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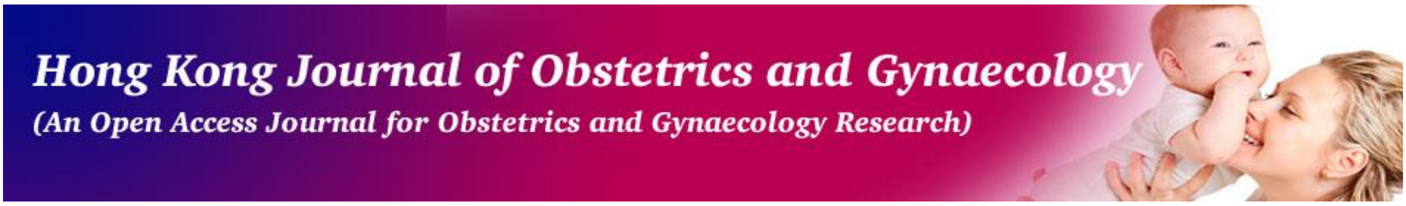


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# Clinical Relevance of Using Local Fetal Biometry Charts as Compared to Intergrowth-21st Standard: A Cross-Sectional Study at Kasr El- Ainy Hospital, Cairo University, Egypt

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## Abstract

**Background:** The Fetal Growth Longitudinal Study (FGLS), part of the INTERGROWTH-21$^{st}$ (IG-21st) Project developed major international standards for fetal size and growth. Our study aimed to formulate reference fetal biometry charts for the Egyptian population and then to compare these novel charts with those of the FGLS to ascertain the statistical significance of differences. And finally to assess the clinical impact of statistical significance between these curves for the diagnoses of abnormal fetal growth and justifying the development of specific local growth curves for clinical practice. **Methods:** A cross-sectional study was carried out at Cairo University Hospital from 2018 to 2020 and including pregnant patients of Egyptian ethnicity, at 14 to 40 gestational weeks. Ultrasound measurements of biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) were retrieved from a prospective clinical database. Based on their characteristics, the included patients were at low risk of abnormal pregnancy outcomes and met proper health and nutritional requirements with the exclusion of cases with major known chronic diseases and undernutrition. All women had an accurate assessment of gestational age at 11+0-13+6 weeks by a crown-rump length measurement. A general linear model (GLM) having the same terms of the same degree as those used in IG-21st for the estimation of the mean (50th centile) of each biometric parameter was used to evaluate the ultrasound growth trajectory of BPD, HC, AC, and FL as a function of gestational age. We decided to use the terms of the same polynomial (including quadratic cubic and logarithmic terms) to allow a comparison aimed at detecting major differences of Egyptian vs IG-21st curves. Finally, major percentiles including 3rd,5th, and 97th were compared to assess possible clinical differences. **Results:** The study group included 540 fetuses (20 per gestational week) meeting the inclusion criteria. The model enabled the construction of curves, with respective percentiles, from 14 - 40 weeks' gestation. All the polynomial terms reached very significant values (all the p-values < 0.001) and the vast majority of the coefficients' values were similar to the IG-21st coefficients. The local group estimated mean values (50th percentile) were on average 2% smaller for BPD and 3% and 4% larger for AC and FL respectively, as compared to the IG-21st standard. Mean HC showed a discordant trajectory, being 4% larger at 14-15 weeks, for progressing reducing to 0% the discrepancy at 30 weeks, and again showing an increasing difference toward larger values after 30 weeks and up to 3% at 40 weeks. Analysis of major percentiles for clinical decision making showed the following: (1) Local BPD 5$^{th}$ and 95th percentiles were smaller corresponding to the 1st and 90th IG-21st centile. (2) Local HC 5th percentile corresponded to the 3rd percentile until 32 weeks and to the 10th percentile after 37 weeks. Local HC 95th percentile was bigger corresponding to the 99th IG-21st percentile. (3) Local FL 5th percentile was quite similar until 32 weeks and then corresponded to the 10th percentile. Local FL 95th percentiles were bigger corresponding to the 99th IG-21st percentile. (4) Local AC 3rd percentile was quite similar to the 3rd IG-21st percentile. The 10th percentile corresponded to 15th on average, and the 95th percentile corresponded constantly to the 99th IG21st percentile. Globally, BPD was constantly smaller and FL and AC constantly bigger respectively. AC percentile values were wider but the 3rd and the 10th percentiles were quite similar to the IG-21st. HC was globally wider and also showed a wider percentile values distribution, despite the crossing growth trajectory with IG-21th. **Conclusion:** We present new reference charts for fetal biometry for the Egyptian population. Our growth curves are very similar to those reported in the IG-21st charts, only HC was slightly non in line with the IG-21st trajectory. The IG-21st charts can be used for accurate fetal biometry and assessment of FGR in an Egyptian population. We present novel reference charts for fetal biometry of the Egyptian population, modeled using identical polynomial terms and degrees of IG-21st curves. Local and IG-21st charts showed minimal differences in BPD and AC (respectively slightly smaller and greater in third-trimester local curves) or FL and HC (globally slightly greater). Overall, there was a very good concordance of estimated AC 3rd and 97th percentiles which are critically important to define abnormal fetal growth. Despite some differences, the clinical impact is likely minimal; therefore, the IG-21st charts can be used for accurate fetal biometry and detection of abnormal fetal growth in an Egyptian population.

**Keywords:** Fetal growth, Growth curves, Intergrowth-21, Polynomial regression, Ultrasound, Biparietal diameter, Head circumference, Abdominal circumference, Femur length.

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## INTRODUCTION

Assessment of fetal well-being is the main target of a proper antenatal care program. Accurate monitoring of fetal growth is crucial to ensure fetal well-being and monitor maternal and fetal complications. There are many challenges in differentiating normal from abnormal growth [1, 2] and fetal biometry is supposed to be an accurate estimate of birthweight that reflects intrauterine fetal growth [3, 4] and recently, intrauterine fetal growth is considered a marker of postnatal life, and many health risks [5]. Usually we compare fetal biometry and estimated fetal weight with reference curves to produce a percentile, with a range of 3rd to 97th percentile considered appropriate for gestational age [1, 6]. Using proper reference growth charts will therefore affect the diagnosis of small and large for gestational age [7].

Many studies both cross-sectional and longitudinal showed racial variations in fetal growth [8, 9, 10]. Turkish and Moroccan women showed fetuses with shorter femur, smaller head, and abdominal circumferences than Belgian women, and in Nigerian women, AC and BPD were found to be smaller than those of the British population [8, 11]. The INTERGROWTH and WHO Fetal studies on fetal growth started with the same assumption, that there would be no differences internationally in fetal growth when conditions were optimal. INTERGROWTH evaluated the differences in crown-rump length (CRL), head circumference (HC), and newborn length among countries, concluding that the differences were small enough before pooling [12].

The aim of this study was: (i) to create standards for fetal biometry in an Egyptian population using a cohort of healthy, well-nourished pregnant women at low risk of adverse maternal and perinatal outcomes; (ii) to compare these novel charts with those of the IG-21st [13, 21], to ascertain the statistical significance of differences; (iii) to assess the clinical impact of any differences for the diagnoses of abnormal fetal growth, and to justify the development of specific local growth curves for clinical practice.

## METHODS

### Study design and participants

This is a prospective cross-sectional study conducted from June 2018 to January 2020 at Cairo University Maternal-Fetal Medicine Unit (CAIFM) - Kasr Al-Ainy Teaching Hospital. All Sonographers had at least 3 years of experience in fetal medicine unit, Cairo university and competent to do fetal biometry according to ISUOG guideline. We used Astraia Software for reporting and saving data.

The study included a cohort of healthy, well-nourished pregnant Egyptian women, considered at low risk for adverse maternal and perinatal outcomes. Spontaneous singleton pregnancies at 14 to 40 weeks were included (20 for each gestational week), with no chronic medical or nutritional disorder and no drug intake except vitamin supplements. Exclusion criteria were: cigarette smoking, alcohol consumption, history of growth restriction or macrosomia in previous pregnancies, congenital anomalies, or chromosomal defects. Maternal age ranged from 18 to 40 years, BMI from 18.5 to 30 kg/m, and Height was greater than 153cm.

The most common reasons for ineligibility were maternal age younger than 18 years or older than 40 years, maternal height less than 153 cm, and BMI more than 30 kg/m2. We also excluded women who developed severe medical problems during pregnancy or newborn who had low birth weight after delivery.

The study was approved by the scientific ethical committee of the department of obstetrics and gynecology at Kasr El-Ainy Hospital – Faculty of Medicine- Cairo University and signed informed consent was obtained from all patients.

### Procedures

A very precise determination of gestational age is vitally important for constructing these growth standards. A reliable crown-rump length (CRL) at 11-13+6 weeks gestation was done to all patients included in the study. The CRL technique was standardized and all sonographers were trained uniformly with strict quality control measures [14].

CRL is the longest distance in a straight line from the cranial to the caudal end of the body and is the most accurate assessment for pregnancy dating [15] Image (1)


Image (1)

We included 540 (20 for each gestational from 14 -40) women after the initial dating scan. During each scan, fetal head circumference (HC), Occipto-frontal diameter (OFD), biparietal diameter (BPD), abdominal circumference (AC), anteroposterior abdominal diameter (APAD), transverse abdominal diameter (TAD) and femur length (FL) were measured 3 times from 3 separately generated ultrasound images in a “blinded” fashion. The average of the 3 measurements was taken for record. The BPD, OFD, HC, TAD, APAD, AC, and FL images should fill at least 75 % of the monitor screen. We used the detailed measurement protocol and the unique standardization procedures used in the INTERGROWTH -21st study [16].

All scans were performed trans-abdominally using GE Voluson E10 (General Electric, Chicago, IL, USA) by curvilinear probe 5-7MHz

The biometry was done according to ISUOG Guideline [17] where measurements should be performed in a standardized manner on the basis of strict quality criteria

### Biparietal diameter (BPD)

**Anatomy:**

- Cross-sectional view of the fetal head at the level of the thalami.
- Ideal angle of insonation is 90◦ to the midline echoes.
- Symmetrical appearance of both hemispheres.
- Continuous midline echo (falx cerebri) broken in middle by the cavum septi pellucidi and thalamus;
- No cerebellum visualized.

**Caliper placement**

Both calipers should be placed according to a specific methodology, because more than one technique has been described (e.g. outer edge to inner edge or ‘leading edge’ technique vs. outer edge to outer edge), at the widest part of the skull, using an angle that is perpendicular to the midline falx.

In this study we used from outer to inner edge. Image (2)


Image (2)

**Head circumference (HC)**

**Anatomy:**

As described for the BPD, ensuring that the circumference placement markers correspond to the technique described on the reference chart.

**Caliper placement:**

If the ultrasound equipment has ellipse measurement capacity, then the HC can be measured directly by placing the ellipse around the outside of the skull bone echoes. Image (3)


Image (3)

**Abdominal circumference (AC)**

**Anatomy**

- Transverse section of the fetal abdomen (as circular as possible);
- Umbilical vein at the level of the portal sinus;
- Stomach bubble visualized;
- Kidneys should not be visible.

**Caliper placement**

The AC is measured at the outer surface of the skin line, either directly with ellipse calipers or calculated from linear measurements made perpendicular to each other, usually the anteroposterior abdominal diameter (APAD) and transverse abdominal diameter (TAD). To measure the APAD, the calipers are placed on the outer borders of the body outline, from the posterior aspect (skin covering the spine) to the anterior abdominal wall. To measure the TAD, the calipers are placed on the outer borders of the body outline, across the abdomen at the widest point. Image (4)


Image (4)

**Femur diaphysis length (FDL)**

**Anatomy:**

The FDL is imaged optimally with both ends of the ossified metaphysis clearly visible.

The longest axis of the ossified diaphysis is measured.

The same technique as that used to establish the reference chart should be used with regard to the angle between the femur and the insonating ultrasound beams.

An angle of insonation between 45◦ and 90◦ is typical.

Caliper placement. Each caliper is placed at the ends of the ossified diaphysis without including the distal femoral epiphysis if it is visible. This measurement should exclude triangular spur artifacts that can falsely extend the diaphysis length. Image (5)


Image (5)

**Statistical analysis**

To compare our curves with the IG-21st curves [12, 13] and to evaluate their degree of similarity, we used a general linear model (GLM) with "a priori definition" of terms and degrees as those used in IG-21st. We therefore used in the GLM equations the same terms and degree of the independent variable (GA in weeks) including GA2, GA3, lnGA, and (lnGA)2 as estimated by the fractional polynomials method used to generate the IG-21st curves.

We calculated the centiles of interest including 3rd, 5th, 10th, 25th, 75th, 90th, 95th, and 97th. Comparison of major centiles of interest (including 5th 95th and for AC also the 3rd) with expected IG-21st percentiles was performed.

**RESULTS**

We Studied 540 pregnant women (20 for each week from14-40 weeks' gestation) attending the CAIFM who met the eligibility criteria. Informed consent was taken from all patients.

The 3rd, 5th, 10th, 50th, 90th, 95th, and 97th fitted percentile curves for BPD, OFD, HC, AC, APAD, TAD, and FL according to gestational age, which represents the standard charts for fetal growth in a sample of the Egyptian population, are presented in **tables 1-7** respectively.

**Table 1:** Growth chart for fetal biparietal diameter.

| Gestational age (week) | Biparietal diameter (mm) | | | | | | |
|---|---|---|---|---|---|---|---|
| | **5°%** | **10°%** | **25°%** | **50°%** | **75°%** | **90°p%** | **95°%** |
| 14 | 22.25 | 23.33 | 25.13 | 27.13 | 29.13 | 30.93 | 32.01 |
| 15 | 25.99 | 27.08 | 28.89 | 30.91 | 32.93 | 34.75 | 35.84 |
| 16 | 29.64 | 30.74 | 32.57 | 34.61 | 36.65 | 38.48 | 39.58 |
| 17 | 33.20 | 34.31 | 36.16 | 38.22 | 40.28 | 42.13 | 43.23 |
| 18 | 36.68 | 37.79 | 39.66 | 41.74 | 43.81 | 45.68 | 46.80 |
| 19 | 40.06 | 41.19 | 43.07 | 45.17 | 47.27 | 49.15 | 50.28 |
| 20 | 43.36 | 44.50 | 46.40 | 48.51 | 50.63 | 52.53 | 53.67 |
| 21 | 46.57 | 47.72 | 49.64 | 51.77 | 53.90 | 55.82 | 56.97 |
| 22 | 49.69 | 50.85 | 52.79 | 54.94 | 57.09 | 59.03 | 60.18 |
| 23 | 52.73 | 53.90 | 55.85 | 58.02 | 60.19 | 62.14 | 63.31 |
| 24 | 55.67 | 56.85 | 58.82 | 61.01 | 63.20 | 65.17 | 66.35 |
| 25 | 58.53 | 59.72 | 61.71 | 63.91 | 66.12 | 68.11 | 69.30 |
| 26 | 61.30 | 62.50 | 64.50 | 66.73 | 68.96 | 70.96 | 72.16 |
| 27 | 63.98 | 65.19 | 67.21 | 69.46 | 71.70 | 73.72 | 74.93 |
| 28 | 66.58 | 67.80 | 69.83 | 72.10 | 74.36 | 76.40 | 77.62 |
| 29 | 69.08 | 70.31 | 72.37 | 74.65 | 76.93 | 78.99 | 80.22 |
| 30 | 71.50 | 72.74 | 74.81 | 77.11 | 79.42 | 81.49 | 82.73 |
| 31 | 73.83 | 75.08 | 77.17 | 79.49 | 81.81 | 83.90 | 85.15 |
| 32 | 76.07 | 77.33 | 79.44 | 81.78 | 84.12 | 86.22 | 87.48 |
| 33 | 78.23 | 79.50 | 81.62 | 83.98 | 86.34 | 88.46 | 89.73 |
| 34 | 80.29 | 81.57 | 83.71 | 86.09 | 88.47 | 90.61 | 91.89 |
| 35 | 82.27 | 83.56 | 85.72 | 88.11 | 90.51 | 92.67 | 93.96 |
| 36 | 84.16 | 85.46 | 87.63 | 90.05 | 92.47 | 94.64 | 95.94 |
| 37 | 85.96 | 87.27 | 89.46 | 91.90 | 94.33 | 96.52 | 97.83 |
| 38 | 87.68 | 89.00 | 91.20 | 93.66 | 96.11 | 98.32 | 99.64 |
| 39 | 89.30 | 90.63 | 92.86 | 95.33 | 97.80 | 100.03 | 101.36 |
| 40 | 90.84 | 92.18 | 94.42 | 96.91 | 99.41 | 101.65 | 102.99 |

**Table 2:** Growth chart for fetal occiputo-frontal diameter.

| Gestational age (week) | Occipital frontal diameter (mm) | | | | | | |
|---|---|---|---|---|---|---|---|
| | **5°%** | **10°%** | **25°%** | **50°%** | **75°%** | **90°%** | **95°%** |
| 14 | 27.24 | 28.48 | 30.55 | 32.85 | 35.15 | 37.22 | 38.46 |
| 15 | 32.24 | 33.51 | 35.64 | 38.00 | 40.36 | 42.49 | 43.76 |
| 16 | 37.08 | 38.38 | 40.57 | 42.99 | 45.42 | 47.60 | 48.91 |
| 17 | 41.76 | 43.10 | 45.34 | 47.83 | 50.32 | 52.56 | 53.90 |
| 18 | 46.29 | 47.66 | 49.96 | 52.51 | 55.07 | 57.36 | 58.74 |
| 19 | 50.66 | 52.06 | 54.42 | 57.04 | 59.65 | 62.01 | 63.42 |
| 20 | 54.87 | 56.31 | 58.72 | 61.40 | 64.09 | 66.50 | 67.94 |
| 21 | 58.93 | 60.41 | 62.87 | 65.62 | 68.36 | 70.83 | 72.31 |
| 22 | 62.83 | 64.34 | 66.87 | 69.67 | 72.48 | 75.01 | 76.52 |
| 23 | 66.58 | 68.12 | 70.70 | 73.58 | 76.45 | 79.03 | 80.57 |
| 24 | 70.17 | 71.75 | 74.39 | 77.32 | 80.26 | 82.90 | 84.47 |
| 25 | 73.60 | 75.22 | 77.91 | 80.91 | 83.91 | 86.60 | 88.22 |
| 26 | 76.88 | 78.53 | 81.28 | 84.34 | 87.40 | 90.16 | 91.80 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 27 | 80.00 | 81.68 | 84.49 | 87.62 | 90.75 | 93.56 | 95.24 |
| 28 | 82.97 | 84.68 | 87.55 | 90.74 | 93.93 | 96.80 | 98.51 |
| 29 | 85.78 | 87.53 | 90.45 | 93.71 | 96.96 | 99.88 | 101.63 |
| 30 | 88.43 | 90.22 | 93.20 | 96.51 | 99.83 | 102.81 | 104.60 |
| 31 | 90.93 | 92.75 | 95.79 | 99.17 | 102.55 | 105.59 | 107.40 |
| 32 | 93.28 | 95.13 | 98.22 | 101.66 | 105.11 | 108.20 | 110.05 |
| 33 | 95.46 | 97.35 | 100.50 | 104.01 | 107.51 | 110.66 | 112.55 |
| 34 | 97.49 | 99.41 | 102.62 | 106.19 | 109.76 | 112.97 | 114.89 |
| 35 | 99.37 | 101.32 | 104.59 | 108.22 | 111.85 | 115.12 | 117.07 |
| 36 | 101.08 | 103.07 | 106.40 | 110.09 | 113.79 | 117.11 | 119.10 |
| 37 | 102.65 | 104.67 | 108.05 | 111.81 | 115.57 | 118.95 | 120.97 |
| 38 | 104.05 | 106.11 | 109.55 | 113.37 | 117.19 | 120.63 | 122.69 |
| 39 | 105.30 | 107.39 | 110.89 | 114.78 | 118.66 | 122.16 | 124.25 |
| 40 | 106.40 | 108.52 | 112.07 | 116.02 | 119.98 | 123.53 | 125.65 |

**Table 3:** Growth chart for fetal head circumference.

| **Gestational age (week)** | **Head circumference (mm)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | **5°%** | **10°%** | **25°%** | **50°%** | **75°%** | **90°%** | **95°%** |
| 14 | 84,27 | 88,09 | 94,47 | 101,57 | 108,66 | 115,04 | 118,86 |
| 15 | 96,30 | 100,25 | 106,84 | 114,17 | 121,51 | 128,10 | 132,04 |
| 16 | 108,07 | 112,15 | 118,95 | 126,52 | 134,09 | 140,90 | 144,97 |
| 17 | 119,59 | 123,79 | 130,81 | 138,61 | 146,42 | 153,44 | 157,64 |
| 18 | 130,84 | 135,17 | 142,40 | 150,45 | 158,49 | 165,73 | 170,06 |
| 19 | 141,84 | 146,29 | 153,74 | 162,03 | 170,31 | 177,76 | 182,21 |
| 20 | 152,58 | 157,16 | 164,82 | 173,34 | 181,86 | 189,53 | 194,11 |
| 21 | 163,06 | 167,77 | 175,64 | 184,40 | 193,16 | 201,04 | 205,75 |
| 22 | 173,28 | 178,12 | 186,21 | 195,20 | 204,20 | 212,29 | 217,13 |
| 23 | 183,25 | 188,21 | 196,52 | 205,75 | 214,98 | 223,29 | 228,25 |
| 24 | 192,95 | 198,05 | 206,56 | 216,03 | 225,51 | 234,02 | 239,12 |
| 25 | 202,40 | 207,62 | 216,35 | 226,06 | 235,77 | 244,50 | 249,72 |
| 26 | 211,59 | 216,94 | 225,89 | 235,83 | 245,78 | 254,72 | 260,07 |
| 27 | 220,53 | 226,00 | 235,16 | 245,34 | 255,53 | 264,69 | 270,16 |
| 28 | 229,20 | 234,81 | 244,18 | 254,60 | 265,02 | 274,39 | 280,00 |
| 29 | 237,62 | 243,35 | 252,94 | 263,59 | 274,25 | 283,84 | 289,57 |
| 30 | 245,78 | 251,64 | 261,44 | 272,33 | 283,23 | 293,03 | 298,89 |
| 31 | 253,68 | 259,67 | 269,68 | 280,81 | 291,95 | 301,96 | 307,95 |
| 32 | 261,32 | 267,44 | 277,66 | 289,03 | 300,41 | 310,63 | 316,75 |
| 33 | 268,71 | 274,95 | 285,39 | 297,00 | 308,61 | 319,05 | 325,29 |
| 34 | 275,83 | 282,20 | 292,86 | 304,70 | 316,55 | 327,21 | 333,58 |
| 35 | 282,70 | 289,20 | 300,07 | 312,15 | 324,24 | 335,10 | 341,60 |
| 36 | 289,31 | 295,94 | 307,02 | 319,34 | 331,67 | 342,75 | 349,37 |
| 37 | 295,67 | 302,42 | 313,72 | 326,28 | 338,83 | 350,13 | 356,88 |
| 38 | 301,76 | 308,64 | 320,15 | 332,95 | 345,75 | 357,25 | 364,14 |
| 39 | 307,60 | 314,61 | 326,33 | 339,36 | 352,40 | 364,12 | 371,13 |
| 40 | 313,18 | 320,32 | 332,25 | 345,52 | 358,80 | 370,73 | 377,87 |

**Table 4:** Growth chart for fetal abdominal circumference.

| **Gestational Age (week)** | **Abdominal Circumference (mm)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | **5°%** | **10°%** | **25°%** | **50°%** | **75°%** | **90°%** | **95°%** |
| 14 | 70.49 | 73.83 | 79.41 | 85.61 | 91.82 | 97.40 | 100.73 |
| 15 | 81.53 | 84.97 | 90.73 | 97.14 | 103.54 | 109.30 | 112.75 |
| 16 | 92.48 | 96.03 | 101.97 | 108.58 | 115.18 | 121.13 | 124.68 |
| 17 | 103.34 | 107.00 | 113.12 | 119.93 | 126.74 | 132.86 | 136.52 |
| 18 | 114.12 | 117.89 | 124.19 | 131.20 | 138.21 | 144.51 | 148.28 |
| 19 | 124.81 | 128.69 | 135.17 | 142.38 | 149.59 | 156.08 | 159.95 |
| 20 | 135.42 | 139.40 | 146.07 | 153.48 | 160.89 | 167.55 | 171.54 |
| 21 | 145.94 | 150.03 | 156.88 | 164.49 | 172.10 | 178.95 | 183.04 |
| 22 | 156.37 | 160.57 | 167.60 | 175.41 | 183.23 | 190.25 | 194.45 |
| 23 | 166.72 | 171.03 | 178.24 | 186.25 | 194.26 | 201.47 | 205.78 |
| 24 | 176.98 | 181.40 | 188.79 | 197.00 | 205.22 | 212.61 | 217.02 |
| 25 | 187.15 | 191.68 | 199.25 | 207.67 | 216.09 | 223.65 | 228.18 |
| 26 | 197.24 | 201.88 | 209.63 | 218.25 | 226.87 | 234.62 | 239.25 |
| 27 | 207.25 | 211.99 | 219.92 | 228.74 | 237.56 | 245.49 | 250.24 |
| 28 | 217.17 | 222.02 | 230.13 | 239.15 | 248.17 | 256.28 | 261.13 |
| 29 | 227.00 | 231.96 | 240.25 | 249.47 | 258.69 | 266.99 | 271.95 |
| 30 | 236.74 | 241.81 | 250.29 | 259.71 | 269.13 | 277.60 | 282.67 |
| 31 | 246.40 | 251.58 | 260.23 | 269.86 | 279.48 | 288.14 | 293.31 |
| 32 | 255.98 | 261.26 | 270.10 | 279.92 | 289.75 | 298.58 | 303.87 |
| 33 | 265.47 | 270.86 | 279.87 | 289.90 | 299.93 | 308.94 | 314.33 |
| 34 | 274.87 | 280.37 | 289.56 | 299.79 | 310.02 | 319.22 | 324.72 |
| 35 | 284.18 | 289.79 | 299.17 | 309.60 | 320.03 | 329.40 | 335.01 |
| 36 | 293.41 | 299.13 | 308.69 | 319.32 | 329.95 | 339.51 | 345.22 |
| 37 | 302.56 | 308.38 | 318.12 | 328.95 | 339.78 | 349.52 | 355.35 |
| 38 | 311.61 | 317.55 | 327.47 | 338.50 | 349.53 | 359.45 | 365.39 |
| 39 | 320.59 | 326.63 | 336.73 | 347.96 | 359.20 | 369.30 | 375.34 |
| 40 | 329.47 | 335.62 | 345.90 | 357.34 | 368.77 | 379.06 | 385.20 |

**Table 5:** Growth chart for fetal abdominal antero-posterior diameter.

| **Gestational age (week)** | **Abdominal antero-posterior diameter (mm)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | **5°%** | **10°%** | **25°%** | **50°%** | **75°%** | **90°%** | **95°%** |
| 14 | 22.23 | 23.33 | 25.16 | 27.2 | 29.24 | 31.07 | 32.17 |
| 15 | 25.61 | 26.75 | 28.67 | 30.81 | 32.94 | 34.86 | 36.00 |
| 16 | 28.96 | 30.16 | 32.16 | 34.39 | 36.62 | 38.62 | 39.82 |
| 17 | 32.30 | 33.54 | 35.63 | 37.95 | 40.27 | 42.36 | 43.61 |
| 18 | 35.61 | 36.91 | 39.08 | 41.49 | 43.91 | 46.08 | 47.38 |
| 19 | 38.90 | 40.25 | 42.50 | 45.01 | 47.52 | 49.77 | 51.12 |
| 20 | 42.16 | 43.56 | 45.90 | 48.51 | 51.11 | 53.45 | 54.85 |
| 21 | 45.41 | 46.86 | 49.28 | 51.98 | 54.67 | 57.10 | 58.55 |
| 22 | 48.63 | 50.13 | 52.64 | 55.43 | 58.22 | 60.73 | 62.23 |
| 23 | 51.83 | 53.38 | 55.98 | 58.86 | 61.74 | 64.34 | 65.89 |
| 24 | 55.01 | 56.61 | 59.29 | 62.27 | 65.25 | 67.92 | 69.53 |
| 25 | 58.17 | 59.82 | 62.58 | 65.66 | 68.73 | 71.49 | 73.14 |
| 26 | 61.31 | 63.01 | 65.85 | 69.02 | 72.18 | 75.03 | 76.73 |
| 27 | 64.42 | 66.17 | 69.10 | 72.36 | 75.62 | 78.55 | 80.30 |
| 28 | 67.51 | 69.31 | 72.33 | 75.68 | 79.03 | 82.05 | 83.85 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 29 | 70.58 | 72.43 | 75.53 | 78.98 | 82.43 | 85.52 | 87.38 |
| 30 | 73.63 | 75.53 | 78.71 | 82.26 | 85.80 | 88.98 | 90.88 |
| 31 | 76.65 | 78.61 | 81.87 | 85.51 | 89.14 | 92.41 | 94.37 |
| 32 | 79.66 | 81.66 | 85.01 | 88.74 | 92.47 | 95.82 | 97.83 |
| 33 | 82.64 | 84.69 | 88.13 | 91.95 | 95.77 | 99.21 | 101.26 |
| 34 | 85.60 | 87.70 | 91.22 | 95.14 | 99.05 | 102.58 | 104.68 |
| 35 | 88.53 | 90.69 | 94.30 | 98.31 | 102.31 | 105.92 | 108.08 |
| 36 | 91.45 | 93.66 | 97.35 | 101.45 | 105.55 | 109.24 | 111.45 |
| 37 | 94.34 | 96.60 | 100.37 | 104.57 | 108.77 | 112.54 | 114.80 |
| 38 | 97.21 | 99.52 | 103.38 | 107.67 | 111.96 | 115.82 | 118.13 |
| 39 | 100.06 | 102.42 | 106.36 | 110.75 | 115.13 | 119.08 | 121.43 |
| 40 | 102.89 | 105.3 | 109.33 | 113.81 | 118.28 | 122.31 | 124.72 |

**Table 6:** Growth chart for fetal transverse abdominal diameter.

| **Gestational Age (week)** | **Transverse Abdominal Diameter (mm)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | **5°%** | **10°%** | **25°%** | **50°%** | **75°%** | **90°%** | **95°%** |
| 14 | 20.23 | 21.47 | 23.53 | 25.82 | 28.12 | 30.18 | 31.41 |
| 15 | 23.83 | 25.10 | 27.23 | 29.60 | 31.97 | 34.10 | 35.37 |
| 16 | 27.38 | 28.69 | 30.89 | 33.34 | 35.78 | 37.98 | 39.29 |
| 17 | 30.88 | 32.24 | 34.51 | 37.03 | 39.54 | 41.81 | 43.17 |
| 18 | 34.35 | 35.74 | 38.08 | 40.67 | 43.27 | 45.60 | 47.00 |
| 19 | 37.76 | 39.20 | 41.60 | 44.27 | 46.94 | 49.35 | 50.78 |
| 20 | 41.14 | 42.61 | 45.08 | 47.83 | 50.58 | 53.05 | 54.52 |
| 21 | 44.47 | 45.98 | 48.52 | 51.35 | 54.17 | 56.71 | 58.22 |
| 22 | 47.75 | 49.31 | 51.92 | 54.82 | 57.71 | 60.32 | 61.88 |
| 23 | 50.99 | 52.59 | 55.27 | 58.24 | 61.21 | 63.89 | 65.49 |
| 24 | 54.19 | 55.83 | 58.57 | 61.62 | 64.67 | 67.41 | 69.05 |
| 25 | 57.35 | 59.03 | 61.84 | 64.96 | 68.09 | 70.90 | 72.58 |
| 26 | 60.46 | 62.18 | 65.05 | 68.26 | 71.46 | 74.33 | 76.05 |
| 27 | 63.52 | 65.28 | 68.23 | 71.51 | 74.78 | 77.73 | 79.49 |
| 28 | 66.54 | 68.35 | 71.36 | 74.71 | 78.06 | 81.08 | 82.88 |
| 29 | 69.52 | 71.36 | 74.45 | 77.87 | 81.30 | 84.38 | 86.22 |
| 30 | 72.46 | 74.34 | 77.49 | 80.99 | 84.49 | 87.64 | 89.53 |
| 31 | 75.34 | 77.27 | 80.49 | 84.07 | 87.64 | 90.86 | 92.79 |
| 32 | 78.19 | 80.16 | 83.44 | 87.10 | 90.75 | 94.03 | 96.00 |
| 33 | 80.99 | 83.00 | 86.35 | 90.08 | 93.81 | 97.16 | 99.17 |
| 34 | 83.75 | 85.80 | 89.22 | 93.02 | 96.83 | 100.25 | 102.3 |
| 35 | 86.46 | 88.55 | 92.04 | 95.92 | 99.80 | 103.29 | 105.38 |
| 36 | 89.13 | 91.26 | 94.82 | 98.78 | 102.73 | 106.29 | 108.42 |
| 37 | 91.76 | 93.93 | 97.55 | 101.59 | 105.62 | 109.24 | 111.41 |
| 38 | 94.34 | 96.55 | 100.24 | 104.35 | 108.46 | 112.15 | 114.36 |
| 39 | 96.88 | 99.13 | 102.89 | 107.07 | 111.26 | 115.02 | 117.27 |
| 40 | 99.37 | 101.66 | 105.49 | 109.75 | 114.01 | 117.84 | 120.13 |

**Table 7:** Growth chart for fetal femur length.

| Gestational age (week) | Femur length (mm) | | | | | | |
|---|---|---|---|---|---|---|---|
| | 5°% | 10°% | 25°% | 50°% | 75°% | 90°% | 95°% |
| 14 | 10.32 | 11.27 | 12.87 | 14.64 | 16.41 | 18.01 | 18.96 |
| 15 | 13.43 | 14.39 | 16.01 | 17.8 | 19.59 | 21.2 | 22.17 |
| 16 | 16.48 | 17.45 | 19.08 | 20.89 | 22.7 | 24.33 | 25.30 |
| 17 | 19.46 | 20.45 | 22.09 | 23.92 | 25.74 | 27.39 | 28.37 |
| 18 | 22.38 | 23.37 | 25.03 | 26.88 | 28.72 | 30.38 | 31.37 |
| 19 | 25.23 | 26.23 | 27.91 | 29.77 | 31.63 | 33.31 | 34.31 |
| 20 | 28.02 | 29.03 | 30.72 | 32.60 | 34.48 | 36.17 | 37.18 |
| 21 | 30.74 | 31.76 | 33.46 | 35.36 | 37.26 | 38.96 | 39.98 |
| 22 | 33.39 | 34.42 | 36.14 | 38.06 | 39.97 | 41.69 | 42.72 |
| 23 | 35.98 | 37.02 | 38.75 | 40.69 | 42.62 | 44.36 | 45.40 |
| 24 | 38.50 | 39.55 | 41.3 | 43.25 | 45.2 | 46.95 | 48.00 |
| 25 | 40.95 | 42.01 | 43.78 | 45.75 | 47.72 | 49.49 | 50.54 |
| 26 | 43.34 | 44.41 | 46.19 | 48.18 | 50.17 | 51.95 | 53.02 |
| 27 | 45.67 | 46.74 | 48.54 | 50.55 | 52.55 | 54.35 | 55.43 |
| 28 | 47.92 | 49.01 | 50.83 | 52.85 | 54.87 | 56.68 | 57.77 |
| 29 | 50.11 | 51.21 | 53.04 | 55.08 | 57.12 | 58.95 | 60.05 |
| 30 | 52.24 | 53.34 | 55.19 | 57.25 | 59.30 | 61.15 | 62.26 |
| 31 | 54.30 | 55.41 | 57.28 | 59.35 | 61.42 | 63.29 | 64.40 |
| 32 | 56.29 | 57.42 | 59.30 | 61.39 | 63.48 | 65.36 | 66.48 |
| 33 | 58.22 | 59.35 | 61.25 | 63.36 | 65.46 | 67.36 | 68.49 |
| 34 | 60.08 | 61.22 | 63.13 | 65.26 | 67.39 | 69.30 | 70.44 |
| 35 | 61.88 | 63.03 | 64.95 | 67.10 | 69.24 | 71.17 | 72.32 |
| 36 | 63.60 | 64.77 | 66.71 | 68.87 | 71.03 | 72.97 | 74.14 |
| 37 | 65.27 | 66.44 | 68.4 | 70.58 | 72.75 | 74.71 | 75.88 |
| 38 | 66.86 | 68.05 | 70.02 | 72.22 | 74.41 | 76.39 | 77.57 |
| 39 | 68.40 | 69.59 | 71.58 | 73.79 | 76.00 | 77.99 | 79.18 |
| 40 | 69.86 | 71.06 | 73.07 | 75.30 | 77.53 | 79.54 | 80.73 |

Comparison with IG-21st curves was performed only for these fetal parameters: BPD, HC, AC, and FL. The model enabled the construction of curves, with respective percentiles, from 14 to 40 weeks gestation. (figures 1-4)

All the polynomial terms reached significant values (all the p-values < 0.001) and the vast majority of the coefficient values were similar to the IG-21st coefficients. Again, many of the 95% CI intervals of the local curves were coherent, including the IG-21st coefficient (Tables 8-11). The local group estimated mean values (50th centiles) were on average 2% smaller for BPD and 3% and 4% larger for AC and FL respectively, as compared to the IG-21st standard. Mean HC showed a discordant trajectory, being 4% larger at 14-15 weeks, progressively reducing to 0% the discrepancy at 30 weeks and again showing an increasing difference toward larger values after 30 weeks and up to 3% at 40 weeks.

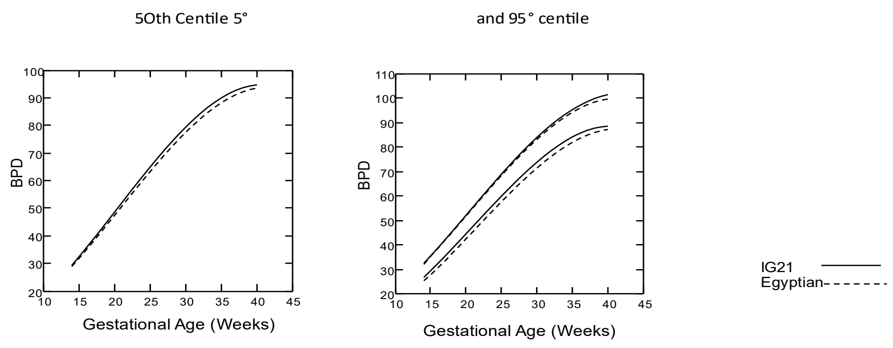


**Figure 1:** Comparison of smoothed 50th , 5th and 95th of our BPD curves with those reported in IG-21st.

smaller

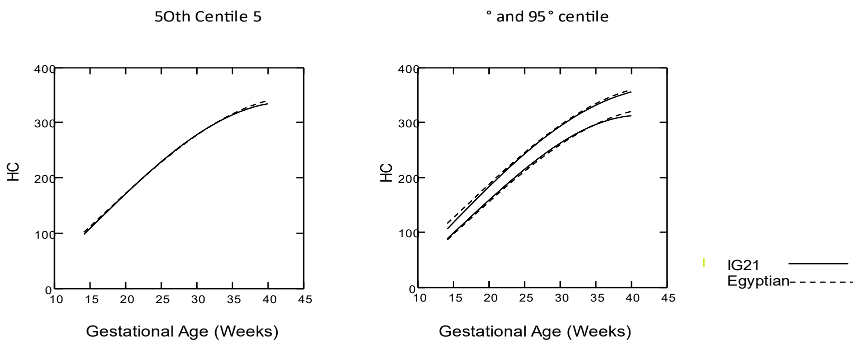


**Figure 2:** Comparison of smoothed 50th , 5 th and 95th of our HC curves with those reported in IG-21st

bigger

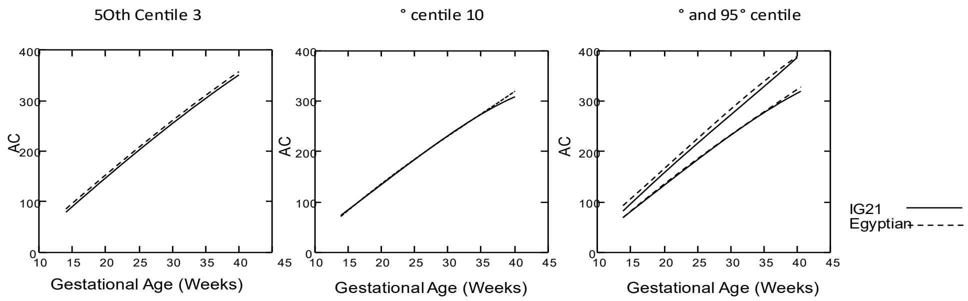


**Figure 3:** Comparison of smoothed 50th , 3rd, 10th and 95th of our AC curves with those reported in IG-21st

bigger

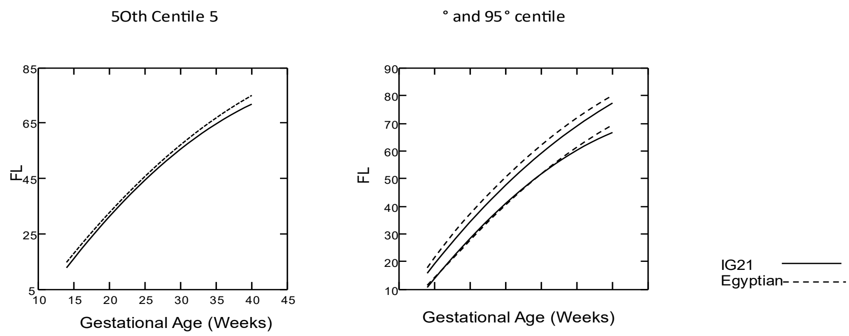


**Figure 4:** Comparison of smoothed 50th, 5th and 95th of our FL curves with those reported in IG-21st

bigger

**Table 8:** Comparison of estimated β coefficients with the original reported in IG21 equations for 50th centile of biparietal diameter. IG21 coefficients that are not included within the 95%CI of our population are marked with [1]

| Parameter | β | Std. Err | t | P-value | Confidence Bound 95% | | IG21 β-Coefficient |
|---|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound | |
| Intercept | 5.227 | 0.788 | 6.638 | <0.001 | 3.680 | 6.775 | 5.60878 |
| $GA^2$ | 0.155 | 0.003 | 45.751 | <0.001 | 0.149 | 0.162 | 0.158369 |
| $GA^3$ | -0.003 | 7.996E-5 | -31.364 | <0.001 | -0.003 | -0.002 | -0.00256379[1] |

**Table 9:** Comparison of estimated β coefficients with the original reported in IG21 equations for 50th centile of head circumference. IG21 coefficients that are not included within the 95%CI of our population are marked with [1]

| Parameter | β | Std. Err | t | P-value | Confidence Bound 95% | | |
|---|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound | IG21 β-Coefficient |
| Intercept | -16.766 | 3.416 | -4.907 | <0.001 | -23.478 | -10.054 | -28.2849[1] |
| $GA^2$ | 1.563 | 0.038 | 40.864 | <0.001 | 1.488 | 1.638 | 1.69267[1] |
| $GA^2$ * lnGA | -0.363 | 0.010 | -36.258 | <0.001 | -0.383 | -0.344 | -0.397485[1] |

**Table 10:** Comparison of estimated β coefficients with the original reported in IG21 equations for 50th centile of abdominal circumference. IG21 coefficients that are not included within the 95%CI of our population are marked with [1]

| Parameter | β | Std. Err | t | P-value | Confidence Bound 95% | | IG21 β-Coefficient |
|---|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound | |
| Intercept | -76.572 | 6.122 | -12.508 | <0.001 | -88.598 | -64.545 | -81.3243 |
| GA | 11.709 | .363 | 32.292 | <0.001 | 10.997 | 12.442 | 11.6772[1] |
| $GA^3$ | -0.0001 | 0.000 | -3.467 | <0.001 | -0.001 | -0.000256379 | -0.000561865 |

**Table 11:** Comparison of estimated β coefficients with the original reported in IG21 equations for 50th centile of femur length. All IG21 coefficients are included within the 95%CI of our population.

| Parameter | β | Std. Err | t | P-value | Confidence Bound 95% | | IG21 β-Coefficient |
|---|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound | |
| Intercept | -36.576 | 1.801 | -20.304 | <0.001 | -40.115 | -33.037 | -39.9616 |
| GA | 4.120 | 0.143 | 28.744 | <0.001 | 3.838 | 4.401 | 4.32298 |
| $GA^2$ | -0.033 | 0.003 | -12.411 | <0.001 | -0.039 | -0.028 | -0.0380156 |

Analysis of major percentiles for clinical decision making showed the following: (1) Local BPD 5th and 95th centiles were smaller corresponded to the 1st and 90th IG-21st centile. (2) Local HC 5th centile corresponded to the 3rd centile until 32 weeks and to the 10th centile about after 37 weeks. Local HC 95th centile was bigger corresponded to the 99th IG-21st centile. (3) Local FL 5th centile was quite similar until 32 weeks and then corresponded to the 10th centile. Local FL 95th centiles were bigger corresponded to the 99th IG-21st centile. (4) AC is the most important parameter for the definition of FGR and we evaluated the centiles that are used for the definition of early and late FGR according to Delphi Criteria [20]. Local AC 3rd centile were quite similar to the 3rd and 10th IG-21st centile. 95th centile corresponded constantly to the 99th IG21st centile. Table 12 shows the estimated IG-21st centile for the 3rd and 10th AC centile of our curve stratified for gestational age from 14 to 40 weeks. The impact of these differences on the FGR diagnosis should be very small and should result in higher sensitivity and a higher false-positive rate for FRG.

**Table 12:** Estimated IG21 centile for 3rd and 10th AC centile of our own curves stratified for gestational age from 14 to 40 weeks.

| Gestational age (week) | IG21 corresponding centile for 3rd centile estimation from our own curve | IG21 corresponding centile for 10th centile estimation from our own curve |
|---|---|---|
| 14 | 0.51 | 8.88 |
| 15 | 1.17 | 11.59 |
| 16 | 1.94 | 13.62 |
| 17 | 2.65 | 14.98 |
| 18 | 3.21 | 15.79 |
| 19 | 3.57 | 16.17 |
| 20 | 3.76 | 16.23 |
| 21 | 3.80 | 16.01 |
| 22 | 3.72 | 15.60 |
| 23 | 3.57 | 15.07 |
| 24 | 3.37 | 14.50 |
| 25 | 3.16 | 13.89 |
| 26 | 2.95 | 13.30 |
| 27 | 2.77 | 12.78 |

| | | |
|---|---|---|
| 28 | 2.62 | 15.89 |
| 29 | 2.51 | 16.17 |
| 30 | 2.46 | 16.53 |
| 31 | 2.48 | 16.99 |
| 32 | 2.55 | 17.55 |
| 33 | 2.71 | 18.24 |
| 34 | 2.97 | 19.04 |
| 35 | 3.34 | 19.98 |
| 36 | 3.85 | 21.04 |
| 37 | 4.53 | 22.22 |
| 38 | 5.43 | 23.50 |
| 39 | 6.56 | 24.89 |
| 40 | 7.98 | 26.35 |

Globally, BPD was constantly smaller and FL and AC constantly bigger, respectively. AC percentile values were wider but the 3rd and 10th centile were quite similar to the IG-21st. HC was globally wider and also showed a wider percentile values distribution, despite the crossing trajectory with IG-21th.

**DISCUSSION**

This study showed first that it is possible to build up robust and reliable growth curves for the Egyptian population based upon the polynomial equations of IG21st for BPD, HC, AC, FL; second, the differences of these growth curves as compared to that of IG-21st are minimal, based upon a comparison of coefficients and confidence intervals; thirdly, given the extent of the differences in the coefficients and trajectories, the potential clinical impact of these differences in the diagnosis of abnormal fetal growth is minimal.

Ultrasound assessment of fetal biometry is considered a fundamental part of proper antenatal care to determine and follow up fetal growth. Proper choice of reference charts is important to guarantee accurate assessment [21]. Many studies have shown the effect of ethnicity on fetal growth [8, 22].

The INTERGROWTH-21st (IG-21st ) project 2014 prospectively enrolled 4607 pregnant women from eight different populations who were well-nourished and at low risk of FGR. This was the first, population-based, large, multi-ethnic, longitudinal, fetal growth standard based on early assessment of gestational age. These standards are for use worldwide to diagnose FGR uniformly. They recommended the use of their charts for the interpretation of routine ultrasound measurements across different populations [12].

The IG-21st proved the concept that optimal fetal growth would be the same across various populations, provided maternal nutrition and condition were optimal. Thus, they designed their study to establish a single growth standard by pooling growth data from different populations [25].

However, the fetal growth study published by The National Institute of Child Health and Development (NICHD) in 2015 found that Significant differences in fetal growth were found among 4 enrolled groups in the USA ( of various ethnic origins). They recommended the use of Racial/ethnic-specific Growth Charts to improve the decisions in evaluating fetal growth [26].

Similarly The World Health Organization (WHO), in 2017 constructed new fetal growth charts for common fetal biometric measurements and fetal weight, based on a longitudinal study of 1387 low-risk pregnant women from 10 countries, including Egypt. The study showed that significant differences existed between countries; indicating ethnic, cultural, and geographic variations; and that maternal factors influenced fetal size as well as growth progress [25].

The results of the WHO study indicate that populations, even under optimal nutritional conditions and environment, vary and that fetal growth varies and should be considered when the WHO fetal growth charts or any growth references are applied [25].

What is apparent from all 3 mentioned studies is the wide differences in fetal growth and weight of birth even when conditions are optimized [17, 25, 26].

Another study by YKY Chang, *et al*. (2016) compared differences between the IG-21st charts and their existing Chinese biometry charts which were found to be large enough that it would not be possible to change to using IG-21st, without leading to a significant number of fetuses being misdiagnosed as small [27].

Our study described the optimal fetal growth for singleton pregnancies in an Egyptian population, who are known to be healthy, well-nourished women. The cohort of women was prospectively enrolled, had a low risk of adverse maternal and perinatal outcomes (including fetal growth restriction) according to their clinical profiles and socioeconomic and demographic characteristics. All participants were recruited from the Cairo fetal medicine unit which is a very busy unit at university with 80 - 100 attending patients daily. All were confirmed to have no congenital anomalies and to be followed up till birth at the unit. All our sonographers were well trained in standardized measurement techniques.

However, unlike previously mentioned studies we showed that no significant differences are present in the equations of the means when compared to the IG-21st study. Some differences were instead observed for the percentile estimations but the vast majority of them were comprised within the 95% CI in a Bland and Altman plot. Given a bigger mean AC, the percentile estimation is slightly shifted so that 3rd and 10th percentiles resulted in a slightly higher than expected percentile for the IG-21st standard.

A limitation of our study is that we used for measuring the BPD outer to inner technique while the IG-21st used the outer to outer one. This could explain why Egyptian BPD is smaller than IG-21st.

Another limitation is that we did not include fetal weight charts and postnatal follow-up. This was difficult because not all these pregnant women were finally delivered at our hospital and many of them did not follow a strict antenatal care schedule.

**CONCLUSION**

According to our results, we recommend the use of the IG-21st charts fetal biometry for our Egyptian population to detect normal and abnormal growth. We recommend undergoing a prospective study using the IG-21st charts on our Egyptian population for follow-up of fetal growth.

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