Are we missing at-risk babies? Comparison of customised growth charts v. standard population charts in a diabetic population

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Background. Diabetes in pregnancy is associated with both accelerated fetal growth and intrauterine growth restriction.
Objective. To compare the difference in occurrence of large-for-gestational-age (LGA) and small-for-gestational-age (SGA) fetuses in a pregnant diabetic population using population-based growth charts and customised growth charts.
Methods. Retrospective observational study at Steve Biko Academic and Kalafong hospitals, Pretoria, South Africa. Information from an electronic database was used to retrospectively generate customised centiles using a web-based tool (www.gestation.net). The first fetal growth scan of the third trimester, as determined by ultrasound, was plotted for each patient on both the population-based and customised growth charts. We compared the growth category on the population-based growth chart with that on the customised growth chart.
Results. Of the patients, 44 had type 1, 66 type 2 and 173 gestational diabetes. The growth of 79/283 fetuses would have been reclassified had customised growth charts been used. Of cases in which fetal growth was classified as appropriate for gestation on the population-based growth charts, 58 fetuses would have been LGA and 14 SGA had customised growth charts been used. Four of the fetuses that were SGA and three that were LGA on the population-based growth charts would have been classified as appropriately grown on the customised growth charts. This was a statistically significant difference ($p<0.001$), with a Cohen's kappa of 0.45 indicating moderate agreement.
Conclusions. Customised growth charts identified more babies with aberrations of growth, who may need vigilant antenatal care and elective delivery and may be at increased health risk in the future.

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Pregnancies in diabetic patients may be complicated by abnormal fetal growth.[1-3] Identifying these fetuses as either large for gestational age (LGA) or small for gestational age (SGA) may result in invasive procedures or premature delivery, in an attempt to reduce adverse perinatal outcomes. Both LGA infants and infants with intrauterine growth retardation have an increased risk of long-term complications in adult life,[4] but there is little evidence to suggest that the long-term outcome of appropriately grown fetuses is likely to be impaired.[5]

The estimated fetal weight is usually classified using population-based birth weight centiles. A potentially superior approach is to utilise large population-based data sets that incorporate fetal gender, maternal parity, ethnicity, height, weight and age, and exclude pathological variables such as maternal smoking, hypertension, diabetes and preterm birth to create an ultrasound-based, customised, optimal growth curve.[5] Several studies comparing the use of population-based growth centiles with customised centiles for prediction of SGA or LGA fetuses and perinatal adverse outcomes have concluded that customised growth charts were better able to predict fetuses at risk of perinatal morbidity and mortality.[6-10]

The aim of this study was to compare the difference in classification of fetuses as LGA and SGA in a pregnant diabetic population using both population-based and customised growth charts.

Methods

We conducted a retrospective observational study at two tertiary care centres with a high-risk diabetic antenatal clinic in Pretoria, South Africa. This study included all patients captured prospectively on an electronic database from January 2010 to February 2013. Patients were managed according to the population-based growth charts. The study included patients with type 1, type 2 and gestational diabetes mellitus (GDM). Gestational age was determined by early ultrasound before 24 weeks' gestation, the last normal menstrual period, or transcerebellar diameter. Information from the first fetal growth scan done in the third trimester was plotted on both the population-based and the customised growth charts, which were generated retrospectively. A customised growth chart was generated for each patient on a web-based tool (www.gestation.net). Fetuses that were below the 10th percentile were defined as SGA, and fetuses above the 90th percentile for gestational age as LGA.

Descriptive statistics were used to describe the study population. Continuous data were described with analysis of variance (ANOVA) and the *t*-test, and categorical variables were compared with the χ^2 test. The McNemar test and Cohen's kappa was used to assess the significance of differences in classification between the population-based and customised growth charts.

Results

There were 379 pregnancies complicated by DM recorded on the database from its inception in 2010 until February 2013. We analysed 283 of these pregnancies. Multiple pregnancies and pregnancies with congenital anomalies ($n=6$) were excluded, as these fetuses have different growth potentials. Ninety other pregnancies were

excluded because data were incomplete and customised growth charts could not be generated (Table 1).

Hypertensive disease was present in 82 patients in the study population. This included chronic hypertension and pre-eclampsia. There were five patients (1.8%) with diabetic ketoacidosis, of whom one presented with diabetes for the first time. Hypoglycaemia was experienced at least once a week in 37 patients (13.1%). Hypoglycaemia was severe enough to require admission in two patients (0.7%). Target organ damage was found in nine patients.

Amniocentesis was performed to establish fetal lung maturity in 65 patients (23.0%). Fifty-three babies (18.7%) were admitted to the neonatal intensive care unit (NICU). There were 15 perinatal deaths, giving a perinatal death rate of 51.2/1 000 births. One baby had a fractured femur as a result of birth trauma.

On the standard population-based growth charts, 26 fetuses (9.2%) were categorised as SGA, 215 (76%) were appropriate for gestational age (AGA), and 42 (14.8%) were LGA. When categorised by customised growth charts, 36 (13.8%) were SGA, 150 (53%) AGA and 97 (34.3%) LGA.

Forty-two fetuses were categorised as LGA on the population-based growth charts, but 97 would have been classified as such had customised growth charts been employed (Table 2). There was one (2.4%) perinatal death in the LGA group determined by population-based growth charts, and two (2.1%) among the 97 determined by customised growth charts. On population-based growth charts, 13 LGA babies (31%) were admitted to the NICU, in comparison with 23 (23.7%) LGA babies if customised growth chart classification had been used.

There were 26 fetuses classified as SGA on the population based growth chart and 36 when the customised growth chart was used (Table 2). There were 2 perinatal deaths (7.7%) in the SGA group determined by population-based growth charts and 5 (13.9%) when determined by customised growth charts. Whether classified by the population-based or customised growth charts, 7 SGA babies were admitted to the NICU.

Table 1. Comparison of study population and patients excluded from study

	Study population (*N*=283)	Patients excluded (*N*=96)
Age (years), mean (range)	33.61 (16 - 49)	33 (20 - 49)
Parity, median (range)	2 (0 - 5)	1 (0 - 5)
Diabetes mellitus, *n* (%)		
GDM	173 (61.1)	30 (31.3)
Type 1 diabetes	44 (15.5)	25 (26.0)
Type 2 diabetes	66 (23.3)	41 (42.7)
Gestational age at delivery (weeks), median (range)	37 (26 - 41)	37 (23 - 40)
Route of delivery, *n* (%)		
Caesarean section	193 (68.2)	54*
NVD	88 (31.1)	18
Assisted delivery	2 (0.7)	1
Birth weight (g), median (range)	3 050 (600 - 4 560)	3 200 (460 - 4 770)

GDM = gestational diabetes mellitus; NVD = normal vaginal delivery.
*Data for routes of delivery incomplete, so patients do not add up to 96.

Table 2. Cross-tabulation of fetal growth on population-based growth charts and customised growth charts

	Population-based charts			
Customised charts	**SGA**	**AGA**	**LGA**	**Total, *n* (%)**
SGA	22	14	0	36 (12.7)
AGA	4	143	3	150 (53.0)
LGA	0	58	39	97 (34.3)
Total, *n* (%)	26 (9.2)	215 (76.0)	42 (14.8)	283 (100)

On population-based growth charts, 4 fetuses (8.7%) of type 1 diabetic women were LGA, but 17 (37%) of the fetuses were LGA when customised charts were used ($p<0.001$). In this group, 4 (8.7%) of fetuses were SGA on population-based charts, but 7 (15.2%) were SGA on customised growth charts ($p<0.001$).

For type 2 diabetic women, 10 (15.2%) and 19 (28.8%) of fetuses were LGA on population and customised growth charts, respectively ($p<0.001$). In this group, 8 (12.1%) fetuses were SGA on population-based charts and 12 (18.2%) on customised growth charts ($p<0.001$).

In the GDM group, 29 of fetuses (16.8%) were LGA on population growth charts and 63 (36.4%) on customised growth charts ($p<0.001$); 13 fetuses (7.5%) were SGA on population-based charts and 16 (9.2%) on customised growth charts ($p<0.001$).

The growth of 79 fetuses (27.9%) would have been reclassified had customised growth charts been used instead of the standard population-based growth charts (Table 2). The overall agreement in classification of growth of fetuses of diabetic mothers between the population-based and customised growth charts is significantly different (p<0.001), and there is a moderate agreement based on Cohen's kappa of 0.45.

Discussion

Customised growth centiles based on individual fetal growth potential enhance our ability to differentiate between physiological and pathological growth derangements. Numerous studies have found similarities in the way fetal growth varies with maternal and pregnancy-related characteristics.

Every year more women are diagnosed with diabetes. In keeping with this trend, more women are also being diagnosed with GDM. These women have an increased risk of delivering macrosomic and growth-restricted babies, with their related risks. We therefore need to predict fetal growth accurately.

Routine care of an uncomplicated DM pregnancy entails fetal growth assessment per trimester. However, it is recommended that growth-restricted and LGA fetuses are followed up every two weeks, as these fetuses are at risk of perinatal mortality and may require preterm delivery.[11] In addition, LGA fetuses are at increased risk of birth trauma, neonatal metabolic and physiological disturbances, and respiratory

distress syndrome as a result of delayed fetal lung maturity. The fetuses that were in fact AGA rather than SGA or LGA would have had fewer interventions and not required amniocentesis and preterm delivery. Similarly, those fetuses classified as AGA that were in fact SGA or LGA on customised growth charts may have required closer monitoring to prevent neonatal morbidity.

Previous studies have shown conflicting results, with some showing no benefit in using customised growth charts[12] and others showing that customised centiles identified more SGA babies.[13-14]

In this study, the reclassification of growth based on customised centiles was prevalent in all types of DM. There was a significant difference in fetal growth classification depending on whether a population-based growth chart or a customised growth chart was used. The 'one-size-fits-all' premise is not appropriate.

Study limitations

As this was a retrospective study, we were unable to obtain adequate, complete information regarding the perinatal outcomes of the babies. All patients were managed according to a standard protocol using population-based growth charts. We are unable to draw conclusions as to whether correctly classifying fetal growth would translate into improved neonatal outcome.

Conclusion

The customised growth charts identified more babies as being LGA and SGA. These babies need more vigilant antenatal care and may need preterm delivery. We cannot ascertain whether using customised growth charts would improve perinatal outcome, and would therefore like to do a prospective randomised trial.

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