The reality of Estimating Fetal Weight (EFW): Expectations and Weaknesses...Obstetricians and neonatologists should sing from the same hymn sheet regarding the baby's weight.

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A recent publication of a systematic review has suggested that Hadlock's 3-parameters formula (HC, AC and FL) is associated with least error in estimating EFW [1,2] and may perform better in fetal weight estimation than the 2-parameter formula we developed recently[3]. Because our commitment is to base our recommendations on the results of systematic reviews, we present herein a newly developed prescriptive standard for EFW based upon this formula of estimating fetal weight ($EFW = 10^{(1.326 + 0.0107\times HC + 0.0438\times AC + 0.158\times FL - 0.00326\times AC\times FL)}$). This formula was applied to fetal biometric measures from our original study of optimally grown fetuses[4].

After calculating the estimated weight for each fetus using this method, we applied a second-degree fractional polynomial functional form and found the best fit using a 3-parameter Box-Cox Gaussian distribution (i.e. the LMS method) for the response variable, defining three distributional functions of gestational age ($\lambda(GA)$, $\mu(GA)$ and $\sigma(GA)$). All analyses were carried out in R statistical software (https://www.r-project.org) using the Generalised Additive Models for Location, Scale and Shape (GAMLSS) framework[5]. The gestational age-specific centiles for EFW are presented in Figure 1 in comparison with the one published previously based on the 2-parameter only based EFW. The corresponding equations for $\lambda(GA)$, $\mu(GA)$ and $\sigma(GA)$, are presented in Table 1 and the main centiles are shown in Table 2.

One has to understand that using the Hadlock's 3-parameters formula [2] rather than the 2-parameter approach we developed previously[3], will lead to some different interpretations:

- First, the computation of the EFW is based on different formulas that combine differently routine biometric measurements, such as head circumference (HC), abdominal circumference (AC) and femur length (FL);

- Secondly, the obtained estimate will be plotted on a different gestational age–specific INTERGROWTH-21st standard, as illustrated in Figure 1.

As an example, a fetus with the following measurements : HC = 29 cm; AC= 26 cm ; FL= 5.7 cm at 32+0 weeks would have an EFW 1499 g and 1558 g based on the IG and Hadlock formula respectively, corresponding to the 5th and 10th centiles, respectively.

It must be highlighted that these discrepancies - and more generally the controversies about which equation or chart to use when evaluating fetal weight - illustrate the fact that the use of ultrasound to estimate fetal weight at the time of making delivery decisions and interacting with neonatologists is a practice that needs to be challenged.

Both obstetricians and neonatologists apply the information, often in conjunction with other parameters, to make life-changing decisions about the need to deliver a baby or whether to transfer an undelivered mother to a facility with a higher-level neonatal unit. However, using in this context, an estimate of fetal weight, as a proxy for newborn viability, on a summary of ultrasound measures of the fetal head, abdomen and femur, each with their own individual technical errors, is questionable. The wide confidence intervals of such estimates, often obscured by the focus on their mean values, may not be appreciated by clinicians and are rarely communicated to parents: the mean percentage error can range from -6.9% to 22.2%, with the standard deviation varying from 7.5% to 17.8% [6].

Given such wide confidence intervals, we deliberately chose not to present a summary measure for estimated fetal weight (EFW), when we first published the INTERGROWTH-21st international fetal growth standards[4]. Rather, we provided all the parameters used for calculating EFW separately, and promoted that clinicians make a more informed judgement based on a pathophysiological assessment of the individual growth parameters. However, there is still the clinical situation, during fetal growth monitoring of uncomplicated pregnancies or those with moderate risk, where obstetricians like to add EFW to complement individual US parameters or to communicate with parents. Indeed, estimating fetal weight has been suggested as a potential tool to screen for intrauterine growth restriction[7]. In fetuses with optimal growth, no environmental constraints, and quality controlled ultrasound measurements, we have demonstrated that the best estimate of fetal weight can be obtained from the cephalic and abdominal perimeters only[3]. However, the latter has been challenged recently [1]. In the general fetal population screened in daily practice, intrinsic errors associated with the ultrasound technique, equipment and operator; as well as the fact that the three most commonly used fetal parameters –HC, AC and FL – may deviate more significantly from optimal trajectories, and contribute differently to total weight across gestational age, may partly explain the greater accuracy of the 3-parameter based Hadlock's equation to calculate EFW.

Regardless of the equation used, only a modest prediction at term is achievable, and there is an important need to improve our practice. Importantly, at early gestational ages the error made by EFW is approximated by a rule of thumb presenting a ±15% range around the estimate. So, when the obstetrician informs the neonatologists that the EFW is 1200g at 30+2 weeks' gestation, what is actually meant is that the value could lie anywhere between 1020g and 1380g. That variation for a girl's birth weight at 30+2 weeks' gestation corresponds to an 8th to 56th centile range according to the published INTERGROWTH-21st Very Preterm Size at Birth Reference Charts.[9] Therefore, caution must be exercised and - if EFW is to be computed - then it has to be interpreted and taken into account using prescriptive standards describing how individuals should grow. This is the reason why the gestational age–specific standard for EFW has to be developed using healthy selected population.

There are other pathophysiological problems with using EFW to estimate neonatal risk. Indeed, each of the biometric parameters summarized in the EFW value has different risk implications. For example, in a recent systematic review and meta-analysis, third-trimester ultrasound screening for late-onset fetal growth restriction (FGR) performed better when based on AC than EFW, and there is a close association between AC in the third trimester and neonatal morbidity [8]. On the other hand, an isolated, mid-trimester, short FL is associated with an increased risk of FGR and preterm birth, in the absence of aneuploidy, congenital anomalies, skeletal dysplasias, and early-onset FGR [9]. To complicate matters further, neonatal mortality, although strongly associated with gestational age at birth, was best predicted in a systematic review by multivariable models rather than birth weight or gestational age alone in very preterm infants, the priority group for this clinical dilemma [10].

That brings us to the last component of the problem with EFW: the neonatologist has to decide which chart to use to judge the implications of the EFW provided by the obstetrician. We strongly believe that for risk assessment of the newborn, the same chart that assesses weight for gestational age should logically be used by obstetricians and neonatologists - otherwise, the same pregnancy may be evaluated on the same day using two different tools, resulting in two separate risk assessments being made. On the one hand, because FGR is over-represented in premature deliveries, the use of birth weight curves to interpret EFW may miss the diagnosis of FGR [11] (preterm infants are known to be somewhat smaller than are fetuses of the same gestational age while still in utero)[12]. On the other hand, the ultimate objective of estimating fetal weight is for the neonatologist to assess risk, to refine the infant's clinical management and to communicate the likelihood of death or disability to the parents. Hence, there should be no need for EFW charts in this context of immediate neonatal risk assessment.

In short, when using EFW for the specific task of *neonatal* risk assessment, comparison must be made with the **newborn size at birth standards** [12,13] as this is the goal. Figure 2 illustrates the difference in interpretation according to the use of EFW or BW standards.

In summary, we recommend:

1) that fetal growth should not be evaluated using a single summary measure. Rather fetal growth should be assessed over time based on the trajectory of individual parameters, plotted separately against the INTERGROWTH-21st Fetal Growth Standards to enable growth/size to be evaluated for each gestational period.
2) If an EFW value is added to complement the individual parameter during fetal growth monitoring, the most evidence-based strategy is to use the EFW we have presented here; these standards match methodologically the INTERGROWTH 21ST Fetal Growth Standards
3) If we are interacting with the neonatologist to decide clinical actions, the INTERGROWTH-21st Newborn Birth Weight Standards (33-43 weeks' gestation) [14] or Very Preterm Reference Charts (<33 weeks' gestation)[9] allow evaluation of neonatal size and risk by week of gestation. This change of standards is required, even if it complicates the process, because neonatal size at birth and risk is different from EFW (Figure 2)
4) The responsible next step is always to provide the parents with the specific centiles or z-scores of the error range of the birthweight estimation. If the newborn is to be delivered prematurely, postnatal growth can then be monitored on the neonatal unit and in the pediatric follow-up clinic using the INTERGROWTH-21st Preterm Postnatal Growth Standards[15] that were constructed specifically to ensure continuity of care, using the same pregnant cohort as the fetal and newborn standards.

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TABLE

Table 1. Equations for parameters and computation of Z-scores and centiles for EFW in relation to gestational age in exact weeks (GA). Abbreviations: GA is for gestational age, in exact weeks; EFW: estimated fetal weight in g. The log function denotes the natural logarithm (base e).

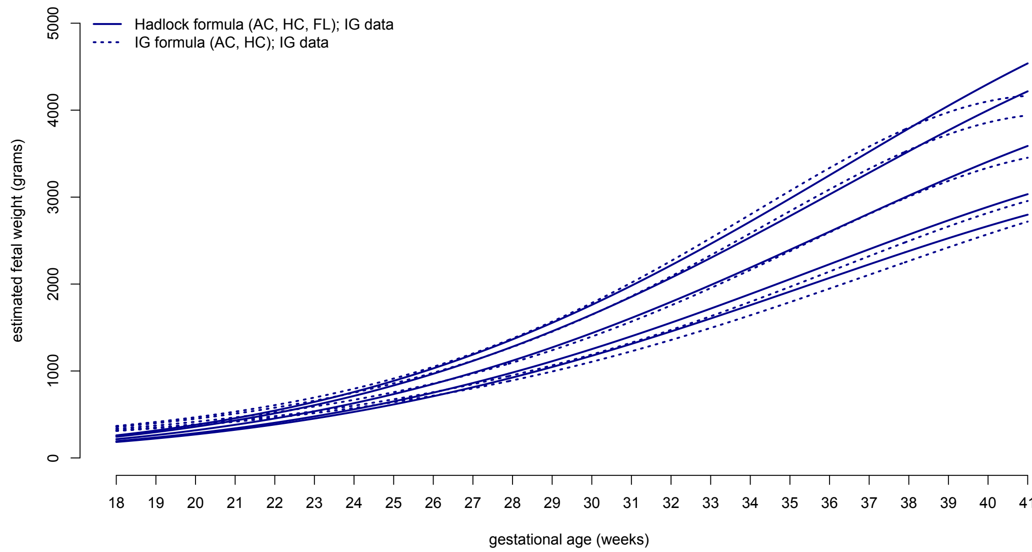
Skewness $\lambda(GA) = 9.43643 + 9.41579*(GA/10)^{-2} - 83.54220 * \ln(GA/10)*(GA/10)^{-2}$
Mean $\mu(GA) = -2.42272 + 1.86478*GA^{0.5} - 1.93299e\text{-}5 * GA^{3}$
Coefficient of variation $\sigma(GA) = 0.0193557 + 0.0310716 * (GA/10)^{-2} - 0.0657587 * \ln(GA/10)*(GA/10)^{-2}$
Z-score $Y=\log(EFW)$ If $\lambda(GA)=0$, $Z(GA) = \sigma(GA)^{-1} \times \log[Y/\mu(GA)]$ If $\lambda(GA)\neq 0$, $Z(GA) = [\sigma(GA) \times \lambda(GA)]^{-1} \times [(Y/\mu(GA))^{\lambda(GA)} - 1]$
Centiles Z_α defined by $\Pr(z \leq Z_\alpha)=\alpha$ for $z \sim N(0,1)$, i.e. $Z_\alpha = \Phi^{-1}(\alpha)$ If $\lambda(GA)=0$, $\log[C_\alpha(GA)] = \mu(GA) \times \exp[\sigma(GA) \times Z_\alpha]$ If $\lambda(GA)\neq 0$, $\log[C_\alpha(GA)] = \mu(GA) \times [Z_\alpha \times \sigma(GA) \times \lambda(GA) +1]^{1/\lambda(GA)}$

FIGURE

Figure 1: Gestational age-specific centiles for EFW presented in in comparison with the one published previously based on the 2-parameter only.

Figure 2: Comparison of the EFW standards based on the Hadlock formula with the INTERGROWTH-21st Newborn Birth Weight Standards (33-43 weeks' gestation) [14] or Very Preterm Reference Charts (<33 weeks' gestation)[9]

Figure 1.


Hadlock formula (AC, HC, FL); IG data
IG formula (AC, HC); IG data
estimated fetal weight (grams)
0
1000
2000
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4000
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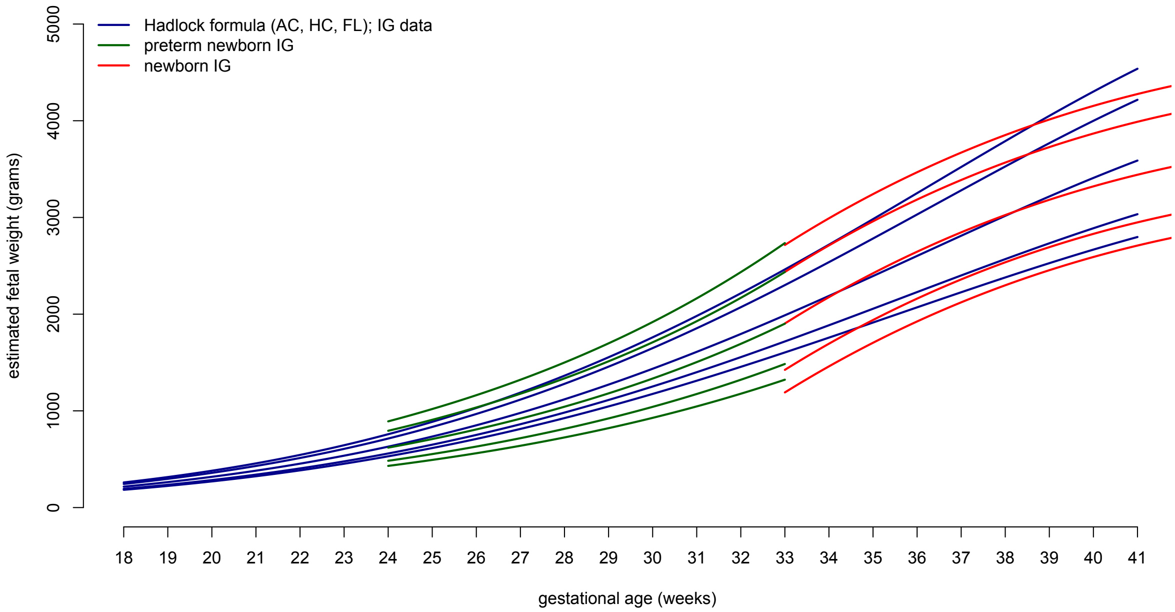
41
gestational age (weeks)

Figure 2.


Hadlock formula (AC, HC, FL); IG data
preterm newborn IG
newborn IG
estimated fetal weight (grams)
0
1000
2000
3000
4000
5000
18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41
gestational age (weeks)

Appendix: centiles for EFW in table format per week. 32 weeks stands for 32weeks and 0 days

GA (weeks)	p3	p5	p10	p50	p90	p95	p97
18	184	187	193	216	244	253	260
19	224	228	235	263	297	308	316
20	271	276	284	318	359	372	381
21	324	330	341	381	430	446	457
22	385	392	405	454	513	532	544
23	453	463	478	537	607	629	645
24	530	541	559	630	714	740	758
25	616	629	650	734	834	865	887
26	710	726	751	851	968	1005	1030
27	813	832	862	979	1116	1160	1189
28	925	947	982	1119	1279	1330	1364
29	1046	1072	1113	1272	1457	1515	1554
30	1175	1205	1252	1435	1649	1716	1760
31	1312	1346	1400	1610	1854	1930	1981
32	1455	1494	1556	1795	2072	2158	2216
33	1604	1648	1718	1988	2300	2397	2462
34	1757	1807	1885	2189	2538	2646	2719
35	1913	1968	2056	2394	2782	2902	2983
36	2070	2131	2228	2602	3031	3163	3251
37	2226	2293	2400	2811	3280	3425	3522
38	2379	2453	2569	3017	3527	3684	3789
39	2527	2607	2733	3217	3768	3937	4051
40	2667	2753	2888	3409	3999	4180	4302
41	2798	2889	3034	3588	4217	4409	4538