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ORIGINAL ARTICLE

Customized birthweight standard for an Iranian population

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ABSTRACT

Objective: To produce a customized birthweight standard for Iran.

Method: Retrospective study of a pregnancy database collected from five hospitals across Iran. The cohort consisted of 4994 consecutive term births with complete data, delivered between July 2013 and November 2014. Coefficients were derived using a backwards stepwise multiple regression technique.

Results: Maternal height, weight in early pregnancy and parity as well as the baby's sex were identified as significant physiological variables affecting birthweight. Paternal height and weight were also significant although weaker factors. The expected 280-day birthweight, free from pathological influences, of a standard size mother (height 163 cm, weight 64 kg) in her first pregnancy was 3390 g. Pathological factors found to affect birthweight in this cohort included village housing, anemia, preexisting and gestational diabetes and preeclampsia.

Conclusion: The analysis confirmed the main physiological variables that affect birthweight in other countries and shows paternal factors also to be significant variables. Development of a country-specific customized birthweight standard will aid clinicians in Iran to distinguish between fetuses that are either constitutionally or pathologically small, thereby avoiding unnecessary interventions, and improving identification of at-risk pregnancies and perinatal outcome.

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Introduction

Fetal growth restriction (FGR) or intrauterine growth restriction (IUGR) is the failure of the fetus to reach its growth potential [1]. As often full information about longitudinal growth is not available, it is commonly assessed by its proxy, small for gestational age (SGA), usually defined as birthweight or fetal weight below the 10th centile [2]. Fetal growth restriction is associated with an increased risk of perinatal morbidity and mortality [3] but in practice most cases of FGR or SGA remain undetected prenatally [4].

There is a growing body of evidence supporting the role of customized rather than population based growth and birthweight charts in improving detection of FGR and decreasing false-positive diagnoses [5–9]. Implementation of customized charts has been associated with a decrease in stillbirths [10,11]. The Royal College of Obstetricians and Gynecologists in the United Kingdom has recommended the use of customized charts for the assessment of fetal growth and birthweight [12].

The process of developing customized growth charts is based on three steps. First, developing a statistical model using population data to predict optimal birthweight adjusted for physiological factors: maternal parity, ethnicity, height and weight, and fetal gender. Second, identifying and adjusting the model to be free from pathological factors (such as preeclampsia and diabetes) that significantly affect fetal growth in the population. Last, the customized optimal birth weight at term is projected backward for all gestational age points (GROW = gestation-related optimal weight), using an ultrasound estimated fetal weight based proportionality curve to outline how the fetus is

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expected to reach its growth potential at the end of a normal term pregnancy [13].

In this study, we aimed to produce a customized growth and birthweight standard based on the variables found to be significant in an Iranian multicenter population.

Materials and methods

Study population

This retrospective cohort study included data from five Iranian hospitals based on deliveries between July 2013 and November 2014. The hospitals were in Tehran (Akbarabady, Milad and Baharloo), Mashhad (Omolbanin) and Arak (Taleghani).

Data collection and inclusion criteria

Data on each delivery were collected in each of the five centers by trained midwives retrospectively within 12 h after delivery. The information was first recorded by the midwife on a proforma and then transferred into an electronic database. Data items included maternal characteristics such as height and weight in early pregnancy, parity, ethnicity, education and employment, type of residence and medical history; and pregnancy characteristics including length of gestation, gender and weight at birth, as well as fetal anomalies and pregnancy outcome. One-minute Apgar score and paternal weight & height were also collected but were only completed in about 50% of cases.

Gestational age was determined by ultrasound between 7 and 14 weeks of pregnancy. Ethnicity, parity, paternal height and weight and other variables were based on self-reporting by the mother. To obtain reliable birthweight, the same scales were provided to all five hospitals. From an original cohort *n* of 9338 deliveries collected, preterm deliveries (<37.0 weeks), congenital anomalies, stillbirths, women of non-Persian ethnicity, multiple pregnancies and cases with missing/incomplete data were excluded, leaving a study cohort of 4994 pregnancies. The biggest reason for exclusions was missing data.

Ethics and consent

The protocol was approved by the research ethics committee at Tehran University. As the study was retrospective and did not affect management, and no identifiable data were stored, mothers were asked for verbal consent only.

Statistical analysis

Physiological and pathological coefficients for customized birthweight centiles were derived according to methods described previously [13]. Multivariate linear regression with stepwise backward elimination was used to obtain coefficients for significant variables with cutoff at probability .05.

The regression analysis was run on the 4994 pregnancies with complete data. However, paternal height and weight were completed in only about 50% of pregnancies and to estimate the missing cases, the multiple imputation by chained equations (MICE) [14] method was used. Tests for differences between the imputed and actual values found no significant differences.

The covariates used for the multiple regression are described in Table 1 and the results in Table 2. To allow comparison with previous studies [15–17], the analysis was centered on a "standard" mother with height 163 cm, early pregnancy weight 64 kg and parity zero, with the baby's sex undefined, that is, neutral or "averaged" between male and female. Paternal height and weight and gestation at delivery were centered on the median for the cohort. To allow

Table 1. Characteristics of the study population ($n = 4994$).

Characteristics	*n* (%)	Mean	SD	Median	IQR
Maternal age (y)		28.0	5.4	27.5	7.0
<20	292 (6.1)				
20 < 28	2,357 (49.1)				
28 < 34	1443 (30.1)				
≥35	705 (14.7)				
Maternal height (cm)		161.2	5.7	161.0	7.0
Paternal height (cm)		174.8	5.7	174.9	5.7
Maternal weight (kg)		64.1	11.7	63.0	15.0
Paternal weight (kg)		79.7	9.7	79.2	9.0
Body mass index (BMI, kg/m^2)		24.6	4.3	24.2	5.5
<18.5	284 (5.7)				
18.5 < 25	2584 (51.7)				
25 < 30	1,571 (31.5)				
≥30	555 (11.1)				
Parity					
0	2,117 (42.3)				
1	1779 (35.5)				
2	725 (14.6)				
≥3	373 (7.6)				
Housing					
City/town	4,458 (89.3)				
Village	536 (10.7)				
History of diabetes	58 (1.2)				
History of preeclampsia	70 (1.4)				
Maternal thyroid disorders	201 (4.0)				
Anemia	42 (0.9)				
Preexisting diabetes	13 (0.3)				
Gestational diabetes	378 (7.6)				
Gestational hypertension	23 (0.5)				
Preeclampsia	144 (2.9)				
Gestation at delivery (d)		274.2	7.3	274.0	11.0
Birthweight (g)		3238.2	404.8	3235.0	520.0
Sex					
Male	2,532 (50.7)				
Female	2,462 (49.3)				

Table 2. Results of multiple regression analysis in grams ($n = 4994$).

	Coeff	SE	95% CI
Constant at 274 days	3242.7		
Constant adjusted to 280 days	3390.0		
Gestational age (from 274 d)			
Linear	16.839	0.722	15.424–18.253
Quadratic	−0.3072	0.0869	−0.4775 to −0.1369
Sex			
Male	63.5	10.4	43–83.9
Female	−63.5	10.4	−83.9 to −43
Maternal height (from 163 cm)			
Linear	6.419	0.989	4.48–8.358
Maternal weight (from 64 kg)			
Linear	5.355	0.527	4.323–6.388
Quadratic	−0.1046	0.0242	−0.152 to −0.0572
Paternal height (from 174 cm)			
Linear	5.537	1.049	3.481–7.593
Paternal weight (from 79 kg)			
Linear	2.739	0.668	1.43–4.048
Quadratic	−0.0800	0.0264	−0.1317 to −0.0283
Parity			
Para 1	53.8	12.0	30.4–77.3
Para $\geq$ 2	82.6	14.1	54.8–110.3
Village housing	−54.8	16.9	−87.9 to −21.7
Anemia	−130.4	58.6	−245.2 to −15.6
Preexisting diabetes	321.0	101.8	121.4–520.6
Gestational diabetes	84.8	19.8	46.1–123.6
Preeclampsia	−101.0	32.1	−163.9 to −38.2

CI: confidence interval; SE: standard error. Model is centered on the median gestational age at delivery (274 days), with coefficients expressed for a "standard mother" (parity 0, maternal height 163 cm, initial weight 64 kg) and gender neutral baby. Constant (optimized by excluding all pathological factors listed): 3242.7 g, SE = 366.1, CV = 0.11, $R^2 = 0.182$.

comparison with other analyses, the constant of the regression model was adjusted to 280 days using the previously described proportionality equation [13]. As maternal and paternal height and weight tend to have a nonlinear relationship to birthweight, they were entered as polynomials up to the third power. Pathological factors were included as categorical variables to quantify their effect on birthweight and to separate their effect out from the optimal constant. This was done also for high and low body mass index and maternal age. All analyses were performed using Stata (version 15.1; StataCorp, College Station, TX).

Results

Table 1 displays the characteristics of the 4994 pregnancies that met the inclusion criteria after exclusion of incomplete data and outliers for gestational age, birthweight and maternal height and weight.

Table 2 lists the significant coefficients affecting birthweight together with their standard error and confidence intervals. The overall adjusted R^2 of the model was 0.182. The covariates were both physiological (gestational age, maternal as well as paternal height and weight, parity, ethnicity and baby's sex) and pathological (village housing, anemia, pre-existing diabetes, gestational diabetes and preeclampsia). The pathological factor with the largest effect was preexisting diabetes (+321 g). History of diabetes, history of preeclampsia, maternal thyroid disorders, gestational hypertension and high and low BMI and maternal age were also entered but were not significant.

The birthweight constant was 3242.7 g at the median gestation of this cohort (274 days) and 3390 g when adjusted to 280 days, for a standard size mother (height 163 cm, weight 64 kg) in her first pregnancy and free from any of the listed pathological factors.

Discussion

This is to our knowledge the first study to report coefficients for customized birthweight in an Iranian population. In this homogeneous ethnic group, similar maternal characteristics as demonstrated elsewhere [13,15,17–19] are shown to affect birthweight: maternal height, weight in early pregnancy and parity. Previous analyses have shown that "customized" SGA determined by a standard adjusted for such characteristics, better reflects the association between SGA with perinatal mortality than population standards that do not take such variation into consideration [20].

In this dataset we were able to study the effect of paternal height and weight and found it to also have a significant, albeit lesser effect on birthweight. This is consistent with previous studies [21–23] and confirms that this association is independent of maternal and other factors on birthweight. Antenatally, studies [24,25] have also found the significant association of

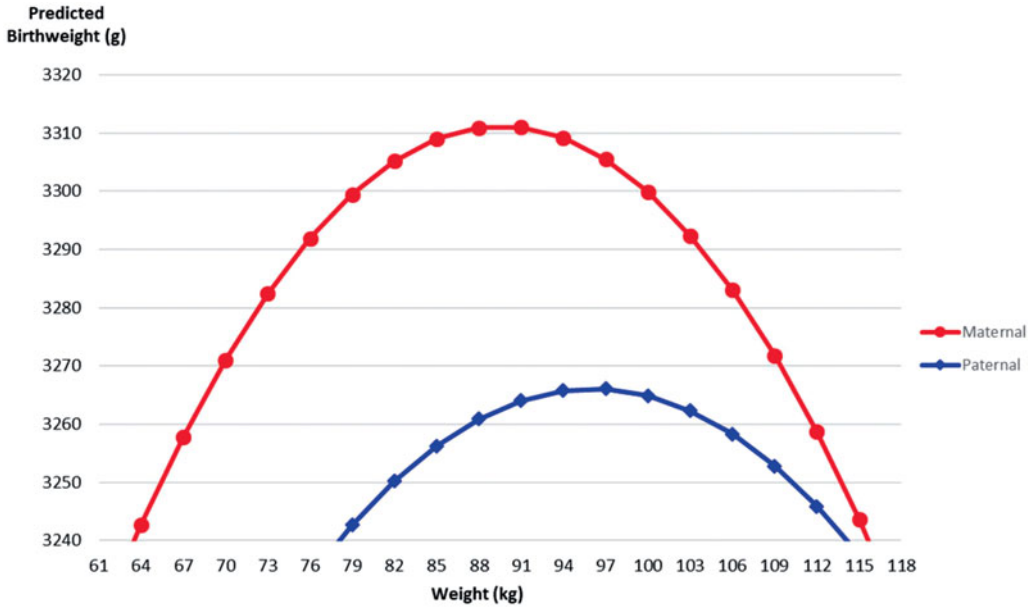

Figure 1. The effect of maternal and paternal weight on average birthweight. Predicted birthweight is represented for an Iranian "standard mother" (parity 0, maternal height 163 cm), paternal height 174 cm, a gender-neutral baby, and absence of any pathological factors listed in Table 2.

paternal height when determining standards for ultrasound fetal biometry including parameters such as biparietal diameter, head and abdominal circumference and femur length, which are related to ultrasound estimated fetal weight and birthweight.

Comparison with datasets from other countries is facilitated by centering the model on a standard mother, defined as a nullipara with height 163 and weight 64 kg, and a gestation length of 280 days [13]. The constant, or birthweight for such a "standard mother" in Iran was 3390 g (Table 2), which is smaller than that derived from the main ethnic group in England (3456 g), the USA (3453 g), Australia (3464 g) and New Zealand (3464 g) [17] as well as Slovenia (3451 g) [19]; and larger than that from France (3346 g) [9], Spain (3319 g) [26] and India (3292 g) [27].

Figure 1 displays the respective effects of maternal and paternal weight on average birthweight of a baby of a standard Iranian mother. The graph demonstrates that: once a specific maternal weight (90 kg, BMI: 33.9 kg/m^2) is reached, the effect on birthweight lessens - e.g. average birthweight at 90 kg is 3311 g, and at 100 kg it is 3300 g. This is an effect of the quadratic relationship between birthweight and maternal weight, and also consistent with previous findings that high BMI has a negative effect on birthweight [17,19]. A similar but smaller effect is seen in the paternal weight graph, an effect which has to our knowledge not been observed previously. Although there is a significant ($p < 0.01$) correlation between paternal and maternal weight, it is weak ($r = 0.167$).

Of the pathological factors identified, village housing is shown to have a negative effect on birthweight (−54.8 g), possibly as an indicator of socioeconomic differences. The data were able to differentiate between pre-existing and gestational diabetes: consistent with previous studies, pre-existing diabetes had a much higher effect on birthweight (+321 g) than gestational diabetes (+85 g) [28] and was higher than that observed in other studies (US: +242 g [17], Ireland: +137 g [29]). Such variation may reflect differential effects of diabetes on growth in different populations, or could be associated with effectiveness of blood sugar control during pregnancy.

The inclusion of pathological variables in the analysis allows the derivation of a constant which is free from pathological influence and allows adjustment of the term optimal weight according to the physiological/constitutional characteristics of the mother, reflecting the baby's growth potential. For example, according to the coefficients listed in Table 2, two mothers who are only slightly below and above the standard height and weight, and with the same BMI (say height 155 cm and weight 58 kg, versus 170 cm and 70 kg; both BMIs = 24 kg/m^2) would expect to have babies weighing 3156 and 3316 g respectively, a 161 g difference. At the normal limits of the distribution, a 160 g difference in birthweight would result in "SGA" being mis-classified in about 40% of cases [11].

SGA based on customized growth potential is more strongly associated than SGA based on respective population standards with pregnancy complications

and adverse outcomes, including abnormal antenatal Doppler, fetal distress, cesarean section, admission and length of stay in neonatal intensive care, and stillbirths and neonatal deaths [6–9,30]. A customized standard has also proved superior to the recently promoted INTERGROWTH 21st international population-based standard [31], identifying more infants as SGA and at-risk [32]. This has recently been confirmed in a comparative study of a database of 1.2 million births from 10 countries [27].

The strength of our study was an ethnically homogenous population with complete data for deriving customized birthweight standards. Variables were collected according to a standardized methodology and clear definitions. A potential weakness is manual data input which may be incorrect due to human or computer error. However, this was mitigated by an OB/GYN specialist checking accuracy of data entered into the online application in each collaborating center. Another potential weakness was that paternal height and weight was based on self-reporting, with only about 50% of cases entered. We were able to address this through the multiple imputation technique by chained equations (MICE) [14]. Differences between the means and variance of the imputed and actual values were tested and no statistically significant differences were found, suggesting that the imputed values were robust.

Availability of an Iranian set of coefficients for an adjustable standard will allow improved calculation of birthweight centiles and the computer-assisted prediction of the "term optimal weight" for each pregnancy. This in turn is combined with a fetal weight proportionality formula [13] to produce customized antenatal growth curves ("gestation related optimal weight", GROW) for surveillance of fetal weight gain [29].

In conclusion, analysis of Iranian data has confirmed physiological and pathological variation in birthweight observed elsewhere and allows the development of an Iranian customized birthweight standard. This will enhance the clinical distinction between normal and abnormal growth [9], thereby avoiding unnecessary intervention and improving perinatal outcome.

Disclosure statement

No potential conflict of interest was reported by the authors.

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