

# Gestational age estimation from ultrasound fetal biometrics in China

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## Summary

**Objective:** To establish a new gestational age estimation equation in China and compare them with commonly used equations of 2017 and 1984. **Methods:** A prospective cross-sectional study was performed in 3208 fetuses between 15 and 40 weeks of gestation. The following biometric variables were recorded: biparietal diameter, head circumference, abdominal circumference, and femur length. Women with a certain gestational age were confirmed by the last menstrual period with a regular cycle of 26–32 days. Subsequently, a mixed regression model was used for regression analysis for the estimation equation of gestational age. Additionally, validation set was used to verify the accuracy of the equation. Estimation error was defined as the mean square deviation between the estimation equation and observed gestational age and its accuracy was compared with that analyzed by Hadlock and National Institute of Child Health and Human Development (NICHD) equations. **Results:** The gestational age estimation errors of the new equation are within 9.62 days from 15 to 20 weeks, 7.90 days from 21 to 25 weeks, 11.76 days from 26 to 30 weeks, 9.35 days from 31 to 35 weeks, and within 11.30 days from 36 to 40 weeks of gestation. Compared to the results evaluated by the Hadlock and NICHD equations, the estimation of the new equation has significantly improved gestational age determination in the second and third trimesters. **Conclusions:** The estimation results of the new equation is superior to those of the Hadlock and NICHD equations and provides more accurate results for gestational age estimation with ultrasonic examination.

**Key words:** Biparietal diameter; Head circumference; Abdominal circumference; Femur length.

## Introduction

Determination of pregnancy is important for pregnant women and their newborns. Fetal ultrasound management technology can estimate the gestational age and improve the measurement of pregnancy [1]. The gestational age guides the timing of interventions as related to the timing of delivery and help balance the risk of fetal death with neonatal morbidity and mortality [2]. It has also been reported that premature babies (i.e. < 37 weeks gestation) are at risk for many short-term and long-term morbidities [3]. Although it is well known that preterm birth is the leading cause of morbidity and mortality in developing countries [4], accurate assessment of gestational age to determine the risk profile of these infants remains challenging. Methods have been reported previously to estimate the age of pregnancy [5–14] but the most commonly used is ultrasound biometry to estimate the gestational age [13–15]. Furthermore, the equation standard developed in an older report is still utilized for ges-

tational age estimation [13]. For example, Hadlock *et al.* recruited 361 women from area in Houston, MA, U. S. A. Their regression analysis for the individual parameters included the linear, quadratic and cubic terms of each parameter [13]. Moreover, the stepwise regression for the combinations of parameters also included the linear, quadratic and cubic terms of the individual parameters as well as all the cross-products of these terms. In the condition that the significance of all statistical items is less than 0.05, the highest  $R^2$  and the smallest standard deviation are selected for the final model [13]. However, a more recent publication indicates that reference equations in these ultrasound instruments are outdated and unsuitable for fetal health diagnosis [16]. Meanwhile, ultrasound imaging technology has been advancing, both in terms of image quality and measurement methods, enabling the possibility to obtain more precise fetal ultrasound biometrics to estimate gestational age [17, 18]. The recent gestational age ultrasound biometric estimation study was reported by Skupski DW *et al.* [14]. The

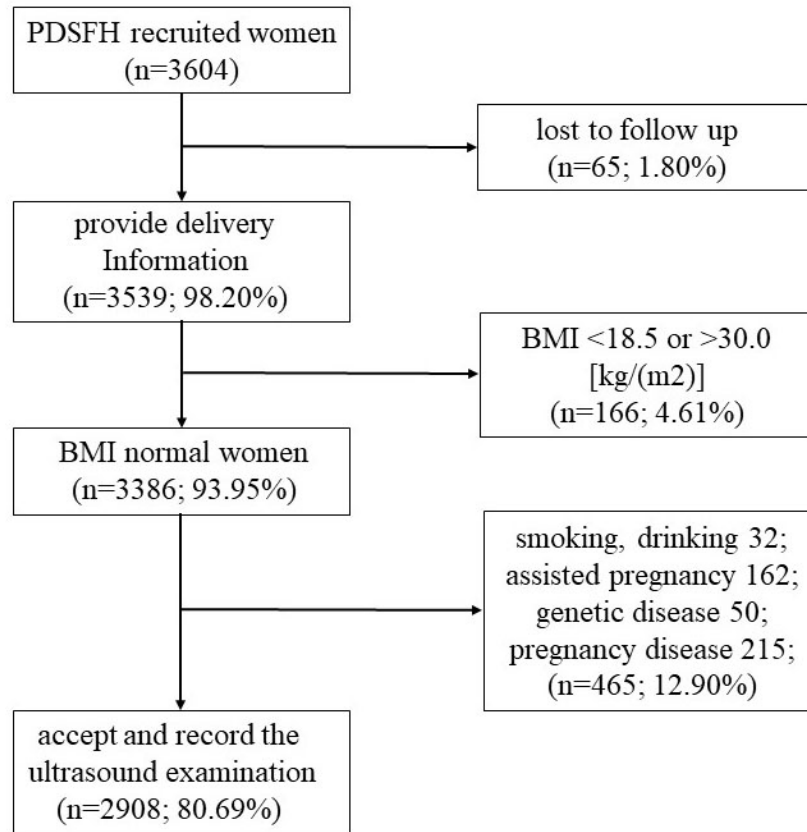


Figure 1. — Flow diagram of study participants. From 2016 to 2018. BMI, body mass index.

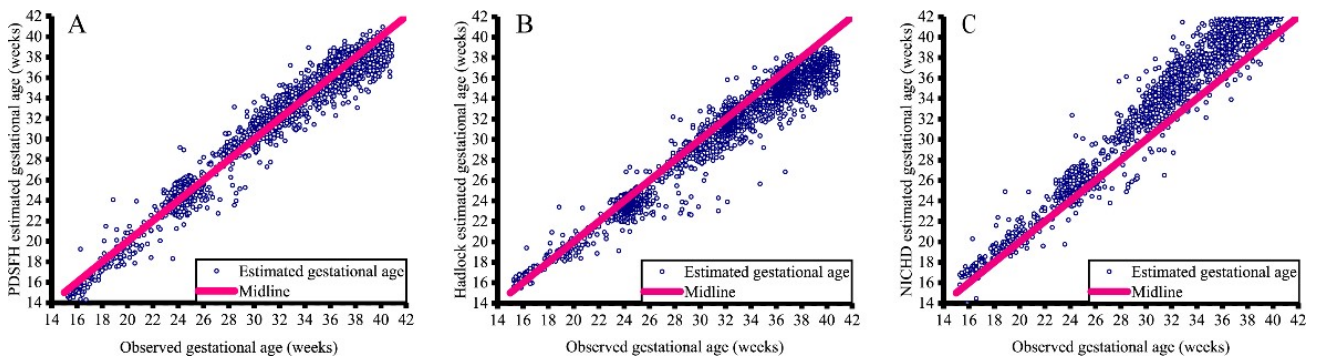


Figure 2. — Comparison of estimated and observed gestational ages from 15 to 40 weeks respectively with PDSFH, Hadlock, NICHD equations, in which observed gestational age are obtained from the last menstrual periods. Figure A uses the PDSFH model to calculate the estimated gestational age, Figure B uses the Hadlock model, and Figure C uses the NICHD model.

National Institute of Child Health and Human Development (NICHD) developed its gestational age estimation model in 2017, which included recruited four ethnic groups including 611 non-Hispanic black, 649 Hispanic, 614 non-Hispanic white and 460 Asian or Pacific Islander women [14]. The NICHD estimation model has utilized a backward elimination regression technique that initially contains all biometric measurements (biparietal diameter, head circumference, abdominal circumference and femur length), including first-order quadratic and interaction terms [14]. It then removes the least significant terms until terms that are sig-

nificant at the 0.05 level remained [14]. However, several publications have shown that fetal growth is significantly related to ethnic [19–21], geographic and socioeconomic differences [22, 23]. Therefore, with fetal biometric values as variables, application of the Hadlock and NICHD models in China will not achieve adequate results. China is a country with a population of 1.3 billion people. A large significant number of pregnant women have ultrasound pregnancy examinations every day. Hence, there is an urgent need to establish a more precise reference equation for gestational age estimation via fetal ultrasound biometrics in China.

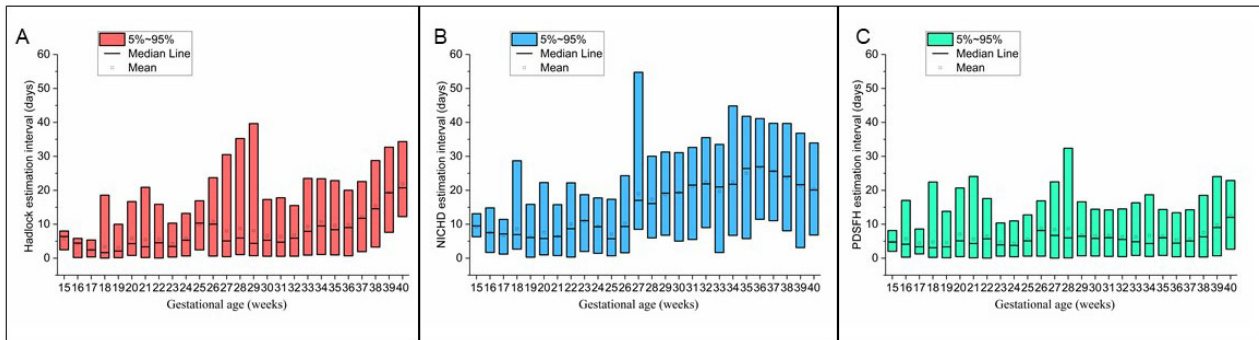


Figure 3. — Comparison of estimated errors in days for gestation at each week. The estimation error of three equations is compared by absolute mean, median, and 5th to 95th percentiles.

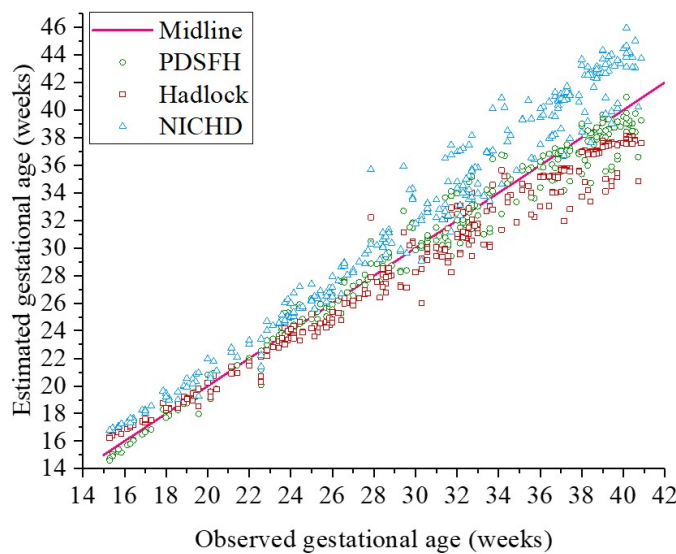


Figure 4. — In validation set data, comparisons of estimated and observed gestational ages from 15 to 40 weeks are respectively plotted with three equations (PDSFH, Hadlock, NICHD), in which observed gestational ages are obtained from the last menstrual periods.

The Precise and digital screening of fetal health (PDSFH) research project based on ultrasound imaging technology has provided a unique opportunity for fetal growth research and establishment of the reference equation for gestational age estimation through fetal ultrasound biological measurements.

The aim of this study is to establish the estimation model of gestational age based on fetal growth parameters of pregnant women recruited by PDSFH during ultrasonic pregnancy examination, as well as to compare this equation with Hadlock and NICHD equations to ensure the accuracy of the new equation.

## Materials and Methods

The PDSFH research project was a prospective cross-sectional study in China that recruited women with gestational age from 15 to 40 weeks. All women had low-risk pregnancies with optimal conditions for fetal growth. The

gravidity of women recruited were either first- or second-born. All had a single gestation and neonates were born with normal outcomes. The frequency of visits for ultrasound examination for each women was based on physicians' recommendations and was not performed weekly on each patient. Gestational age was confirmed by obtaining their last self-reported menstrual period (LMP) with a regular cycle of 26–32 days [1, 14]. The fetal crown-rump length was measured in their early first trimester ultrasound test (11–15weeks) [24]. The inclusion criteria were as follows: women had an ultrasound examination at 15 to 40 weeks of gestation for maternal health status associated with normal fetal growth (age, 18–40 years); body mass index [calculated as weight (kg)/[height (m)]<sup>2</sup>] ranges from 18.5–29.9 for the pregnant woman; healthy lifestyle and living conditions [see the exclusion criteria subsequently]; low-risk medical and obstetric history. Body mass index was calculated based on the self-reported weight and height

Table 1. — Characteristics of the Study Population (N = 2908).

Characteristic	Value
Age	29.52 ± 4.56
Self-reported height (cm)	159.08 ± 4.78
Self-reported weight (kg)	53.25 ± 7.85
BMI (kg/m <sup>2</sup> )	21.04 ± 3.03
Education	
No college	124 (4.26%)
Some college	1652 (56.81%)
College graduate	846 (29.09%)
Postgraduate degree	286 (9.84%)
Monthly family income	
Less than USD 1,500	1125 (38.69%)
USD 1,500–2,999	1453 (49.96%)
USD 3,000–4,499	218 (7.50%)
USD 4,500 or greater	112 (3.85%)
Parity	
1	1774 (61%)
2	1134 (39%)
Neonatal sex	
Male	1506 (51.79%)
Female	1402 (48.21%)

BMI, body mass index.

Table 2. — Estimating the regression model of gestational age.

Variable	Estimate	SE	P-value	R <sup>2</sup>
Intercept	4.230360	0.120308		
BPD	0.071633	0.006921		
HC	0.003865	0.001474	P < 0.001	0.965370
AC	0.039038	0.001629		
FL	0.178828	0.008472		

SE, standard error; BPD, biparietal diameter; HC, head circumference; AC, abdominal circumference; FL, femur length; GA, gestational age. The P-value of less than 0.05 indicates statistical significance. R<sup>2</sup> is based on randomly selected one sample for each participant.

The equation is: Gestational age (weeks) = 4.2304 + 0.0716 × BPD + 0.0039 × HC + 0.039 × AC + 0.1788 × FL.

of the patient prior to pregnancy and was confirmed by measurements at later visits. It cannot be determined if their first weight measured during pregnancy was their pre-pregnancy weight.

The exclusion criteria in the PDSFH project were extensive: current pregnancy with multifetal gestation; history of abortions > 2; previous fetal congenital malformation; irregular menstrual cycle; cigarette smoking or illicit drug use in the past 6–12 months; daily intake of one or more alcoholic drinks during pregnancy; pregnancy with complications (including gestational diabetes, gestational hypertension, hypothyroidism and hyperthyroidism); history of

Table 3. — Error of estimation in days for different gestational age windows.

Gestational age window	PDSFH model	NICHD model	Hadlock model
1 15-20	9.62	10.46	7.94
2 21-25	7.90	10.95	8.37
3 26-30	11.76	17.04	15.34
4 31-35	9.35	18.08	13.66
5 36-40	11.30	18.81	16.14
6 15-40	10.23	20.69	15.14

The estimated error is obtained by 1.96 times the standard deviation ( $\pm$  SD × 1.96).

non-communicable diseases for the pregnant woman or her husband (autoimmune disorders, cancer, diabetes mellitus, epilepsy or seizures requiring medication, hematologic disorders, hypertension, psychiatric disorders, renal disease, hyperthyroidism or hypothyroidism), fetal malformation; and amniotic fluid abnormality.

Pregnant women recruited in this project had ultrasound examinations multiple times at 15–40 gestational weeks based on physicians' recommendations, instead of undergoing ultrasonic measurement every week. All ultrasound examinations were performed using GE Voluson E8 and GE Voluson E10 machines (General Electric Healthcare, U.S.A) in four tertiary hospitals in China (University-Town Hospital of Chongqing Medical University, the Second Affiliated Hospital of Chongqing Medical University, Jiangnan Hospital of Chongqing Medical University and the First Affiliated Hospital of Chongqing Medical University). All the ultrasonographers in the study underwent ante-hoc training and credentialing and their measurement techniques were subjected to rigorous quality assurance [25–27]. The variation in ultrasound measurements between physicians was within 1 mm. The ultrasonographers were blinded to the gestational age of each pregnant woman to avoid measurement bias [28]. From January 2016 to October 2018, the PDSFH project recruited 3,604 women. Women in this study have completed ethnic group information to ensure a uniformity. The program covered residents originally from all over the country and their average monthly income was about 1,500 US dollars. All pregnant women signed an informed consent form.

The fetal biparietal diameter and head circumference measurements were based on standard section, i.e., the cranial cross-section, with left and right symmetric structures, showing the midline of the brain, transparent compartment, and posterior horn of the distal lateral ventricle, while not displaying the cerebellum and tentorial structures. The biparietal diameter was measured at the level of the thalami and cavum septa pellucida or the cerebral peduncles, i.e., linear distance from the outer edge of the proximal to the inner edge of the distal skull. The head circumference containing no extra cranial soft tissue along the outer edge of the fetal skull was directly measured using the elliptical function key. The fetal abdomen measurement was

Table 4. — Error of estimation for gestational age by each gestational week.

Gestational age	n	Hadlock	NICHD	PDSFH
		Error of estimation (days*)	Error of estimation (days*)	Error of estimation (days*)
15 to less than 16	21	3	7	5
16 to less than 17	36	7	9	9
17 to less than 18	22	3	7	5
18 to less than 19	33	12	16	14
19 to less than 20	38	6	9	8
20 to less than 21	20	10	12	12
21 to less than 22	18	10	8	12
22 to less than 23	14	9	12	11
23 to less than 24	193	7	9	8
24 to less than 25	394	8	11	8
25 to less than 26	66	9	13	7
26 to less than 27	23	15	14	11
27 to less than 28	31	18	22	14
28 to less than 29	52	19	16	17
29 to less than 30	60	20	15	10
30 to less than 31	158	10	16	9
31 to less than 32	200	13	15	9
32 to less than 33	266	11	17	9
33 to less than 34	102	13	19	9
34 to less than 35	89	17	22	12
35 to less than 36	108	14	21	8
36 to less than 37	326	14	18	9
37 to less than 38	242	13	18	9
38 to less than 39	153	15	19	12
39 to less than 40	179	14	19	13
40 to less than 41	64	14	18	13

The estimated error was obtained by 1.96 times the standard deviation ( $\pm SD \times 1.96$ ). Bold value is the minimum error for a specific gestational week.

based on standard fetal abdominal cross-section, showing the stomach, ventral umbilical vein segment, left and right branches of the portal vein and spinal cross-section. The normal stomach should be located in the left abdominal cavity of the fetus. The cross-section of the fetal abdomen was kept in a circular shape. Care was taken to not apply excessive force on the abdominal wall of the pregnant woman while using the probe to avoid deforming the fetal abdomen or making the boundaries of the abdominal wall unclear. The fetal abdominal circumference was determined by measuring the perimeter of the fetal outer abdominal wall with the elliptical function key. Measurement of the femur length requires a standard section that shows the full length of the femur and the angle between the femoral long axis and sound beam had to be greater than  $60^\circ$ . The measurement point was placed at the midpoint of the femoral diaphysis, excluding the epiphyseal end. All fetal growth parameters were measured three times and the mean values were obtained.

The gestational age assessment model uses a reverse elimination regression technique [14]. In details, it first considered all biological measurements (biparietal diameter, head circumference, abdominal circumference and fe-

mur length), included the first order, second order, and interaction items, and then deleted the insignificant parameters until the significance of all parameters reached 0.01 [13, 14]. These first, second, and exchange terms were variable transformations. The final selected model (referred to as the PDSFH model) was suitable for all pregnant women in the database from 15 to 40 weeks of gestation. This model was validated using the technique of tenfold cross-validation, a paradigm that divides sample data into 10 parts, nine of which are used to build a model with the remaining one being tested [29]. Then, the sample data was randomly re-distributed and the tenfold cross-validation method was repeated 100 times. The average values of the coefficient of the validation model was used to derive the estimated gestational age model.

The estimation error is defined as the mean square error between the estimated gestational ages, and the observed gestational age as well as the accuracy of the model as determined by several methods [7]. First, the study estimated the standard deviation of the error through the PDSFH model compared with the Hadlock and NICHD models at several different gestational age windows (15–40 weeks, 15–20 weeks, 21–25 weeks, 26–30 weeks, 31–35 weeks, and

Table 5. — Comparison of different error equations at different gestational age windows.

Equation	In range*	Out of range*	P-value
15-20 weeks			
Hadlock	163 (95.9%)	7 (4.1%)	< 0.001
NICHHD	145 (85.3%)	25 (14.7%)	
PDSFH	150 (88.2%)	20 (11.8%)	
21-25 weeks			
Hadlock	530 (77.4%)	155 (22.6%)	< 0.001
NICHHD	297 (43.4%)	238 (56.6%)	
PDSFH	597 (87.2%)	88 (12.8%)	
26-30 weeks			
Hadlock	269 (83.0%)	55 (17.0%)	< 0.001
NICHHD	89 (27.5%)	235 (72.5%)	
PDSFH	279 (86.1%)	45 (13.9%)	
31-35 weeks			
Hadlock	561 (73.3%)	204 (26.7%)	< 0.001
NICHHD	79 (10.3%)	686 (89.7%)	
PDSFH	620 (81.0%)	145 (19.0%)	
36-40 weeks			
Hadlock	451 (46.8%)	513 (53.2%)	< 0.001
NICHHD	107 (11.1%)	857 (88.9%)	
PDSFH	814 (84.4%)	150 (15.6%)	

In range\*, 15–20 weeks estimation error within  $\pm 10$  days, 21–25 weeks  $\pm 8$  days, 25–30 weeks  $\pm 12$  days, 30–35 weeks  $\pm 10$  days, 35–40 weeks  $\pm 12$  days. Out of range, when measurements are outside these ranges.

36–40 weeks). Second, we estimated the standard deviation of the error through the PDSFH model from 15 to 40 weeks in comparison with the Hadlock and NICHHD models. Third, the estimated error distribution of the PDSFH model from 15 to 40 weeks is compared with the Hadlock and NICHHD models. Next, we compared the estimated mean, median, and 5th to 95th percentile of the new equation from 15 to 40 weeks with the results obtained by Hadlock and NICHHD equations. Then the study compared the accuracy of the same estimation error range among the PDSFH, Hadlock, and NICHHD models in clinical trials. Finally, 300 data were selected as a validation set to verify the accuracy of the PDSFH, Hadlock and NICHHD models. The data in the validation set was selected randomly. It is new data collected after the new model has been established, i.e., it has not participated in the establishment of the previous estimation model. The criteria for collecting the validation set data is consistent with the criteria in the data collection that builds the model. The estimated error of the model was obtained from  $\pm SD$  (standard deviation)  $\times 1.96$ , which was interpreted as the difference between the estimated gestational age and observed gestational age of 95% of patients. The SD was defined as the mean squared difference between estimated and observed (project) gestational age. All analyses were performed using IBM SPSS 24.0 (IBM Inc., New York).

## Results

A total of 3604 pregnant women were enrolled in the study, of which 2908 were eligible for screening after post-hoc exclusions (Figure 1). Table 1 lists the details of the individual women. Table 2 shows the fitting equation of gestational age estimate and their correlation coefficients ( $R^2 = 0.965$ ) as well as the standard error. All  $P$ -values were less than 0.001, indicating statistical significance.

Figure 2 shows the relationship between observed gestational age and estimated gestational age based on the last menstrual period (LMP). Figures 2A, 2B, and 2C show the results based on our new equation, Hadlock equation, and NICHHD equation, respectively. The red solid line indicates that it is completely consistent with the observed gestational age. Based on estimated gestational age distribution on the two sides of the red solid line, it can be seen that the gestational age estimated by Hadlock equation is younger than the observed gestational age. The gestational age estimated by NICHHD equation is older than the observed gestational age; and the result estimated by our new equation is closest to the observed gestational age.

Figure 3 shows compared the three equations using the mean, median, and 5th to 95th percentiles, and found that the error distribution of the new equation is more stable than the Hadlock and NICHHD equations. The error distribution of the three equations has no obvious pattern over gestational age. At 36–40 weeks, the average estimation error of the new equation is significantly smaller than that of the Hadlock and NICHHD equations. The mean estimation of the Hadlock model is relatively low before 23 weeks, while the PDSFH model error is low after 23 weeks, and begins to increase after 32 weeks. However, the mean estimation of the NICHHD model is older than that of the other two models.

Table 3 shows the estimation error results for different gestational age windows. Judging from the gestational age window 6, the estimation error of the new equation is the smallest ( $\pm 10.23$  days), which is more accurate than the Hadlock equation ( $\pm 15.14$  days) that is currently in use. In gestational age window 1, the gestational age estimation of Hadlock equation is more accurate than NICHHD and PDSFH equation ( $\pm 7.94$  days). In gestational age window 1 and 2, the difference of gestational age estimation of the new equation is similar to Hadlock. In five gestational age windows from 2–6, the gestational age estimation of the new equation is more accurate ( $\pm 7.90$  days,  $\pm 11.76$  days,  $\pm 9.35$  days,  $\pm 11.30$  days and  $\pm 10.23$  days) compared with that of the Hadlock equation and NICHHD equation.

Table 4 reveals that the estimated error intervals from 15 to 40 weeks. The estimation error of Hadlock model is the minimum in the gestational age 15–20 weeks. The estimation error of PDSFH model is similar to that of the Hadlock model (within 2 days). Aside from 21 and 28 weeks, the estimation error of NICHHD is greater than the other two estimation equations. Meanwhile, the new equation possesses the smallest estimation error from 29–40 weeks.

Table 5 illustrates the accuracy of comparison with the

Hadlock equation and the NICHD equation about the estimated error range of each gestational age window [14]. It indicates that Hadlock equation accuracy is the highest in gestational age window 1, but from gestational age windows 2-5, the new equation accuracy is the highest. Meanwhile, the NICHD accuracy is relatively lower in these 5 gestational age windows.

As is shown in Figure 4, the models of the PDSFH, Hadlock and NICHD models have been verified with additional 300 data points that are not involved in the modeling as the verification set. On the whole, the estimated value of the new equation is closer to the observed value, the estimated value of Hadlock is younger, and the estimated value of NICHD is older. Within the estimated error range for each gestational age window, the highest accuracy rate of the PDSFH model is to be 84.7%. The estimation accuracy of Hadlock model is 70.3% and 42.7% for NICHD model.

## Discussion

Compared with Hadlock and NICHD, our sample size is larger and more reliable as the samples are all from the same ethnic group and are able to reduce the impact of ethnic differences [19-21]. Our exclusion criteria are extensive, which also improves the quality of the study. For example, maternal smoking has an impact on fetal growth which may result in a negative effect on fetal lung function and low fetal birth weight [30]. Exposure to alcohol during pregnancy could also cause impaired growth, stillbirth, and fetal alcohol spectrum disorders [31]. Use of cocaine during pregnancy may lead to an increased incidence of congenital malformations, stillbirths and intrauterine growth retardation [32]. Use of heroin and opioids does not seem to increase the incidence of major congenital malformations, but it affects fetal growth and increases intrauterine fetal mortality [32]. Studies of the developmental outcomes of children born by cocaine or heroin-dependent mothers appear to indicate that children have retarded psychomotor development [32]. Compared with normal pregnancy, the incidence of the gestational hypertension is significantly higher in infants of small gestational age, and lead to higher mortality of infants of small gestational age as well as significantly retarded physical and mental development [33].

At 15-25 gestational weeks, the estimation results of PDSFH and NICHD equations are similar to the Hadlock equation, indicating that fetal biological variation of different ethnic groups is smaller in early pregnancy [14]. The estimation results of the PDSFH equation prove better than the results estimated by the other two equations after 29 weeks. Meanwhile, the estimation error of the NICHD equation is smaller than the other two equations at 21 and 28 weeks, and the other gestational ages having larger error.

Referring to the comparison method of NICHD and Hadlock equations, the study creates Table 5 to prove the significant clinical effect of the improved new equation. As the ultrasound test may have a greater margin of error, it reveals that these findings are particularly important for women at

later gestational ages. At present, the estimated error range of the new equation is considered as a threshold for each gestational age window. In the Hadlock equation, 4%-53% of the estimated error is outside the specified acceptable error range (Table 3), especially in the third trimester. In the NICHD equation, 15%-89% of the estimated error is outside the specified acceptable error interval. With the new equation, 4%-38% of women will have a more accurate pregnancy dating and potentially prevent preterm or postpartum pregnancy (Table 5). For pregnant women in the third trimester, the accuracy rate of the new formula for gestational age estimation is higher than that of ultrasound gestational week estimation (Hadlock equation). In China, a significant number of pregnant women undergo ultrasound pregnancy examinations each year. Utilization of this equation may prevent unnecessary obstetric intervention. Among the women we recruited, one of them had an unknown gestational week and last menstrual period. After emergency admission, the ultrasound test suggested that the gestational age was 36.3 weeks with a risk of preterm birth. However, the later delivery process was uncomplicated with normal umbilical blood gas analysis. This new equation for the ultrasound test data estimated the gestational age as 38.4 weeks resulting in a normal delivery. This example presents that accurate gestational dating is important for managing pregnancy, determining time to terminate pregnancy, reducing unnecessary obstetric interventions and avoiding premature or overdue births.

Previous publications have reported that differences of fetal growth from other ethnic groups are mainly in head circumference and femur length [34, 35]. In addition, fetal bioassay are also affected by environmental and socioeconomic impacts [22, 23]. Therefore, fetal growth presents considerable natural differences in different countries. The age, height, weight and parity of mothers as well as fetal sex could affect fetal growth to some extent [36]. Since Hadlock does not provide the details of the sample data, PDSFH cannot be compared with it directly. But it is clear that the average height and weight of the women in PDSFH are smaller than those recruited by NICHD. The Hadlock and NICHD reference equations are basically based on the examples in high-income countries, i.e., annual incomes of female households recruited by NICHD is generally higher than those in China. The above differences could possibly affect fetal growth and lead to the result that Hadlock and NICHD gestational week estimates based on fetal biometric values may not be applicable in China. Therefore, the emergence of new equations for China is important in accurately estimating gestational age.

There are several possible reasons that led to the improvement of our estimation results. First, all ultrasound physicians have received unified training and blinded to the gestational age of each pregnant woman during ultrasound measurement, ensuring data quality. Second, the ultrasonic images presented by advanced ultrasonic equipment brings better measurement accuracy [37, 38]. Finally, due to the

fact that ethnicity, geographic and socioeconomic factors have an impact on fetal development [19-23], the PDSFH equation is best utilized for gestational age estimation for Chinese pregnant women.

This project has several advantages. First, the study recruited 3604 women from the same ethnic group (Han) in China to ensure consistency of ethnic group and ethnicity. The abundant data enables the new equation to be more suitable for use in China than the other two equations. Second, the linear mixed model is used for analysis and calculation, as well as the optimal gestational age estimation model being selected. Third, the 10-fold cross-validation method is adopted and further improves the accuracy of the model, which was later verified by the verification data set that was not used in building the model. Finally, the accuracy of the new equation, Hadlock model, and NICHD model was compared using various parameters, such as SD, mean, median, and accuracy of clinical estimates.

This study has some limitations. First the data is collected from both GE Voluson E8 and GE Voluson E10. The imaging quality variation due to different instrumentations might affect the judgment of physicians and general applicability of the results to some extent. Second, the ultrasound instruments display the estimated gestational week of the ultrasound measurement. The sonographer performing the measurements may not be blinded to the gestational age and is subject to bias unconsciously, trying to get each measurements consistent with each other. The lack of blindness and inherent bias could lead to an unknown numbers of positive results.

This study has established a gestational age estimation model for Chinese women. Compared with the Hadlock and NICHD models, it was found that from 15 to 25 weeks, the new equation was close to the Hadlock model (estimated gestational age within  $\pm 2$  days), while Hadlock's estimation error was smaller. However from 26 to 40 weeks, the new equation estimates more optimal results for gestational age, especially in the third trimester. Given the high number of births and intervention rates in China each year, the findings of this study may have important implications for child health and quality of maternal care.

### Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of University-Town Hospital of Chongqing Medical University (approval number: ECUTH-CMU2018110601).

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### Conflict of Interest

The authors declare no conflict of interest.

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