinical decisions. This study was undertaken considering this gap in the existing literature.

The primary objective of this study was to systematically evaluate the impact of six maternal and fetal factors on the accuracy of ultrasound-based fetal estimation in an Indian population. In this study, we examined the following factors: maternal age, parity, gestational age (GA), fetal gender, gestational diabetes mellitus (GDM), and pregnancy-induced hypertension (PIH). These factors were selected as they are not studied by the earlier studies from India, and there is still no consensus in the literature on their exact impact.^[6] It has been observed that no single ultrasound-based fetal weight estimation formula is applicable for all the populations^[16]; this has led to the development of many indigenous population-based models. Therefore, the secondary objective of the study was to examine impact of a formula/model selection on the fetal weight estimation accuracy. For this purpose, two Indian population-based models, Hiwale-1 and Hiwale-2,^[17] were compared with the Hadlock-4 model,^[18] which is based on a population from the United States of America.

Subjects and Methods

Study design

For this retrospective study, a de-identified database of pregnant women obtained from a tertiary care hospital was used. The inclusion criteria were a live-birth singleton pregnancy and the last ultrasound scan to a delivery interval less than or equal to 7 days. Cases with suspected chromosomal or structural anomalies or fetal malformation were excluded as they are known to impact the accuracy of fetal weight estimation.^[19,20] Similarly, cases with postpartum maternal or neonatal death were also excluded. Each newborn was weighed immediately after birth. Small for gestational age or large for gestational age newborns

were excluded as general-purpose fetal weight estimation formulas are shown to have high errors at the extreme ends of a birth weight range.^[12,16] The ultrasound scans were performed using standard protocols by experienced radiologists to obtain four fetal biometry parameters: abdominal circumference (AC), biparietal diameter (BPD), head circumference (HC), and femur length (FL). In total, 184 cases met the inclusion and exclusion criteria and were considered for final analysis.

Based on the fetal biometry parameters, fetal weight was estimated using the Hadlock-4, Hiwale-1, and Hiwale-2 models as per the formulas published in the literature [Table 1]. The Hadlock-4 formula was selected for the study as it is one of the most frequently used formulas for fetal weight estimation,^[6,18] and secondly to make sure that results of this study can be compared with other similar studies. In this study, we examined the following parameters: Maternal age, parity, gestational age, fetal gender, GDM, and PIH. For inclusion, gestational age was determined using the date of the last menstrual period; in the case of ambiguity, gestational age by ultrasound examination was considered. For statistical analysis, gestational age was rounded off to the completed weeks. The retrospective data used for the study was obtained in accordance with local regulations after approval of an ethical committee.

Statistical analysis

An estimated fetal weight (EFW) given by the Hadlock-4 formula and the actual birth weight (ABW) were used to calculate percentage error (PE) as follows:

$$\text{Percentage Error} = \left(\frac{\text{EFW} - \text{ABW}}{\text{ABW}} \right) \times 100$$

The relationship between the continuous variables (maternal age and gestational age) and absolute percentage error (APE) was studied using the Spearman's rank correlation coefficient. We observed that many studies in the past have used some categorization for maternal age (e.g., older than 35 years or not) and gestational age (e.g., <37 or >42 weeks, etc.). However, such arbitrary categorizations often lead

Table 1: Details of selected ultrasound-based fetal weight estimation formulas

Model	Population base	Formula
Hadlock-4 ^[18]	USA	$\text{Log}_{10}(\text{EFW}) = 1.3596 + 0.0064(\text{HC}) + 0.0424(\text{AC}) + 0.174(\text{FL}) + 0.00061(\text{BPD})(\text{AC}) - 0.00386(\text{AC})(\text{FL})$
Hiwale-1 ^[17]	India	$\text{Log}_{10}(\text{EFW}) = 2.7843700 + 0.0004197(\text{HC} * \text{AC}) + 0.0008545(\text{AC} * \text{FL})$
Hiwale-2 ^[17]	India	$\text{Log}_{10}(\text{EFW}) = 2.3870211110 + 0.0074323216(\text{HC}) + 0.0186555940(\text{AC}) + 0.0013463735(\text{BPD} * \text{FL}) + 0.0004519715(\text{HC} * \text{FL})$

AC=Abdominal circumference; BPD=Biparietal diameter; EFW=Estimated fetal weight; FL=Femur length; HC=Head circumference; USA=United States of America

to information loss and are not recommended from the statistical point of view.^[21] Therefore, in this study, we did not use any forced categorization for the continuous variables. For the categorical variables such as nulliparity, fetal gender, GDM, and PIH, independent-sample Student *t*-test was used to study the impact of their subcategories on the PE.

The concurrent impact of the maternal and fetal factors on the fetal weight estimation accuracy was studied by computing adjusted odds ratio (OR) with 95% confidence interval (CI) via multivariate logistic regression. For the multivariate analysis, cases were categorized into two subcategories based on the PE. The first category had cases with the PE within $\pm 10\%$; the second category had cases with the PE beyond $\pm 10\%$. The threshold for categorization was set at $\pm 10\%$, as a fetal weight estimation with more than $\pm 10\%$ variation is likely to impact decision making in clinical practice.^[9,16]

The Hadlock-4 and the two Indian population-based formulas were compared using the mean of percentage error (MPE); paired Student *t*-test was used for this purpose. Random errors (standard deviation of MPE) between the formulas were compared using Levene's test. APE between the formulas was compared using Wilcoxon signed-rank test. A number of cases with the PE within $\pm 10\%$ for each formula were compared using Chi-squared test. For all the comparisons, a *P* value < 0.05 was considered a statistically significant difference. All the statistical analyses were performed in R (version 3.4.4) and MATLAB (2016b, Mathworks).

Results

In total, 184 cases met the inclusion and exclusion criteria and were considered for final analysis. The mean maternal age of the study population was 23.70 ± 3.44 years. The nulliparous women constituted 46.2% of the study population. The median gestational age was 38 weeks (range, 32 to 41.2 weeks), with 45 preterm cases. The average duration between ultrasound scan and delivery was 2.7 days; 53.26% cases had it performed within two days before the delivery. The mean birth weight of the study population was 2750.50 ± 386.66 g, with a range of 1680 g to 3860 g; 51 newborns had ABW less than 2500 g. The female babies ($n = 88$) constituted 47.83% of the study population, whereas male babies accounted for 52.17% of the study population. The mean

percentage error (MPE) in the fetal weight estimation was $10.01 \pm 9.97\%$, whereas the absolute percentage error (APE) was $11.66 \pm 7.95\%$ by the Hadlock-4 formula. The MPE for the Hiwale-1 and Hiwale-2 model was $-0.59 \pm 8.75\%$ and $-0.65 \pm 8.70\%$, respectively, whereas APE was $6.68 \pm 5.67\%$ and $6.65 \pm 5.63\%$, respectively.

Univariate analysis

Both the continuous variables, maternal age and gestational age, were found to be weakly correlated with the APE [Table 2]. The maternal age was found to have a negative correlation with the APE; this means an increase in maternal age was associated with less APE in fetal weight estimation. However, this association was weak and statistically nonsignificant. Birth weight was also found to have a negative correlation with APE; albeit stronger than age, but statistically nonsignificant. On the other hand, gestational age had a weak positive correlation with APE.

The MPEs in the two subcategories of nulliparity, fetal gender, GDM, and PIH are summarized in Table 3. Out of these factors, only fetal gender was found to have a statistically significant difference in the accuracy [Figure 1], with the male fetuses having significantly less MPE ($8.45 + 9.34\%$) as compared to the female fetuses ($11.71 + 10.34\%$).

Multivariate analysis

For multivariate analysis, the study population was divided into two subcategories based on the PE; the demographic characteristics of the cases in these two subcategories are summarized in Table 4. No significant difference was found between the two subcategories for the studied parameters.

Multivariate logistic regression analysis was used to find out a concurrent impact of all the factors on the accuracy of ultrasound-based fetal weight estimation [Table 5]. Both GDM and PIH had less than 10 cases in some individual subcategories and, therefore, were excluded in the multivariate analysis. It was observed that advanced maternal age and male fetal gender were associated with more accurate fetal weight estimation (more cases within $\pm 10\%$ of PE), whereas higher gestational age and nulliparity were found to be associated with less accurate fetal weight estimation. However, based on adjusted OR and 95% CI, none of these factors were found to have any statistically significant impact on the overall accuracy.

Table 2: Relationship of the continuous variables and the absolute percentage error

Characteristic	Mean (\pm SD) ($n=184$)	Spearman's correlation with APE	Statistical significance
Maternal age (year)	23.70 (± 3.43)	-0.049	NS
Gestational age (week)	38.21	0.066	NS
Birth weight (g)	2750.50 (± 386.66)	-0.335	NS

APE=Absolute of percentage error; NS=Nonsignificant; SD=Standard deviation

Comparison of the formulas

It was observed that both the Indian population-based formulas, Hiwale-1 ($-0.59 \pm 8.75\%$) and Hiwale-2 ($-0.65 \pm 8.7\%$), had statistically significant less errors compared to that of Hadlock-4 ($11.67 \pm 7.95\%$) formula [Figure 2]. The Indian formulas also had less random error but it was not significantly different from the Hadlock-4 formula. The Indian formulas also had significantly lower APEs and a significantly higher number of cases

Table 3: Impact of the categorical factors on the accuracy of fetal weight estimation

Characteristic	Subcategory	n	MPE (SD)	Statistical significance
Nulliparity	Yes	85	10.39 (9.84)	NS
	No	99	9.67 (10.11)	
Fetal gender	Male	96	8.45 (9.34)	Significant ($P=0.028$)
	Female	88	11.71 (10.34)	
GDM	Yes	6	3.16 (13.43)	NS
	No	178	10.24 (9.8)	
PIH	Yes	16	11.24 (8.30)	NS
	No	168	9.89 (10.12)	

GDM=Gestational diabetes mellitus; PIH=Pregnancy-induced hypertension; MPE=Mean percentage error; NS=Nonsignificant (by independent-sample Student t-test); SD=Standard deviation

with the PE within $\pm 10\%$ in comparison to the Hadlock-4 formula [Table 6].

Discussion

Excellent safety profile, ease of use, and wide availability have made ultrasound a modality of choice for intrauterine fetal assessment. Given its dominant position in clinical practice, clinicians often take the ultrasound-based weight estimation as a proxy for the actual birth weight; this is usually done without due consideration of the factors, which can affect its accuracy. This is precarious as inaccurate fetal weight estimation can lead to unnecessary or delayed interventions, putting both a mother and fetus at a risk. Considering this, the primary objective of this study was to systematically evaluate the impact of clinical factors and formula selection on the accuracy of ultrasound-based fetal weight estimation. The important findings of this study are: (1) the overall accuracy of ultrasound-based fetal weight estimation by the Hadlock-4 formula was low with high systematic and random error; (2) the male fetuses had significantly less systematic error in comparison to the female fetuses; (3) all studied clinical factors had a limited

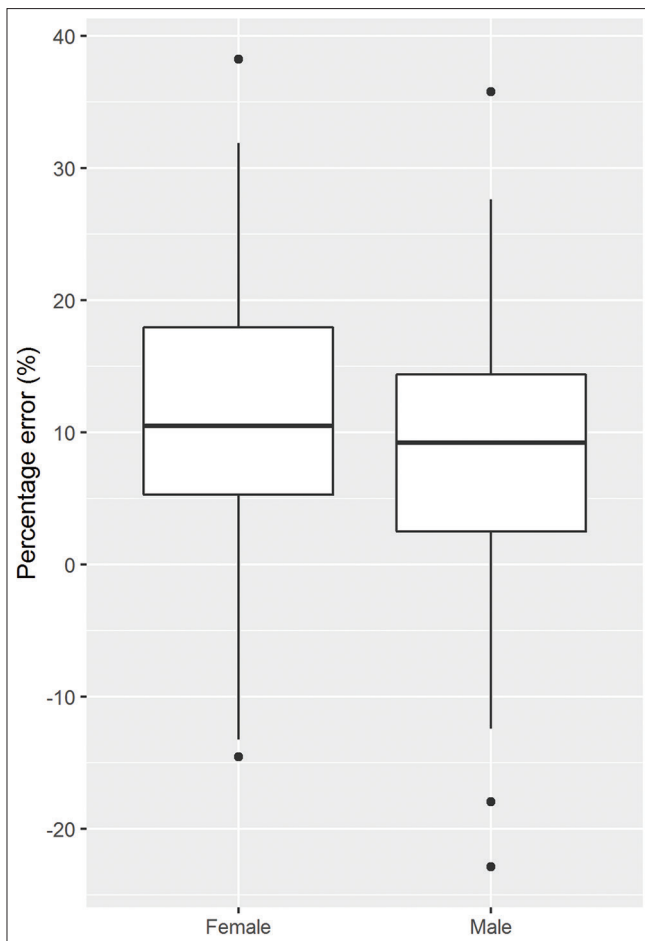


Figure 1: Percentage error in fetal weight estimation according to the fetal gender

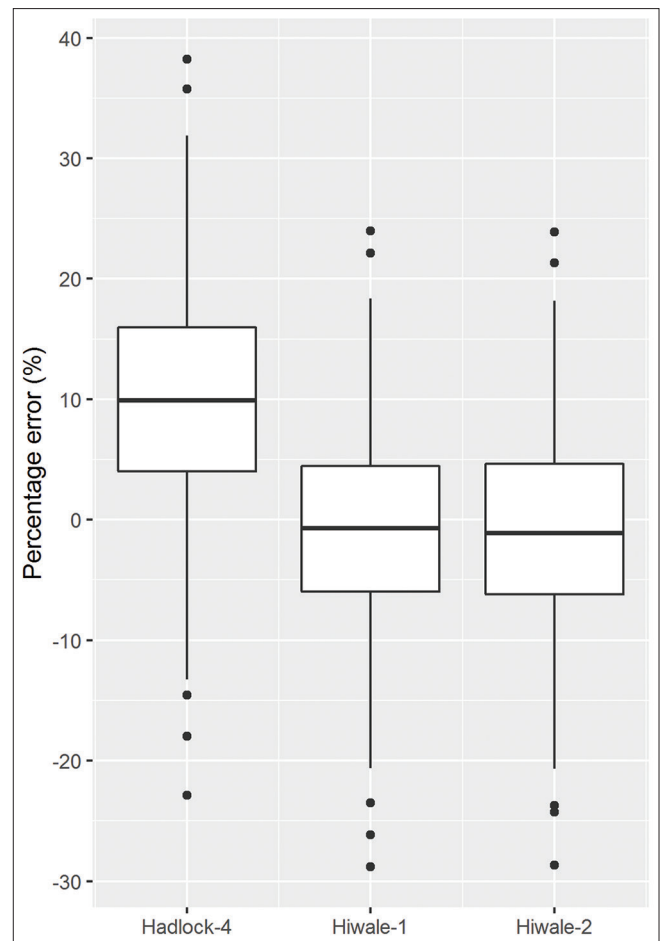


Figure 2: Percentage error in the fetal weight estimation by the different formulas

Table 4: Distribution of the study population in the two PE-based categories

Characteristic	Subcategory	Study population (n=184)	PE within ±10% (n=86)	PE beyond ±10% (n=98)	Statistical significance
Maternal age (year)		23.70 (±3.43)	23.82 (±3.66)	23.59 (±3.24)	NS*
Gestational age (week)		38.21 (±1.20)	37.5 (±1.60)	37.66 (±1.45)	NS*
Nulliparity	Yes	85	38	47	NS†
	No	99	48	51	
Fetal gender	Male	96	48	48	NS†
	Female	88	38	50	
GDM	Yes	6	1	5	NS‡
	No	178	85	93	
PIH	Yes	16	6	10	NS†
	No	168	80	88	

Numerical values are expressed in mean (± standard deviation); for categorical factors, frequency of occurrence is given. GDM=Gestational diabetes mellitus; PIH=Pregnancy-induced hypertension; NS=Nonsignificant (by *Student's t-test; †Chi-squared test; ‡Fisher exact test); PE=Percentage error

Table 5: Concurrent impact of the different parameters on the accuracy of fetal weight estimation by multivariate analysis

Risk factor	Adjusted OR	CI lower limit	CI upper limit	P
Maternal age (Year)	1.013	0.927	1.106	0.776
Gestational age (Week)	0.952	0.779	1.160	0.626
Nulliparity (Yes/No)	0.895	0.489	1.635	0.719
Fetal gender (Male/Female)	1.278	0.709	2.309	0.414

CI=95% confidence interval; OR=Odds ratio

Table 6: Accuracy performance of the different formulas

Model	MPE (SD)	P*	APE (SD)	P†	PE within ±10%	P‡
Hadlock-4	10.01 (9.97)	-	11.67 (7.95)	-	86	-
Hiwale-1	-0.59 (8.75)	<0.01	6.68 (5.67)	<0.01	142	0.030
Hiwale-2	-0.65 (8.70)	<0.01	6.65 (5.63)	<0.01	144	0.026

APE=Absolute percentage error; PE=Percentage error; MPE=Mean percentage error; SD=Standard deviation. *by Student t-test; †by Wilcoxon signed-rank test; ‡by Chi-squared test, with Hadlock-4 formula as a reference

impact on the accuracy as per the PE-based categorization; and (4) formula selection had a significant impact on the accuracy with the Indian population-based formulas having statistically significant less error compared to that of the Hadlock-4 formula.

The error in ultrasound-based fetal weight estimation can be divided into two components: systematic error and random error. The Hadlock-4 formula showed both high systematic and random error in our population. Systematic error is due to an inherent limitation in use of ultrasound-based fetal biometry parameters as a surrogate measure for fetal weight estimation. Any factor that influences fetal biometry parameters is thus likely to contribute to systematic error. As it is not possible to eliminate systematic error totally, it is important to identify factors contributing to it, so that appropriate corrective measures can be developed. Random error is due to errors in measurement of fetal biometry parameters. The technical factors, such as variation in measurements due to intra-observer and inter-observer differences, image quality, device calibration,

and experience and education of the sonologist, contribute to the random error. Due to significant variations in the above-mentioned factors, random error of less than 7% has been rarely observed in the literature.^[16,22] Steps such as standardization of measurement techniques, proper device maintenance, and continuous education and training of doctors are likely to reduce this error.

The earlier studies from India have evaluated the impact of amniotic fluid index (AFI)^[13] and fetal weight^[12] on the accuracy of ultrasound-based fetal weight estimation. Wadnere *et al.* found that there is no significant association between AFI and the accuracy of ultrasound-based fetal weight estimation.^[13] However, fetal weight has been found to have a significant impact on the accuracy, with a general tendency of weight overestimation in the low birth weight fetuses and underestimation in the macrosomic fetuses.^[12] In this study, we evaluated six additional maternal and fetal factors, which could contribute to systematic error in fetal weight estimation. We found that accuracy of fetal weight estimation was different only for the fetal gender, with the male fetuses having statistically significant less error. Similar findings have been reported by many studies, and a few of them have also proposed sex-specific models for fetal weight estimation.^[2,23-25] The slow intrauterine growth rate in the female fetus compared to that of the male fetus has been put forward as one possible explanation of this phenomenon.^[23,26] However, there is still no consensus on an exact impact of fetal gender on the accuracy of weight estimation.^[1,4] Although significant on its own, fetal gender alone was not fully adequate to justify the magnitude of overall error. Other studies have also found that contribution of maternal and fetal factors in overall inaccuracy is limited.^[1,2,7,9,27,28]

As a number of factors are shown to have impact on the accuracy of fetal weight estimation, it is very important to study their combined impact on the overall accuracy. However, not many studies have evaluated such impact in the past. In this study, we have used multivariate logistic regression analysis to study a concurrent impact of the

various factors. We found that none of the studied factors had a significant impact on the accuracy. Other studies have also observed a similar trend using multivariate analysis.^[27] This indicates that combined impact of the studied clinical factors on the overall accuracy is also limited.

A number of studies have observed that the formula/model selected for the fetal weight estimation has the maximum influence on the accuracy.^[2,6,9,15,16] As a number of factors such as genetics, anthropometry, nutrition, and population characteristics are known to impact the fetal weight, it is important to use a formula, which is appropriate for the underlying population.^[15] This is the reason that many population-specific models have been developed for fetal weight estimation.^[15] For Indian fetuses, a significant difference has been observed in growth pattern when compared to the Western populations.^[14] In our study, we observed that the India population-based models had a significantly lower systematic and random error as compared to that of Hadlock-4 model. This further highlights the limitation of using models developed on other populations for Indian populations.

The two important limitations of our study are its retrospective design and small sample size. Due to the retrospective design, we could not evaluate the impact of maternal weight gain and BMI on fetal weight accuracy. Similarly, operator-related factors such as education, experience, protocols followed, and technical factors (ultrasound machine calibration, configuration, etc.) also have important bearing on the overall error in fetal weight estimation. However, the current study design also makes it unfeasible to study inter and intra-observer related errors, which are an important source of random error in ultrasound diagnosis. Nevertheless, standardization of protocols, techniques, and proper training are important measures to minimize the random error. The strength of our study lies in being one of the earliest studies on Indian population where various factors are studied systematically using multivariate regression analysis to find their concurrent impact on the accuracy of fetal weight estimation.

To conclude, a number of maternal, fetal, and technical factors are known to impact the accuracy of ultrasound-based fetal weight estimation. Therefore, it is very important that a clinician has detailed knowledge about it. In our study, we observed that among the various factors, which can have an impact on the accuracy of fetal weight estimation, a selection of appropriate models is the most important factor. Hence, we recommend that all available formulas should be thoroughly evaluated with well-designed large prospective studies before selection of a final formula for fetal weight estimation. Furthermore, in an era where personalized medicine is the ultimate target and automation of ultrasound measurements is around the corner, the use

of customized models for a given patient population could be a game-changer for more accurate ultrasound-based fetal weight estimation.

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Conflicts of interest

There are no conflicts of interest.

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