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Prediction of birth weight in pregnancy with gestational diabetes mellitus using an artificial neural network

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Gestational diabetes mellitus (GDM) is common during pregnancy, with the prevalence reaching as high as 31.0% in some European regions (McIntyre et al., 2019). Dysfunction of the glucose metabolism in pregnancy can influence fetal growth via alteration of the intrauterine environment, resulting in an increased risk of abnormal offspring birth weight (McIntyre et al., 2019). Infants with abnormal birth weight will be faced with increased risks of neonatal complications in the perinatal period and chronic non-communicable diseases in childhood and adulthood (Mitanchez et al., 2015; McIntyre et al., 2019). Therefore, accurate estimation of birth weight for neonates from women with GDM is crucial for more sensible perinatal decision-making and improvement of perinatal outcomes. Timely antenatal intervention, with reference to accurately estimated fetal weight, may also decrease the risks of adverse long-term diseases.

Over the past few decades, dozens of estimation formulas have been established for estimating fetal weight; however, none of them are considered sufficiently accurate for use by obstetricians (Scioscia et al., 2008; Hammami et al., 2018), and when it comes to fetal weight prediction in diabetic pregnancy, the accuracy appears to be even lower (Benson et al., 1987; Best and Pressman, 2002; Cesnaite et al., 2020; Pretscher et al., 2020). In this study, we tried using one method of machine learning, an artificial neural network (ANN), to establish a model for predicting birth weight more accurately in pregnancy with GDM. We established a two-layer feed-forward ANN with tanh hidden neurons, and the details of subjects and methods are described in the supplementary materials and methods.

The performance of the derived ANN was assessed with a testing dataset of 492 subjects. The estimated birth weight values obtained with the ANN were approximately consistent with actual birth weight, with mean absolute error (MAE) and mean absolute percentage error (MAPE) being 153.5 g and 4.7%, respectively (Fig. 1, Table 1).

We also compared the performance of this ANN with other prediction models, including formulae reported by Hadlock et al. (1985) and Li et al. (2019). Hadlock formulae are considered to provide a simple and accurate model for predicting fetal weight and have been widely used (Hadlock et al., 1985; Hammami et al., 2018). In the study carried out by Li et al. (2019), the subjects were also Chinese, with sample sizes as large as about 20 000 patients, which suggested that these prediction formulae for fetal weight might be also suitable for another Chinese population. However, the above two sets of formulae did not perform very well in predicting birth weight with the testing datasets of GDM subjects (subjects with ultrasonic data within 3 d before delivery). In our comparisons of the ANN with the two sets of formulae, the MAE and MAPE from the ANN were much lower than those from the two controls (148.5 g vs. 192.2 g and 218.5 g, 4.6% vs. 6.0% and 7.0%, respectively; $P<0.001$ for all); and the proportions of absolute error (<250 g and <100 g) and the proportions of relative error (ratio of absolute error to actual fetal weight;

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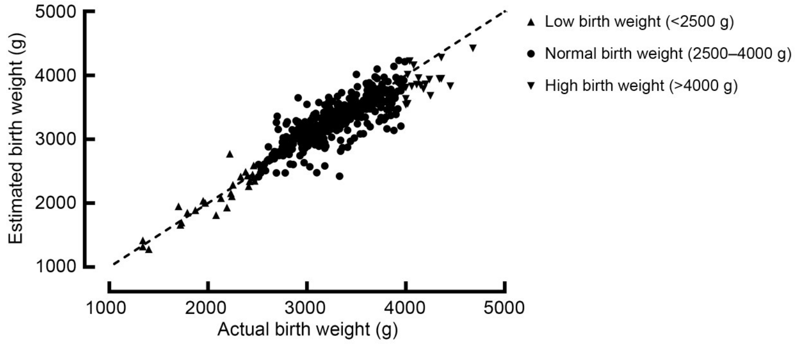

Fig. 1 Estimated birth weight and actual birth weight in the testing dataset. The estimated birth weight was approximately consistent with actual birth weight, and estimation error for birth weight differed for different weight intervals. The dashed line indicates the relation of estimated birth weight equal to actual birth weight.

Table 1 Fetal weight estimation by three methods

Method[1]	MAE (g)	MAPE (%)	Estimation error (%)			
			Absolute error <250 g	Absolute error <100 g	Relative error[2] <10%	Relative error[2] <5%
Hadlock et al. (1985)	192.2±141.0***	6.0±4.4***	71.2***	29.9***	84.5	49.1***
Li et al. (2019)	218.5±147.2***	7.0±4.9***	63.8***	23.2***	75.3***	38.7***
ANN	148.5±145.9	4.6±4.5	80.1	48.3	86.7	66.4
ANN for all	153.5±147.9	4.7±4.5	79.9	48.4	87.4	66.1

[1] Results are from a subset of testing dataset with ultrasonic data within 3 d before delivery, since the estimation methods for birth weight in the studies of Hadlock et al. (1985) and Li et al. (2019) were established with ultrasonic data within 3 d before delivery, except the results of "ANN for all," in which all the testing datasets were used for birth weight estimation. [2] Relative error is the ratio of absolute error to actual fetal weight. The values of MAE and MAPE are expressed as mean±standard deviation (n=272, but n=492 for ANN for all). *** P<0.001 vs. ANN. ANN: artificial neural network; MAE: mean absolute error; MAPE: mean absolute percentage error.

<10% and <5%) were much higher with the ANN model than with the two sets of control formulae (80.1% vs. 71.2% and 63.8%, P<0.001 for both; 48.3% vs. 29.9% and 23.2%, P<0.001 for both; 86.7% vs. 84.5% and 75.3%, P>0.05 for the former and P<0.001 for the latter; 66.4% vs. 49.1% and 38.7%, P<0.001 for both) (Table 1).

In further assessment of the ANN in estimating birth weight, the ANN model showed different degrees of accuracy. It was apparent that the derived ANN was not good at estimating birth weight with high percentiles (birth weight percentiles for the same gestational age) or high birth weight. However, it performed well in predicting birth weight with low and medium percentiles, especially in predicting weight in the interval from the 25th to 75th percentile. In the weight interval from the 3rd to 75th percentile, the absolute estimated errors in the ANN were significantly smaller than those produced by the formulae reported by Hadlock et al. (1985) and Li et al. (2019) (P<0.01 for all; Fig. 2a). In addition, we used a kernel regression fit to describe the variation trend of estimated error across actual birth weight. The absolute estimated error and real estimated error at smoothed curves both sharply increased when the actual birth weight approached 3500 g, in the underestimation direction (Fig. 2b). We also compared the estimated error in different birth weight intervals with certain cut-off points, reaching similar results (Table S1).

Conventional prediction models for GDM newborn birth weight tend to establish formulae using ultrasonic information, but this approach has some limitations: (1) information on time interval to delivery is not included in the final formulae or is simply abnegated; (2) information other than ultrasonic data, like gestational weight gain, is hard to integrate into ultrasonic formulae; (3) the algorithms in conventional formulae are often so simple that information from ultrasonic data cannot be used completely. An ANN is essentially an algorithm more complex than regular arithmetic, allowing a greater capability to explore both linear and non-linear relationships between imputing features and outputs of interest (Kriegeskorte and Golan, 2019). Therefore, the ANN is able to improve

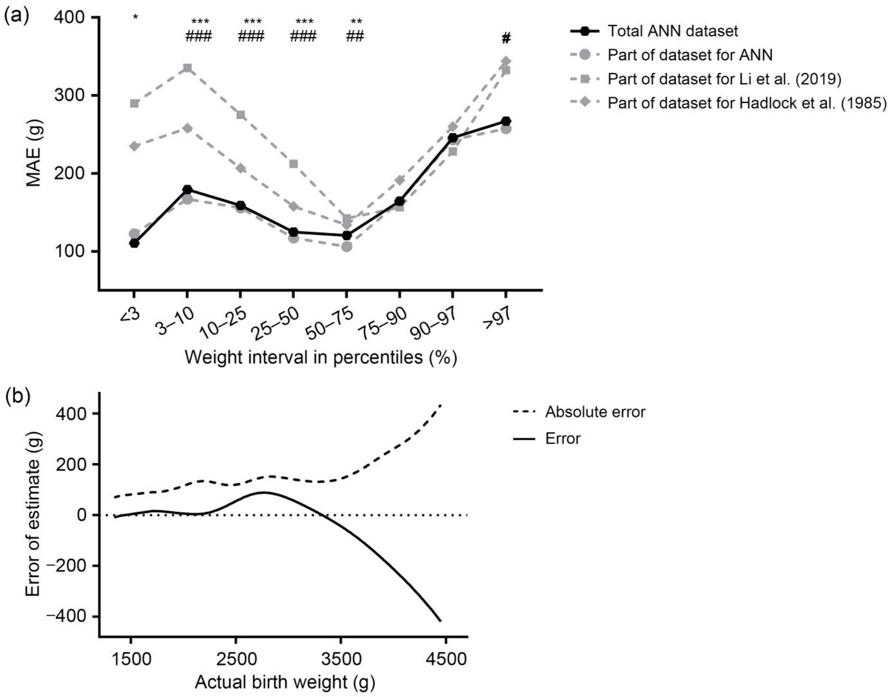

Fig. 2 Variation of estimated error with actual birth weight. (a) Prediction accuracy seemed lower in weight intervals of high percentiles (>200 g); for samples with ultrasonic data within 3 d before delivery, the estimated error with the ANN method was lower than that with the formulae reported by Hadlock et al. (1985) and Li et al. (2019), especially for actual birth weight in the weight interval from the 3rd to 75th percentile. (b) A kernel regression fit was used to describe the variation trend of estimated error across actual birth weight. The curve of absolute estimated error remained relatively stable and suddenly ascended sharply when actual birth weight approached 3500 g; the smoothed real error (estimated weight−actual weight) remained close to zero until actual birth weight approached 3500 g, and then constantly increased along the negative axis. **P*<0.05, ***P*<0.01, ****P*<0.001, for the comparison of the method in Li et al. (2019) with the ANN; $^{\#}$*P*<0.05, $^{\#\#}$*P*<0.01, $^{\#\#\#}$*P*<0.001, for the comparison of the formula of Hadlock et al. (1985) with the ANN. ANN: artificial neural network; MAE: mean absolute error.

the capability of the antenatal data to reflect growth features and remove the limitations of conventional prediction models, to a certain extent, thus theoretically yielding a higher prediction accuracy.

Benson et al. (1987) first reported the prediction accuracy of ultrasonic data in diabetic pregnancy; however, the best result for mean percent error±standard deviation was (−0.9±11.0)%, not presented as absolute error. Following that study, several others showed the accuracies (presented as MAPEs) ranging from 6.07% to 9.00% (Alsulyman et al., 1997; Best and Pressman, 2002; Husslein et al., 2012; Cesnaite et al., 2020; Pretscher et al., 2020), while some studies reported the accuracies as percentage of relative error (PRE) of <10% or <15%, which was also not satisfactory (PRE<15%: 74%; PRE<10%: 70%) (Wong et al., 2001; Valent et al., 2017). The sample sizes of all the above studies were small, ranging from 19 to 756. In the present study, based on a large diabetic pregnancy population (*n*=2462), we used the ANN method to establish a model for predicting birth weight, yielding a higher accuracy (presented as MAE, MAPE, or PRE) than that in similar research. Also, another limitation of previous models was the time interval from ultrasonic data to delivery. Most models required data within 3 to 7 d before delivery, while in the ANN estimation described in this study, the time interval of ultrasonic data is no longer a limitation.

However, there were limitations in the present study. When predicting birth weight with high percentiles or high birth weight, estimation error increased in the direction of underestimation. More to the point, the underestimation tendency began at an actual birth weight of around 3500 g, which was consistent with the conclusions of a previous study (Scioscia et al., 2008). In fact, the ANN did not work accurately either in lower or higher weight percentiles. In higher percentiles, we speculate that extreme percentiles of weight (both lower and higher) are more likely to indicate abnormal growth of fetuses, which is common in diabetic pregnancy because of excessive glucose in maternal and fetal circulation or aggressive glycaemic management (Mitanchez et al., 2015; McIntyre et al., 2019). The lower accuracy in predicting lower or higher birth weight percentiles may be inevitable, since traditional anthropometric parameters or common characteristics probably cannot reflect the growth features of diabetic pregnancy accurately, especially in the case of abnormal growth of fetuses. Although prediction accuracy of abnormal birth weight was improved by the advanced ANN algorithm, the ANN indeed improved the estimating precision, even for birth weight of >3500 g; however, limited by conventional anthropometric parameters as imputers, the underestimation tendency was inevitable. It seems that anthropometric parameters reflecting more growth features, like fractional limb volume, are as important as advanced algorithms for improvement of prediction precision. In addition, the present study was the first trial of the machine learning method for birth weight prediction in diabetic pregnancy, while other machine learning methods such as random forest, support vector machine, or decision tree were not assessed in this study. Their prediction capabilities may be compared with ANNs in future studies.

In summary, we created an ANN model for predicting birth weight in pregnancy with GDM, based on a large Chinese population, and the model yielded a high accuracy, though it tended to underestimate the weight and number of large newborns.

Materials and methods

Detailed methods are provided in the electronic supplementary materials of this paper.

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Author contributions

Menglin ZHOU performed the data analysis, wrote and edited the manuscript. Jiansheng JI and Nie XIE performed the data collection. Danqing CHEN performed the study design, funding support, and process supervision. All authors have read and approved the final manuscript, and therefore, have full access to all the data in the study and take responsibility for the integrity and security of the data.

Compliance with ethics guidelines

Menglin ZHOU, Jiansheng JI, Nie XIE, and Danqing CHEN declare that they have no conflict of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was not obtained since de-identified retrospective data were collected and it was approved by the Institutional Ethics Committee of Women's Hospital, Zhejiang University School of Medicine, Hangzhou, China (No. IRB-20210136-R).

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Supplementary information

Materials and methods; Table S1