New Israeli Sonographic Estimated Fetal Weight Growth Curves as Compared to Current Birth Weight Growth Curves: On What Should Diagnosis of Intrauterine Growth Disorders Be Based?

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ABSTRACT: **Background:** Two types of growth curves are commonly used to diagnose fetal growth disorders: neonatal birth weight (BW) and sonographic estimated fetal weight (EFW). The debate as to which growth curve to use is universal.

Objectives: To establish sonographic EFW growth curves for the Israeli population and to assess whether the use of the BW growth curves currently adapted in Israel leads to under-diagnosis of intrauterine growth disorders.

Methods: Biometric data collected during a 6 year period was analyzed to establish sonographic EFW growth curves between 15–42 weeks of gestation for the Israeli population. Growth curves were compared to previously published sonographic EFW growth curves. A comparison with the Israeli BW growth curves was performed to assess the possibility of under-diagnosis of intrauterine growth disorders.

Results: Out of 42,778 sonographic EFW studies, 31,559 met the inclusion criteria. The sonographic EFW growth curves from the current study resembled the EFW curves previously published. The comparison of the current sonographic EFW and BW growth curves revealed under-diagnosis of intrauterine growth disorders during the preterm period. Four percent of the fetuses assessed between 26–34 weeks would have been suspected of being growth restricted; 2.8 percent of the fetuses assessed between 30–36 weeks would have been suspected of having macrosomia, based on the BW growth curves.

Conclusions: New Israeli sonographic EFW growth curves resemble previously published sonographic EFW curves. Using BW growth curves may lead to the under-diagnosis of growth disorders. We recommend adopting sonographic EFW growth to diagnose intrauterine growth disorders.

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KEY WORDS: fetal growth disorder, birth weight (BW), estimated fetal weight (EFW), growth curves, Israel

Obstetric ultrasound is an accepted practice and is performed frequently throughout pregnancy [1]. Sonographic estimated fetal weight (EFW) is used as a critical diagnostic tool for identifying fetal growth acceleration and restriction. Intrauterine growth restriction (IUGR) and suspected macrosomia are associated with poor obstetrical outcome and may impact pregnancy management. When IUGR or macrosomia are suspected, underlying causes for these conditions should be investigated. Second trimester IUGR may be associated with chromosomal abnormalities and both conditions are associated with preterm delivery, low Apgar score, gestational diabetes, adverse cognitive and behavioral outcomes, and intrauterine fetal death [2,3].

Sonographic EFW is based on biometric measurements such as biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femoral length (FL). Several formulas have been published to improve estimation of fetal weight, yet no formula has been shown to be statistically superior to the one published by Hadlock in 1985 [4]. Following EFW calculations, the result is compared to an established fetal growth curve to assess whether the specific fetus is within the normal range. Fetal growth varies among populations and is associated with geographic distribution and ethnicity [5]. Two types of growth curves are commonly used; neonatal birth weight (BW) growth curves and sonographic EFW growth curves. Over the years, numerous EFW and BW growth curves have been published for different populations [6,7].

Evidence shows that growth restriction is related to preterm delivery. Therefore, applying neonatal BW growth curves can cause under-estimation of IUGR in preterm infants [5,8-11]. The debate as to which growth curve to use is universal. The American College of Obstetrics and Gynecology defines fetuses suffering from IUGR as those smaller than the 10th percentile of either sonographic EFW or BW, while the French College of Gynecologists and Obstetricians is against using BW growth curves and recommends using sonographic EFW growth curves [1,12].

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In Israel, the first population-specific sonographic EFW growth curves were published in 2005 by Romano-Zelekha and co-authors [13]. Those were based on a regression analysis of 857 sonographic EFW studies. Within a year neonatal BW growth curves for the Israeli population based on 787,710 births were published by Dollberg and colleagues [14]. Although recently new fetal biometry in the Israeli population have been published twice, they lacked sonographic growth curves [15,16]. Currently in Israel, the Israel Society of Obstetrics and Gynecology recommends using BW growth curves to identify intrauterine growth disorders [17]. The aims of our study are to establish sonographic EFW growth curves based on a large sample of the Israeli population and to assess whether using BW growth curves, as currently recommended, underestimates intrauterine growth disorders.

PATIENTS AND METHODS

This is a retrospective study. The Shaare Zedek Medical Center institutional review board approved the study (0107-16-SZMC). We included all ultrasound studies that included fetal biometry measurements and were performed in the Fetal Medicine Unit of Shaare Zedek between January 2010 and February 2016. Shaare Zedek is a university-affiliated medical center with a large obstetric department, with approximately 15,000 deliveries annually. Ultrasound exams were performed by either a registered and trained sonographer or a specialist who is trained in maternal fetal medicine. Common indications for these exams included: routine follow-up, fetal anatomical survey, assessment of fetuses from labor and delivery unit. These exams were conducted on both patient populations: women admitted from either labor and delivery or the high-risk unit and outpatients arriving for routine care. We excluded multiple gestations, exams without gestational age (GA) documentation, studies that were performed prior to 15 weeks or later than 43 weeks, and studies with missing or apparently false values. GA calculation was based on last menstrual period, menstrual age was not rounded.

All studies included the measurement of the four parameters: BPD measured from the outer edge of the near calvarial wall to the inner edge of the far calvarial wall on an axial plane that traverses the thalami and cavum septum pellucidum, HC measured in the same plane as BPD, FL measured from the lateral condyle to the greater trochanter, and AC measured at the transverse section through the upper abdomen, which demonstrated fetal stomach, umbilical vein, and portal sinus [18].

STATISTICAL ANALYSIS

Sonographic EFW was calculated by inserting the biometric values of BPD, HC, AC, and FL into the Hadlock 1985 formula [4]. Standard deviation was obtained for every GA, and curves were built for the Israeli population. Mean,1st, 3rd, 5th, 10th, 50th, 90th, 95th, 97th, 99th percentiles of sonographic EFW and confidence intervals were calculated for each complete week of GA from 15 to 42 weeks at 1 week intervals. Furthermore, these percentiles were plotted on a graph. To assess growth rate, the mean sonographic EFW interval between consecutive weeks was calculated and expressed as a percentage.

Following establishment of our growth curves and percentiles, we validated our data by comparing it with the sonographic EFW growth curves published by Hadlock in 1991 [19] for the population in the United States and the Romano-Zelekha growth curves published in 2005 for the Israeli population [13].

We then compared our growth curves with the neonatal BW growth curves published by Dollberg in 2006 [14] to assess potential underestimation of intrauterine growth disorders.

All four studies (Hadlock 1991, Romano-Zelekha 2005, Dollberg 2006, our data) were compared for GA at 24 to 40 weeks for the different percentiles. Although our data includes sonographic EFW for GA less than 24 and greater than 40 weeks, comparisons were not performed for these weeks as the EFW studies lacked information for GA greater than 40 weeks, while the BW study lacked data prior to 22 weeks and had a small sample size for GA of 22 to 24 weeks.

We furthered assessed how many of the fetuses that had sonographic EFW would be suspected to have either IUGR (< 10th percentile) or macrosomia (> 90th percentile) if the current BW growth curve was applied.

RESULTS

A total of 42,778 sonographic EFW exams were performed during the study period. We excluded 3722 studies (8.7%) missing GA, 3559 studies (8.3%) of multiple gestations, 3449 studies (8%) with missing or obviously false sonographic information, and 489 studies (1.1%) that were performed prior to 15 weeks or after 43 weeks. A total of 31,559 studies performed for live singleton fetuses that met the inclusion criteria were included in the study.

Distribution of 1st, 3rd, 5th, 10th, 50th, 90th, 95th, 97th, 99th percentiles, sample size, mean, standard deviation (SD), and interval difference of EFW according to GA in the study population is detailed in Table 1 and the 3rd, 10th, 50th, 90th, and 97th percentiles are plotted on a graph [Figure 1]. We included on average 1654 studies per week with a minimum of 290 exams at week 19 and a maximum of 3552 studies at week 40. The interval difference of EFW declined with advancing GA, showing a 20% interval growth prior to 20 weeks of gestation, 10–20% interval growth between 21–34 weeks, 5–10% interval growth between 34–39 weeks, and less than 5% interval growth in the post date period.

A graphical comparison [Figure 2] of sonographic EFW growth curves describes the 3rd, 10th, 50th, 90th, and 97th percentiles from the current study in relation to the percentiles

Table 1. Sonographic EFW percentiles, number of exams, mean, and standard deviation according to gestational weeks and fetal growth (%) in the consecutive weeks

Gestational age (weeks)	Percentiles											
	1st	3rd	5th	10th	50th	90th	95th	97th	99th	No. of exams	Mean ± SD	Interval EFW (%)
15	87	99	102	109	129	151	158	162	176	678	130 ± 18	
16	90	111	117	129	156	182	194	200	213	550	156 ± 25	20
17	88	103	113	140	191	229	237	241	269	311	187 ± 36	20
18	98	106	125	151	234	280	297	311	326	295	228 ± 50	22
19	95	112	158	219	295	345	368	390	471	290	288 ± 66	26
20	127	204	263	291	360	424	445	459	502	492	355 ± 63	23
21	170	280	316	352	424	489	508	524	570	801	421 ± 70	18
22	211	337	375	415	496	579	605	619	677	795	494 ± 79	17
23	332	406	438	478	575	675	709	738	790	564	575 ± 84	16
24	393	470	512	550	677	797	835	867	929	501	674 ± 104	17
25	409	509	573	645	790	934	975	1022	1090	539	785 ± 124	16
26	564	664	704	771	929	1107	1155	1178	1240	551	929 ± 136	18
27	564	696	774	870	1059	1221	1288	1353	1443	655	1051 ± 159	13
28	716	808	889	990	1200	1407	1473	1514	1629	710	1200 ± 177	14
29	783	937	1006	1130	1363	1614	1684	1726	1809	787	1363 ± 201	14
30	994	1147	1212	1293	1539	1800	1873	1954	2049	847	1534 ± 209	13
31	1100	1252	1329	1445	1738	2031	2135	2203	2443	940	1739 ± 251	13
32	1186	1376	1416	1568	1906	2253	2356	2402	2590	1150	1902 ± 283	9
33	1341	1527	1570	1710	2099	2478	2623	2743	2936	1170	2102 ± 309	11
34	1424	1605	1684	1842	2310	2722	2850	2943	3147	1201	2295 ± 353	9
35	1595	1762	1854	1997	2520	2983	3161	3294	3592	1328	2506 ± 396	9
36	1810	1941	2022	2172	2685	3216	3415	3575	3830	1806	2695 ± 422	8
37	1977	2121	2216	2372	2918	3481	3711	3852	4111	3000	2929 ± 446	9
38	2150	2331	2424	2572	3135	3767	3947	4067	4270	3113	3150 ± 464	8
39	2304	2496	2584	2729	3323	3941	4107	4236	4453	2851	3336 ± 468	6
40	2549	2715	2809	2934	3483	4067	4229	4323	4520	3552	3499 ± 434	5
41	2689	2807	2935	3067	3595	4140	4293	4394	4569	1608	3599 ± 415	3
42	2754	2986	3063	3175	3643	4158	4297	4382	4536	474	3662 ± 388	2

EFW = estimated fetal weight, SD = standard deviation

published by Hadlock (USA population) and Romano-Zelekha (Israeli population) reveals the following:

- The maximal difference between our data and previous publications is not greater than 5% for the 50th, 90th, and 97th percentiles.
- The maximal difference between our data and the Romano-Zelekha data is less than 4% for the 10th percentile.
- The maximal difference between our data and the Hadlock data for the 10th percentile is less than 5% for all gestational weeks except for 34–37 weeks of gestation, where the difference reached 8%.
- The maximal difference between our data and that of Hadlock and Romano-Zelekha for the 3rd percentile is less than 10% for all gestational weeks, except between 25–29 weeks of gestation where it is more than 10% and between 34–37 weeks of gestation where it is roughly 10%.

Comparison of the current study growth curves against the neonatal BW growth curves published by Dollberg and currently used in Israel [Figure 3] reveals the following:

- The 50th percentile of sonographic EFW was consistently larger as compared to the 50th percentile of neonatal BW in the preterm period, with a discrepancy of up to 11% at the 29 weeks of gestation.
- The 10th percentile in our study consistently differed from the 10th percentile of BW. It was 15% higher between 27–32

weeks of gestation and reached 25% difference at 29 week of gestation.

- The 5th percentiles during the same period [27–32 weeks of gestation) reached a maximum difference of 28% at 30 week of gestation.
- The 90th percentile in our study was comparable to the 90th percentile of BW, except for gestational weeks 31–34, where the BW percentile was significantly higher than sonographic EFW percentile with a maximum difference of 36% at 32 week of gestation.
- Comparison of the 95th percentiles during the same period (31–34 gestational weeks) revealed a difference in excess of 40%.

We found in our data of sonographic EFW that only 4% of the fetuses assessed by the current BW growth curve between 26–34 weeks would be suspected to have IUGR and that only 2.8% of the fetuses assessed between 30–36 weeks would be suspected to have macrosomia.

Figure 1. 3rd, 10th, 50th, 90th, 97th percentiles for estimated fetal weight by gestational week

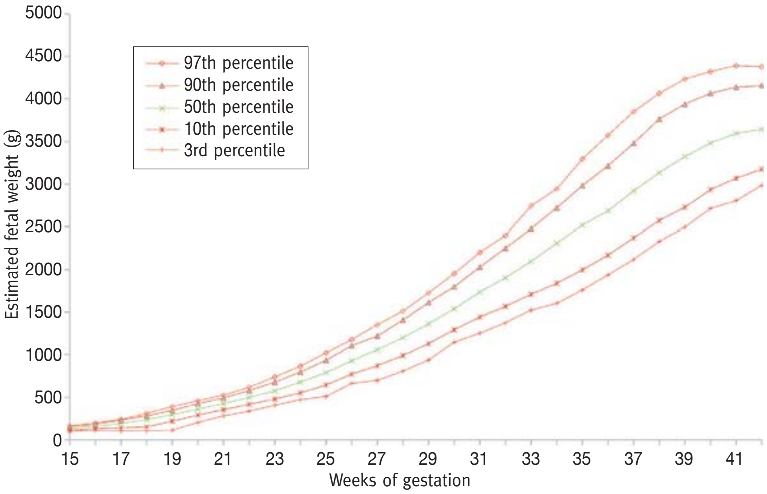
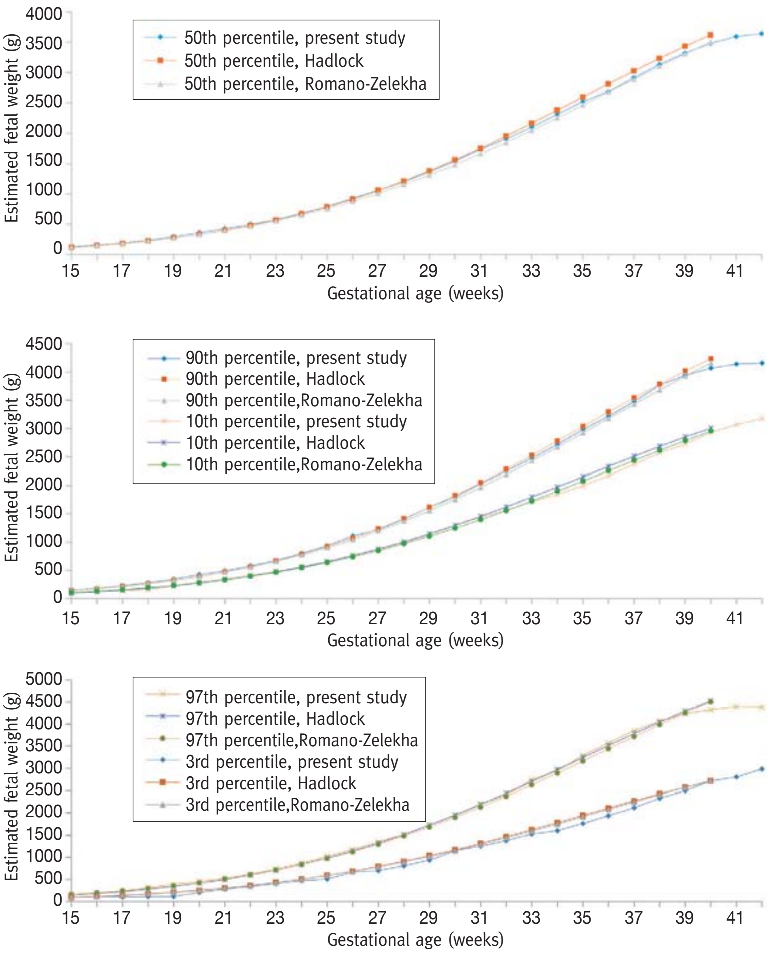


Figure 2. Comparison between the 3rd, 10th, 50th, 90th, and 97th percentiles of the present study compared with Hadlock 1991 [4] and Romano-Zelekha 2005 [13]

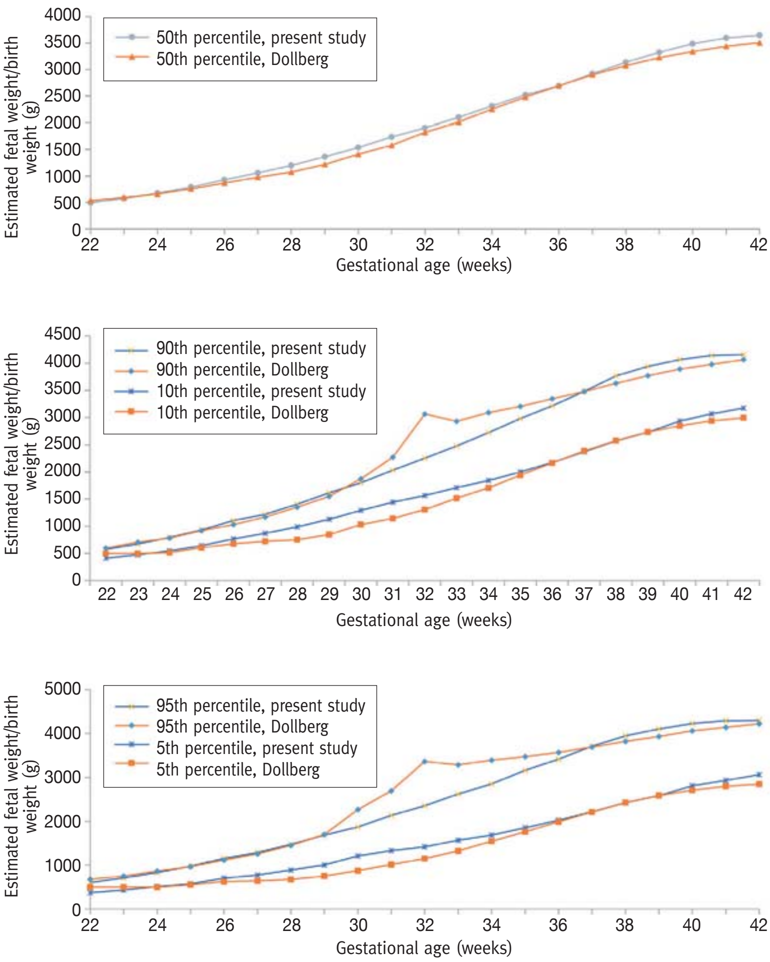


DISCUSSION

In this study, we established sonographic EFW growth curves for the Israeli population based on data from a single large tertiary center. We noted that the growth rate declined with advancing in GA. Comparison of the current study sonographic EFW curves to large international and small Israeli growth curves revealed strong resemblance, thus validating our curves. Furthermore, comparison of the sonographic EFW curves to the BW growth curves currently in use in Israel revealed that the two curves are different. Obviously, only the sonographic EFW curves enable detection of intrauterine growth disorders as early as 15 weeks. Using the BW growth curves would underdiagnose cases of IUGR and macrosomia. In addition, 50th percentiles of sonographic EFW is greater than the 50th percentiles of BW during the preterm period. The 5th and 10th percentiles of the sonographic EFW are significantly greater than the 5th and 10th percentiles of the BW during the early preterm period. The 90th and the 95th percentiles of the sonographic EFW during the early preterm period may be up to 40% less than the corresponding BW percentiles.

These findings suggest that when a sonographic EFW is obtained and plotted on different growth curves the interpretation and hence pregnancy management may differ widely. As noted earlier, only 3–4% of the fetuses assessed for growth were suspected to have growth disorders. To better clarify this point two patients should be considered, the first at 31 weeks with sonographic EFW of 1252 grams. When placed on the BW growth curve currently used in Israel it would be interpreted as 12th percentile, yet when placed on the sonographic EFW growth curve it falls on the 3rd percentile. It is clear that this fetus, suspected to be at the 3rd percentile should be managed accordingly, that is, consideration should be given to obtaining

Figure 3. Comparison between the 5th, 10th, 50th, 90th and 95th percentiles of the present study with Dollberg 2006 [14]



genetic counseling, work up for TORCH (which includes toxoplasmosis, other [syphilis, varicella-zoster, parvovirus B19], rubella, cytomegalovirus, and herpes infections), detailed fetal anatomical survey, fetal echocardiogram, and twice weekly biophysical follow-up including Doppler studies [17]. However, a fetus at 32 weeks where the sonographic EFW is 2402 grams, when placed on the BW growth curve currently used in Israel would be interpreted as 86th percentile, yet when plotted on the sonographic EFW growth curve it falls on the 97th percentile, which is highly suggestive of macrosomia and hence suitable management might include performing oral glucose tolerance test and a follow-up growth study. It appears, therefore, that by using the BW growth curve for the Israeli population, as currently recommended in Israel, there is a potential to under-diagnose fetuses who suffer from IUGR or macrosomia, specifically during the late second and early third trimesters.

The biologic plausibility of under-diagnosing IUGR during the preterm period when using BW growth curves stems from the fact that preterm births are often caused by pathological processes and as such those newborn weights do not reflect the normal birth weights of a normal population. A study from Australia revealed that among preterm births, up to 40% were medically indicated preterm births and these had significantly lower BW ($P < 0.001$) than spontaneous preterm births and births after preterm premature rupture of membranes [20]. It seems clear that using preterm BW for obtaining growth curves while including newborns delivered due to preeclampsia, severe IUGR, and other pathological process skews the curve. Using sonographic EFW growth curves avoids basing the standard on preterm neonatal weights, which by definition are derived from pregnancies with a pathological outcome and hence do not represent normal growth potential [21,22]. Previous studies have demonstrated that the use of BW curves causes underestimation of IUGR in the preterm period [8,9,23]. There is no clear explanation for the difference noted between the current study growth curves and the neonatal BW growth curves at the 90th and 95th percentiles, specifically in the later second and early third trimester.

Our findings regarding under-diagnosis of IUGR are consistent with previous studies. In 2007, Salomon and colleagues [9] obtained biometric data for fetuses between 20–36 weeks of gestation and used the Hadlock formula to create sonographic EFW growth curves in a tertiary care center in France and compared them to BW curves. The comparison revealed that the mean sonographic EFW was higher than the mean BW in the preterm period. Furthermore, at 28–32 gestational weeks, the 50th percentile for BW compared approximately with the 10th percentile for EFW. The authors concluded that the use of BW growth curves may miss the diagnosis of IUGR. In 2015, The French College of Gynecologists and Obstetricians [12] recommended that sonographic EFW growth curves represent physiological growth more reliably than BW growth curves for the identification of SGA at early GA because of the disorders associated with preterm delivery. In 1994, Bernstein and colleagues [24] created a growth curve using cross-sectional BW data of 350 neonates and compared it to a generated sonographic EFW growth curve based on 350 exams performed between 26 and 39 weeks. The mean regression lines of the two curves were significantly different ($P < 0.05$). In 1996, a subsequent study [25] compared a BW growth curve based on 9553 BW of neonates delivered between 24 and 43 weeks of gestation with a sonographic EFW curve based on 1331 exams performed between 24 and 40 weeks of gestation. The authors found that fewer than 2% of the sonographic EFW fell below the 10th percentile of the BW standard in the preterm period [25]. However, neither of these studies demonstrates under-diagnosis of macrosomia.

Our study has strengths and limitations. The strengths of our study include its contemporary large sample size for each week, specifically during the second trimester. It enables the identification of intrauterine growth disorders as early as 15 weeks. All included scans were performed by certified sonographers or maternal fetal medicine specialists. The limitations of the study include its performance at a single center, which may not be representative of the entire Israeli population, yet it has strong resemblance to the previous sonographic EFW growth curves published supports its validity. We did not exclude fetuses with anatomic or chromosomal anomalies because our aim was to provide population-based sonographic EFW curves. In addition, our data rely on dating from maternal report, which may be based on last menstrual period or first trimester ultrasound.

CONCLUSIONS

In conclusion, we have created an Israeli growth curve based on a large sample of sonographic EFW performed by certified sonographers and specialists, which resembles other sonographic EFW growth curves and has the potential to better identify IUGR and macrosomia during the late second and early third trimesters. Hence, we advise using the new curve based on sonographic EFW derived from a local population sample, as recommended in some European countries. Furthermore, a national prospective longitudinal cohort study to assess which growth curve best identifies growth disorders should be performed.

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"We need diversity of thought in the world to face the new challenges"

Tim Berners-Lee, (born 1955), also known as TimBL, is an English engineer and computer scientist, best known as the inventor of the World Wide Web

"The greatest obstacle to being heroic is the doubt whether one may not be going to prove one's self a fool; the truest heroism is to resist the doubt; and the profoundest wisdom, to know when it ought to be resisted, and when it be obeyed"

Nathaniel Hawthorne, (1804–1864), American novelist, dark romantic, and short story writer